THE EFFECT OF DECEREBRATE RIGIDITY ON INTRACRANIAL PRESSURE IN MAN AND ANIMALS

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This thesis is dedicated to
my beloved brother ARGYRIOS who did not
survive to see it finished, and
my parents with greatest respect.

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PUBLICATIONS

Both of my supervisors, Professor F.J. Gillingham and Professor E.R. Hitchcock, considered that the importance of the work merited publication in advance of submission of this thesis. Accordingly, the major part of the work has been already communicated to learned societies or published in scientific journals as shown below. A small part of the work, however, consists of material so far unpublished.

A. Communications to Learned Societies:

1. Scottish Association of Neurological Sciences (S.A.N.S.), Glasgow, 25th February, 1978.

   The effect of decerebrate rigidity on the intracranial pressure.

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2. Proceedings of the Physiological Society, London. 15th - 16th December, 1978

   Torque-resonance relationship in the wrist: sex difference

   S.A. Tsementzis, M.D. Lakie

3. Fourth International Symposium on Intracranial Pressure, Williamsburg, Virginia, U.S.A., 10th - 14th June, 1979.

   The effect of decerebrate rigidity on the ICP as modified by brain elastance.

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4. Proceedings of the 6th European Congress of Neurosurgery, Paris, 15th - 20th July, 1979

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   Acta Neurochir. 40: 191-202

2. Tsementzis, S.A. & Lakie, M.D. : 1978
   Torque-resonance relationship in the wrist: sex difference.
   J. Physiol. 289: 86

3. Tsementzis, S.A., Gillingham, F.J., Hitchcock, E.R. & Gordon, A. : 1979
   The effect of decerebrate rigidity on the intracranial pressure. An experimental study.
   Acta Neurochir. 46: 5-43

4. Tsementzis, S.A., Gordon, A. & Gillingham, F.J. : 1979
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   Acta Neurochir., Suppl. 28: 78-84

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   The effect of decerebrate rigidity on the ICP as modified by brain elastance. (Abstract of paper given at 4th Int. Symp. on Intracranial Pressure).
   Neurosurgery 4, No. 5 : 488

6. Yates, C.M., Tsementzis, S.A., & Wilson, H. : 1979
   Amine metabolites in ventricular cerebrospinal fluid in coma.
   J. Neurol. Neurosurg. Psychiat. (In Press).

7. Tsementzis, S.A., Gillingham, F.J., Gordon, A. & Lakie, M.D.: 1979
   Two methods of measuring muscle tone applied in patients with decerebrate rigidity.
   J. Neurol. Neurosurg. Psychiat. (In Press)

ABSTRACT

Patients with decerebrate rigidity frequently also show intracranial hypertension. The factors responsible for this effect and their inter-relationships were explored in cats and in patients with head injuries.

Animals: The factors examined, separately and in combination, were elevation of central venous, intrathoracic, intra-abdominal and systemic arterial pressures. The baselines thus established were used for the investigation of the effects of these factors on the intracranial pressure (ICP) in cats which had been rendered decerebrate by focal stereotactic mesencephalic lesions.

Little or no change occurred in the ICP when:

1) Rigidity was mainly unilateral.

2) Bilateral limb rigidity was extreme.

Persistent elevation of ICP occurred when

1) Truncal rigidity resulted in the simultaneous elevation of the intrathoracic and intra-abdominal pressures

2) Elevation of the systemic arterial pressure occurred in the presence of defective cerebrovascular homeostasis.

Human: The dynamics and management of the complex clinical problem posed by decerebrate rigidity were investigated in patients with head injuries who exhibited well-developed bilateral rigidity under conditions of altered cerebral elastance.

Rigidity was quantified by measuring the resonant frequency of the wrist induced by a printed-circuit motor. The brain elastance, ICP, intrathoracic and blood pressures were measured throughout the study. The effect of pharmacological muscle paralysis on the ICP and rigidity was examined.

It appeared that well-developed decerebrate rigidity increased the ICP. The relationship was direct; the greater the rigidity or cerebral elastance, the greater the rise in ICP and vice versa. The two factors mainly responsible were muscle hypertonicity and cerebral elastance. The rises in ICP were caused by the rigidity and although it may not always be possible to reduce the abnormally increased elastance, the rigidity can certainly be abolished. As long as the cerebral vascular homeostatic mechanisms were intact, spontaneous waning of the rigidity or its abolition by muscle relaxants returned the ICP to its previous resting level. Pancuronium produced much deeper and more lasting relaxation than either diazepam or chlorpromazine.

During the period of mechanical ventilation, alterations in ICP were of prognostic value as regards the outcome of the injuries.

ABBREVIATIONS

A	Anterior to the intercollicular plane (Stereotactic co-ordinate)
AC	Aqueduct
a	Alpha motorneuron
AV	Arachnoid villi
BBB	Blood brain barrier
BCI	Brachium colliculi inferioris
BCS	Brachium colliculi superioris
C	Brain compliance
CBF	Cerebral blood flow
CBV	Cerebral blood volume
CGL	Corpus geniculatum laterale
CI	Colliculus inferior
CM	Calibration mark (AP = O)
CPM	Chlorpromazine hydrochloride
CPP	Cerebral perfusion pressure
CS	Colliculus superior
CSF	Cerebrospinal fluid
CSFP	Cerebrospinal fluid pressure
Cu	Curarisation
CVP	Central venous pressure
D	Diazepam
d	Change
DA	Dopamine
Diast SAP	Diastolic systemic arterial pressure
DPCS	Decussatio pedunculorum cerebellarium superiorum
DR	Decerebrate rigidity
DTD	Decussatio tegmenti dorsalis
dV/dP	Coefficient of elasticity

E	Brain elastance
ECG	Electrocardiogram
EDP	Epidural pressure
EEG	Electroencephalogram
EMG	Electromyogram
FC	Foramen caecum
FH	Formatio hippocampalis
FLM	Fasciculus longitudinalis medialis
FPT	Fibrae pontis transversae
FRM	Formatio reticularis mesencephali
H	Horizontal plane (Stereotactic co-ordinate)
H	Hippocampus
5-HIAA	5-hydroxyindolylacetic acid
5-HT	5-hydroxytryptamine
HVA	Homovanillic acid
Hz	Hertz
Ia	Afferent fibres
IAP	Intra-abdominal pressure
ICP	Intracranial pressure
II	Afferent fibres
IPPV	Intermittent positive pressure ventilation
ITP	Intrathoracic pressure
Kg	Kilogram
$Kg.m^2$	Kilogram square metre
L	Largactil
L	Left
LM	Lemniscus medialis
μ	micro (10^{-6})
μ g	microgram

MHPG	3-methoxy, 4-hydroxyphenylglycol
ml	millilitre
mm	millimetre
mmHg	millimetres of mercury
mmH_2O	millimetres of water
μ V	microvolt
NA	noradrenaline
NCS	Nursing care stimuli
N/G	Nasogastric tube
NI	Nucleus interpeduncularis
N.m	Newton metre
NO	Nervus oculomotorius
NP	Nuclei pontis
NPV	Nucleus pontis ventralis
NR	Nucleus ruber
NRPC	Nucleus reticularis pontis caudalis
NRPO	Nucleus reticularis pontis oralis
NRTP	Nucleus reticularis tegmenti pontis
NVLL	Nucleus ventralis lemnisci lateralis
OD	Outside diameter
P	Pancuronium bromide
P	Pressure
P	Pyramidal tract
PC	Pedunculus cerebri
PCM	Pedunculus cerebellaris medius
PCS	Pedunculus cerebellaris superior
R	Resistance
rad	Radian
rad/N.m	Radian per Newton metre (Limb compliance)

Rb	Rubrospinal tract
RF	Resonant frequency
Rt	Reticulospinal tract
SAP	Systemic arterial pressure
SGC	Substantia grisea centralis
SN	Substantia nigra
S.R	Spontaneous relaxation
Syst SAP	Systolic systemic arterial pressure
T	Tectospinal tract
$\bar{t}$	Mean transit (circulation) time
TCC	Tractus corticobulbaris et corticospinalis
T.I.M.A.	Torque Induced Motion Analyser
TVR	Tonic vibration reflex
V	Volume
V	Vestibulospinal tract
V	Volts
Vin	Excitation voltage
Vout	Output voltage
VFP	Ventricular fluid pressure
VMT	Vasomotor tone
VO	Venous occlusion
$\bar{x}$	Mean value
γ	Gamma motor neurons
γ_1	Efferent fibres
γ^2	Efferent fibres

INTRODUCTION

Patients often exhibit decerebrate rigidity following a severe head injury, as a result of either primary impact lesions of the brain stem or secondary stem lesions resulting from transtentorial herniation. Classically, the syndrome is manifested by variably severe contractions of the muscles of the limbs and of the thorax and abdomen associated with major haemodynamic and respiratory changes.

Quinke (1891), whilst performing a lumbar puncture on a hydrocephalic patient, was the first to observe an increase in the cerebrospinal fluid pressure (CSFP) during coughing, straining or abdominal compression and measured it by means of an open-ended manometer. This observation has been amply confirmed and the phenomenon is generally attributed to an increase in the intracranial venous blood volume, which is due to slowing of the cerebral venous return by the rise in the intrathoracic pressure (Becht, 1920, Meyrson and Loman 1932, Bedford 1935).

The CSFP was first continuously recorded graphically with an optical manometer by Hamilton et al. (1936) who recorded increases of as much as 60 mmHg during coughing and straining in normal subjects. The clinical significance of this effect was first appreciated by Hunter (1959, 1960). In a discussion of the value of controlled ventilation in neurosurgical practice, he urged that muscle relaxants should be used to prevent increases in the CSFP due to straining during intubation; in these circumstances the increase in intra-abdominal pressure forced blood up the vena cava, distended the veins of the head and neck and raised the intracranial pressure.

Subsequent work by Hamilton et al. (1943) showed that, in the normal human, increases in the CSFP resulted in transient systemic arterial hypertension "produced by the propagation of the increased intrathoracic pressure". Löfgren (1973) found that in normal dogs a 5-fold increase in the brain elastance occurred if the mean arterial pressure were raised from 25 to 200 mmHg. This means that, when the arterial pressure is already elevated a rapid increase in intracranial volume is less readily compensated; a greater increase in CSFP occurs than would be the case were the arterial pressure normal.

The skeletal muscle contractions of decerebrate rigidity may well alter the intrathoracic and intra-abdominal pressures and have secondary effects on the central venous and arterial pressures. Depending on the nature and location of the brain stem lesion, primary arterial pressor responses may be elicited (Lindgren et al. 1956). These, in the presence of defective cerebrovascular homeostasis due to trauma, could result in an uncontrollable increase of the intracranial blood volume and consequently of the intracranial pressure (ICP).

The effect of decerebrate rigidity on the ICP does not appear to have been investigated either clinically or experimentally.

The ICP was normal in one patient with post-traumatic extensor decerebrate rigidity, discussed by Jennett and Plum (1972) and by Jennett and Johnston (1972). Mello et al. (1976) reported that 17 out of 29 patients who showed early signs of decerebration had moderate to severe intracranial hypertension; in the remainder the pressure was normal. They neither monitored

any of the cardiovascular or respiratory parameters nor measured the degree of rigidity, all factors which might have explained their findings.

The few previous reports discounting the possible influence of muscle spasms on the ICP have tended to be more of the nature of casual observations than detailed studies. It seems reasonable to argue that severe decerebrate spasms might, by increasing the craniospinal venous blood volume, play a mechanical role in raising the maintaining the elevation of ICP. The magnitude and rapidity of this effect would obviously be of interest. Craniospinal venous engorgement may be due to either raised intrathoracic (ITP) or intra-abdominal pressure (IAP) or both, or to widespread compression of the intramuscular veins of the limbs and the displacement of their contents into the major capacitance veins. Changes in systemic arterial pressure (SAP) might also play a role in raising the ICP. It could be of great practical importance to know the relative significance of these factors in the elevation of ICP, which, by aggravating transtentorial herniation, may accentuate a brain stem lesion and convert a reversible physiological lesion into a permanent anatomical one.

Answers to these questions could materially influence the management of severe head injuries particularly in children and young adults whose brain stem appears to be relatively resistant (Powiertowski 1970). To date, mechanical ventilation has been employed primarily to correct the systemic arterial hypoxia caused by increased respiratory effort and muscle hypertonicity and thereby prevent the development of

brain swelling (Bracket 1970). The only head injuries which benefit from it, however, are those suffering from systemic arterial hypoxia (Brown 1970). This concept, supported as it is by the well-established value of adequate respiration in the management and prognosis of head injuries, dominates the present management policy in Edinburgh.

While we do not, by any means, underestimate the value of adequate ventilation of a head injury, it is suggested that decerebrate rigidity itself may have a direct mechanical effect in raising and maintaining the raised ICP. It is known that, at pressures above 450-500 mmH_2O, an increase in ICP reduces the cerebral blood flow (CBF) by mechanical vasocompression (Zwetnow 1970), and that this leads (just as does systemic hypoxia) to local cerebral hypoxia (Brock 1970, Siesjo et al. 1970) which, in turn, causes brain tissue acidosis and swelling (Langfitt et al. 1966, Jennett and Johnston 1970).

If rigidity per se has no effect on the intracranial pressure then muscle paralysis and supportive ventilation of these patients is of limited value. If, on the other hand, decerebrate rigidity does increase the ICP, paralysis of striated muscle and ventilation should not only correct blood gas tensions but also should directly reduce the ICP.

The absence of any study of the effect of decerebrate rigidity on ICP led us to consider the effect on the ICP of non-decerebrate spasms such as those of struggling animals, muscular exercise, tetanus or epileptic fits.

The cerebral congestion and elevated intracranial pressure which were found in struggling animals lightly anaesthetised with chloroform or morphia (Roy and Sherrington 1890) were attributed

to the observed rise in systemic arterial and venous pressures. The validity of this conclusion may be questioned, however, because of their inability to control the blood gases and acid-base balance, and also in the light of the later discovery that both of the agents used, chloroform (Koopmans 1939, Finesinger and Cobb 1935) and morphine (Keats and Mithoefer 1955) could themselves cause cerebral vaso-dilatation and a rise in cerebral blood volume by a combination of respiratory depression, carbon dioxide retention and hypoxaemia.

The evolution of cerebral blood flow (CBF) and ICP monitoring techniques in the last few decades now permits an accurate and controlled study of changes in cerebral circulatory homeostasis.

Scheinberg et al. (1953) showed no change in the cerebro-vascular resistance (CVR) and CBF in ten out of twelve patients suffering from pulmonary emphysema and fibrosis while, during muscular exercise, their mean arterial pressure was greatly elevated; the other two patients showed a decrease in CVR and increase in CBF which were attributed to the increase which they observed in the arterial pCO2. Kleinerman and Sancetta (1955) found an increase in CVR and a decrease in CBF during exercise, to which they attributed the rise in CVR and fall in CBF. In a more recent study of four healthy volunteers Hedlund et al. (1962) showed little if any increase in CBF and the cerebral circulation time following muscular exercise, even though marked increases were seen in arterial blood pressure, pulse rate and cardiac output. They concluded that the cerebral blood volume was unaffected by exercise.

Poisoning by the toxin of Cl. tetani is clinically

equivalent to episodic decerebrate spasm and is characterised by the development of skeletal muscle spasms which are often associated with systemic hypertension, tachycardia and increased peripheral vascular resistance. Only six out of ten cases with severe tetanus developed hypertension (Corbet et al. 1969). Because of the marked elevation of urine catecholamines found by Kerr et al. (1968) during tetanus, these cardiovascular disturbances have been attributed to noradrenaline hypersecretion due to overactivity of the sympathetic nervous system (Editorial, B.M.J. 1969, Kerr et al. 1968). We found no study of the effect of the tetanic spasms on cerebrovascular dynamics; this is perhaps because tetanus is treated non-surgically.

Epileptic fits are generally regarded as being similar to those observed during decerebrate rigidity. Marked increases in CBF and ICP have been reported during seizures. The increases were rarely proportional to the amount of muscular activity in either experimentally induced or spontaneous fits. Gibbs et al. (1934) suggested that the great increase in CBF they observed in man during seizures was due to either systemic hypertension or the accumulation of carbon dioxide from the arrest of respiration. Penfield et al. (1939) disagreed and attributed the 4-fold increase in CBF they observed 3 minutes after termination of the seizures to an increase of cerebral metabolites. Plum and Wasterlain (1970), in experimental seizures in rats, showed a 3-fold increase in CBF and at least as great an increase in cerebral metabolic rate as judged by A-V oxygen and carbon dioxide gradients across the brain. Minns and Brown (1978) have recently shown that marked increases in ICP occur in children with various types of epilepsy and may

be maintained for up to 20 minutes after the end of the clinical seizure. They attributed this to the increase in CBF caused by metabolite accumulation.

CONTENTS

PART ONE

SURVEY OF THE LITERATURE

CHAPTER 1

DECEREBRATE RIGIDITY

HISTORICAL NOTE

The long-sustained muscular contraction which results from removal of the cerebral hemispheres and basal ganglia from cats and other mammals (rats, guinea pigs, dogs, monkeys) was called decerebrate rigidity by Sherrington (1897-98) whose discovery and systematic analysis of the phenomenon triggered the rapid development of knowledge of the central and peripheral neuromuscular control mechanisms.

The phenomenon of rigidity had already been described by Magendie (1825, cited by Denny-Brown 1966) in rabbits whose midbrain had been transected; subsequent sectioning of the pons abolished this rigidity. Luciani (1891, cited by Dow and Morruzi 1958) described homolateral rigidity of the fore-limb and opisthotonos following unilateral cerebellar ablation. He thought that the rigidity was due to irritation by haemorrhage at the operation site and also showed that total cerebellar ablation in dogs resulted in opisthotonos and great fore-limb rigidity. Sherrington, on the other hand, attributed rigidity to a central release effect of pontine and medullary centres which allowed the spinal motorneurons to sustain a high level of activity. Liddell and Sherrington (1924) further analysed the rigidity of decerebration and found it to be dependent on a spinal cord reflex which they called the stretch reflex.

GENERAL CHARACTERISTICS OF DECEREBRATE RIGIDITY IN ANIMALS

SHERRINGTONIAN RIGIDITY

The original, meticulously detailed description of decerebrate rigidity by Sherrington (1897-98) was

based on observations made mainly on cats and monkeys. He demonstrated that, within a few minutes (sometimes, however, only after an hour or so) of removal of the forebrain, a strong contraction of the voluntary muscles occurred. The rigidity was present in both flexor and extensor muscles and it was greatest in those muscles which opposed gravity. The animal assumed a posture in which the head and neck were held high, all four limbs were strongly extended (fore-limbs more than hind and proximal joints more than distal) and tail and dorsal hair were erect; if the animal were carefully placed upright it could stand. Sherrington called this posture "a caricature of reflex standing". Hypothalamic dysfunction, characterised mainly by loss of temperature control, was a prominent feature.

Decerebrate rigidity was evident not only in the posture of the animal but also in the resistance of the limbs to passive movement. These were "plastic", in the sense that a limb passively moved from one position to another retained the new position (Sherrington 1909). In particular, when the knee joint, already extended because of decerebrate rigidity, was further extended by lifting it (while the hip was flexed) the knee extensor muscles showed a considerable tonic contraction. If the support were withdrawn, the knee remained extended, maintained thus by contraction of the extensor muscle, which then offered considerable resistance to passive flexion. This phenomenon was called the "shortening reaction" because shortening of the extensor muscle was the stimulus to contraction (and therefore rigidity). The shortening reaction was abolished by sectioning the posterior roots of the spinal cord. It is clearly no more than a tonic shortening reflex in response to

stretch. The receptors involved are these which subserve the phasic stretch reflexes, i.e. the annulo-spiral receptor of the muscle spindle (described later) (Fulton 1943, Monnier 1964). The shortening reaction and the tonic stretch reflex are two aspects of one and the same mechanism; they are the basis of muscle tone.

When an attempt was made to bend the extended knee, the extensor muscle resisted this action until a point was reached at which the resistance melted away and if the pressure on the knee was then withdrawn the knee maintained the degree of flexion to which it had been manipulated; the tonic contraction previously exhibited by the extensor muscle had clearly disappeared. This reaction was called the "lengthening reaction" and it is what is observed in Parkinsonian rigidity and there described as the "clasp knife reaction". (Fulton 1943, Monnier 1964, Sherrington 1909).

Decerebrate rigidity could be completely abolished by the use of anaesthetics (at that time chloroform or ether) and when these were discontinued the rigidity rapidly returned to its previous level.

Denervation of the skin had little effect on the rigidity and an already rigid muscle remained so when its neighbours were denervated. When the corresponding dorsal roots were severed decerebrate rigidity was abolished only in those muscles which had been specifically de-afferentated (Sherrington 1897-98). Decerebrate rigidity was therefore, dependent on a proprioceptive reflex, the receptor of which was located in or near the effector muscle itself. As the trauma of de-afferentation alone might exacerbate rigidity, Sherrington

cut the dorsal roots of some animals several days before decerebration and in these animals, as might have been anticipated, decerebrate rigidity did not develop.

Section of the dorsal funiculi had no effect on decerbrate rigidity whereas section of one lateral column in the upper lumbar region abolished rigidity in the homolateral hindlimb. When both ventrolateral columns were cut at the cervical level the rigidity of both the homolateral fore and hindlimbs was abolished completely. In view of the possibility that the pyramidal tract was involved in the abolition of rigidity, Sherrington sectioned the lateral half of the medulla, well above the decussation of the pyramids. This abolished rigidity of the homolateral limbs which, however, could be restored by stimulation of the site of section.

Sherringtonian rigidity was inhibited by stimulation of central structures such as the anterior lobe of the cerebellum, the cerebral peduncles, pyramidal tracts or the sensorimotor cortical areas (Sherrington 1897-98, 1939, Brown 1914).

The distribution of rigidity was very characteristic, in that excitation, as expressed by contraction of one muscle group, was accompanied by inhibition (i.e. relaxation) of the antagonistic muscle group - the phenomenon of "reciprocal innervation" (Sherrington 1939).

The extensor decerebrate rigidity produced by intercollicular transection was short-lived. Sherrington reported that rigidity could last for up to 4 days in a few young animals. Bazet and Penfield (1922) showed that in chronically decerebrate animals rigidity was maintained for a few days, then steadily decreased and was replaced by flexion reflexes and stepping movements.

"ANAEMIC DECEREBRATE RIGIDITY"

Sherrington's intercollicular decerebration was a crude and mutilating procedure and most of the animals died within a few hours, mainly from uncontrollable haemorrhage.

Pollock and Davis (1923, 1930, 1931) developed the "anaemic method" of decerebration in which both carotid and basilar arteries were tied so that the blood supply was shut off from all structures rostral to the midbrain. The ensuing rigidity was more severe than the Sherringtonian and, like it, was abolished by sectioning the brain stem at the level of the eighth cranial nerve. It differed, however, in that it was not abolished by section of the dorsal roots. This difference was, at the time, attributed to the better preservation of the anaemic preparation but subsequent studies of the micro-vasculature have shown that the "anaemic" cats had sustained damage to their anterior cerebellar lobe, in addition to those structures rostral to the midbrain (diencephalon, basal ganglia and cerebral cortex). The blood supply of the anterior lobe of the cerebellum arises from the arterial tree rostral to the midbrain (Pollock and Davis 1930) and thus was inevitably damaged. The cerebellum, however, remained functionally intact and this, as will be shown later, largely determined the type of rigidity which appeared.

The essential difference between these two types of decerebrate preparation was first demonstrated by Stella (1944, cited by Morruzi and Pompeiano 1957) who prepared Sherringtonian or classical decerebrate animals with de-afferentated and thus flaccid forelimbs; rigidity appeared at once when the anterior lobe of the cerebellum was cooled

or excised. Cardin (1946) showed the same effect in the hind-limbs.

Brain motor centres initiate movement via descending impulses which reach the muscles either directly or through polysynaptic connections to large anterior horn cells (alpha-cells) or indirectly to the small cells (gamma-cells) and their efferent fibres which set up the level of excitation of the alpha neurons (Granit 1955).

Eldred et al. (1953) have shown that in cats with classical decerebration the gamma route predominates. By "listening in" to the single spindle afferents they demonstrated intense facilitation of the gamma system, whereas in the anaemic cats virtually pure alpha facilitation occurred, designating them as having alpha-rigidity.

Matthews and Rushworth (1957) confirmed this by applying procaine solution to the motor nerve near its termination. Gamma decerebrate rigidity was promptly abolished, by selective blockade of the small gamma fibres (they hypothesised), whereas the alpha rigidity could be abolished only by blocking large motor fibres (Matthews 1958).

Granit et al. (1955) showed that cerebellectomy resulted in a gamma paralysis which they considered equivalent to de-afferentation. Because the muscles were not paralysed but remained perfectly accessible to reflex stimulation, they concluded that more excitation must have been directed on to the alpha motorneurons. They introduced, thus, the concept of two routes of excitation, alpha and gamma, equally able to mediate reflex movement; the proportion in which they were activated at any given moment was in some way dependent on

the cerebellum.

Another difference between alpha and gamma rigidity (Pollock and Davis 1927, Sprague and Chambers 1953) is that anaemic preparations - in which the alpha mode of excitation predominates - show a lack of plasticity in their rigidity. Eldred et al. (1953) explained this by showing that an important component in the lengthening reaction is the inhibition of gamma bias, which, clearly, cannot occur if there is no such bias to start with. Plasticity thus appears to be an exclusive property of the gamma mode of excitation. This would adequately explain the absence of a reflex lengthening reaction in the preparations of Pollock and Davis as well as those of Sprague and Chambers. The presence or absence of a lengthening reaction may be of value in the differential diagnosis of the hypertonias.

NECK AND LABYRINTHINE TONIC REFLEXES

The next major advance in our knowledge of the mechanism of the normal postural reflex came from the analysis of its role in decerebrate rigidity by Magnus (1925). He demonstrated that flexion, extension or rotation of the neck of a decerebrate animal altered the pattern of the plastic tone; e.g. strong flexion of the neck resulted in a decrease in rigidity in all four limbs, extension had the converse effect and rotation of the head to one side increased the rigidity homolaterally while decreasing it contralaterally. The impulses responsible for these changes in rigidity pattern were believed to be the proprioceptive input from the neck muscles, joints and tendons, the otic labyrinths and some exteroceptive impulses from the body surface, eyes and ears.

Postural reflexes were distinguished as:

a) "Reflex standing", i.e. reflex muscle action sets up a certain degree of continuing tone in order to prevent the body falling to the ground under the influence of gravity,

b) "normal distribution of tone", i.e. a balance of tone between the extensor (antigravity) and flexor muscles,

c) "attitudinal reflexes", i.e. ensuring the harmonious relationship between parts of the body and,

d) the "righting reflexes", i.e. if an animal's body position is disturbed it is brought back to normal by the operation of a series of reflexes. The righting reflexes are classified as:

i) "labyrinthine righting reflexes",

ii) "body righting reflexes acting on the head"

iii) "neck righting reflexes",

iv) "body righting reflexes acting on the body" and

v) "optical righting reflexes".

The centres regulating these postural reactions are widely dispersed within the brain stem; the attitudinal reflexes caudad to the entrance of the VIIIth nerve, the neck righting reflex in the pons and upper medulla, the righting reflexes in the midbrain and the others rostral to the red nucleus. Ponto-medullary and intercollicular preparations, therefore, would be expected to have lost their righting reflexes, whereas in the thalamic and decorticate animal these and other postural reflexes are preserved except for the visual ones which are lost only in the decorticate animal. Magnus (1925) believed that the red nucleus was the centre for all of the righting reflexes except for those acting on the head, and that the efferent pathway was the rubrospinal tract.

GENERAL CHARACTERISTICS OF DECEREBRATE RIGIDITY IN MAN

Decerebrate rigidity has been recognised in man for almost as long as in the experimental animal. There is room for doubt, however, as to the strict equivalence of the two conditions because the clinician rarely sees cases with complete brain stem lesions which exhibit all the characteristics observed in animals and therefore customarily base the diagnosis largely on the patient's postural attitude.

Magnus and DeKleijn (1912) reported briefly on 5 cases diagnosed as having "decerebrate rigidity" on the basis of postural tonic reflexes rather than on the characteristics of the hypertonia; one hydrocephalic child was completely atonic, another had a spastic, ataxic and paretic gait, a neonate with respiratory distress showed a strong extensor rigidity and tremor, an old man with intraventricular haemorrhage survived for 48 hours with extensor rigidity of all four limbs without convulsions and there was one case of meningitis with convulsions.

Brouer (1916) and Winkler et al. (1917, both cited by Walshe 1923) described similar isolated cases and like Magnus and DeKleijn they were more interested in demonstrating the righting reflexes than in establishing the presence of true decerebrate rigidity.

Wilson (1920) reported a series of cases which he divided into those with "decerebrate rigidity" and those without tonic fits. He expressed the opinion that many of the involuntary postures of a limb in various nervous diseases, as well as the transient positions assumed in chorea and athetosis were

aspects of decerebrate rigidity. His cases covered a wide clinical spectrum - spastic paralysis, extrapyramidal syndromes and cerebellar symptoms, even tetany and hysterical spasm. Only two of his cases (Nos. 6 and 9) showed the typical decerebrate state as we understand it today.

According to Sherrington, the physiologic characteristics of true decerebrate rigidity are:

1. the rigidity should affect the extensor muscles more than the flexors, which, by the law of reciprocal innervation, should be relaxed or at least less active.
2. the rigidity should be plastic, which is known to result from the reflex shortening and lengthening reactions.
3. the presence of righting reflexes is not necessary, because in the case of a ponto-mesencephalic lesion they might be absent; their presence, however, is strong evidence in favour of the diagnosis.

Tonic fits do not occur in the decerebrate animal except as a result of haemorrhage or irritative trauma to the medulla (Bazet and Penfield 1922). The intercollicular animal gradually loses thermoregulation but there are no irregularities of pulse or respiration if the lesion spares the medullary centres and if convulsions do not occur; in an animal with tonic fits, however, bradycardia, cyanosis, fixed and dilated pupils, head retraction and opisthotonos all occur and soon lead to death but are no part of reflex decerebrate rigidity.

Strychnine, tetanus and meningitis produce a posture similar to that of decerebrate rigidity but, in fact, fundamentally different; these are irritative phenomena whereas decerebrate rigidity represents a release of central motor activation mechanisms.

Despite some minor differences, human spasticity is very similar to classical decerebrate rigidity in that both are due to a release of stretch reflexes of the antigravity muscles. In both conditions, de-afferentation abolishes the increased tone (Sherrington in animals 1939, Foerster in man 1911) and lengthening reactions ("clasp knife" rigidity) can be elicited. Spasticity is well exemplified by the posture adopted in man following a capsular haemorrhage; this is described as muscle hypertonia, predominantly in the flexors of the arms and extensors of the legs and is accompanied by hyperactive proprioceptive reflexes and clonus. This type of mixed (upper limb flexor and lower limb extensor) rigidity in man can be regarded as "decorticate" because it is induced by lesions which interrupt cortical impulses. It differs, however, from the experimental decorticate rigidity of cats and other animals in that these show extensor hypertonia of all four limbs.

Walshe (1923) presented a young woman who survived in coma for four weeks following operation for a suprasellar cyst. Her arms were held semiflexed across the body at the elbows, the forearms slightly pronated and the wrists and fingers flexed, while the legs were held extended and adducted with the feet in plantar flexion. The rigidity was plastic and typically "clasp knife" in character, tendon reflexes were brisk and showed shortening reactions and the Magnus and DeKleijn reflexes were present. The pulse and respiration were regular but the temperature was persistently subnormal. The description matches that of experimental intercollicular rigidity but for the attitude, which was that of decorticate rigidity.

Another typical case of decorticate rigidity was reported by Davis (1925): a child with a suprasellar cyst which compressed

the brain stem sufficiently to produce symptoms similar to these of experimental rigidity. Necropsy showed an anatomically incomplete lesion of the brain stem.

Nielson (1941) presented three cases with "decerebrate rigidity" and attempted to establish a clinical distinction between "decorticate" and "decerebrate" rigidity. At necropsy, however, all three showed lesions similarly located in pons and cerebral peduncles.

It is generally accepted that strictly localised lesions like these made in experimental animals are very rare indeed. Decorticate rigidity (arms flexed, lower limbs extended) is a common result of severe anoxia, a variety of encephalitides and some metabolic disorders of the brain (Ritchie Russell 1961).

Extensor rigidity with marked internal rotation of all four limbs is commonly seen as a result of midbrain damage from transtentorial herniation as a result of raised supratentorial pressure. Extensor decerebration in man is produced by e.g. massive haemorrhage at the mesencephalic level and is usually followed by extreme extensor rigidity of all four extremities (Henneman 1974, Mettler 1978).

Bricolo et al. (1977) carried out a comprehensive study of the motor patterns described as decerebrate rigidity in 800 head injuries. His combined clinical and electromyographic studies showed that 35% developed classical decerebrate rigidity, 7% decorticate rigidity, 11% unilateral rigidity, 7% combined rigidity and the remaining 40% alternating rigidity, either extensor or flexor, in the same limb.

STRETCH REFLEX

DEFINITION

The resistance which was observed, mainly in the anti-gravity muscles, in animals with decerebrate rigidity led Liddell and Sherrington (1924) to study the "myotatic" or "stretch" reflex. This was done on the quadriceps muscle of a decerebrate cat whose hind limb had been denervated except for this muscle; slight stretching of the muscle developed a greater tension than would have been anticipated from the elastic properties of the muscle itself. When the nerve was then severed a much smaller tension was developed. They concluded that the tension was due to reflex contraction of the muscle because interruption of its reflex pathway (dorsal roots, spinal cord) abolished the contraction. The receptor organs were in the muscle itself since the reflex was restricted to the stretched muscle and the injection of local anaesthetic into the tendon had no effect on it (Fulton 1943).

It is generally agreed that there are two components of the stretch reflex; a phasic reaction which corresponds to the period of increasing stretch and a postural or tonic reaction which corresponds to the period of maintenance of stretch, so that alteration or maintenance of the posture occurs. The latter is considered to be the basis of muscle tone (Lance 1970). The integrated view of the stretch reflex and posture can be expressed as "posture is basically the stretch reflex, the result of gravitational pull on the antigravity muscles themselves" (Rushworth 1964).

Subsequent knowledge has demanded no revision of the original concept of the stretch reflex. The reflex arc is constituted

by an afferent fibre which originates from receptors within the specialised fibres of the muscle spindle and which synapses with a motor neuron, the axon of which supplies the striated extrafusal muscle fibres which surround the muscle spindle as it lies parallel with the ordinary muscle fibres (Fig. 1-1).

MUSCLE SPINDLES

Muscle spindles are found in all striated muscles. Cooper and Daniel (1956, 1963) working with human and Boyd (1956) with cat muscle found two types of intrafusal muscle fibres as regards size and appearance:

a) the larger, "nuclear bag fibre", has a prominent non-contractile central area containing many nuclei and only the extremities of the fibre are striated and contractile.

b) the thinner and shorter, "nuclear chain fibre", is striated throughout its length and multiple nuclei are arranged as a central, longitudinal chain.

Efferent nerves of muscle spindles

The contractile regions of the muscle spindle fibres are innervated by small fibres which, because their conduction velocity of 30m/sec was the same as of the gamma group of Erlanger and Gasser (1937) were labelled gamma fibres (Leksell 1945). Two types of gamma fibre can be distinguished (Boyd (1962): $gamma_1$ and $gamma_2$. The larger $gamma_1$ fibre terminates in one or more motor end-plates at the pole of a nuclear bag fibre while the finer $gamma_2$ fibre terminates in a network, (a "trail ending"), in the para-equatorial region of a nuclear chain fibre. The gamma neurons from which these fibres originate are located close to the anterior horn cells of the spinal cord (Fig. 1-1).

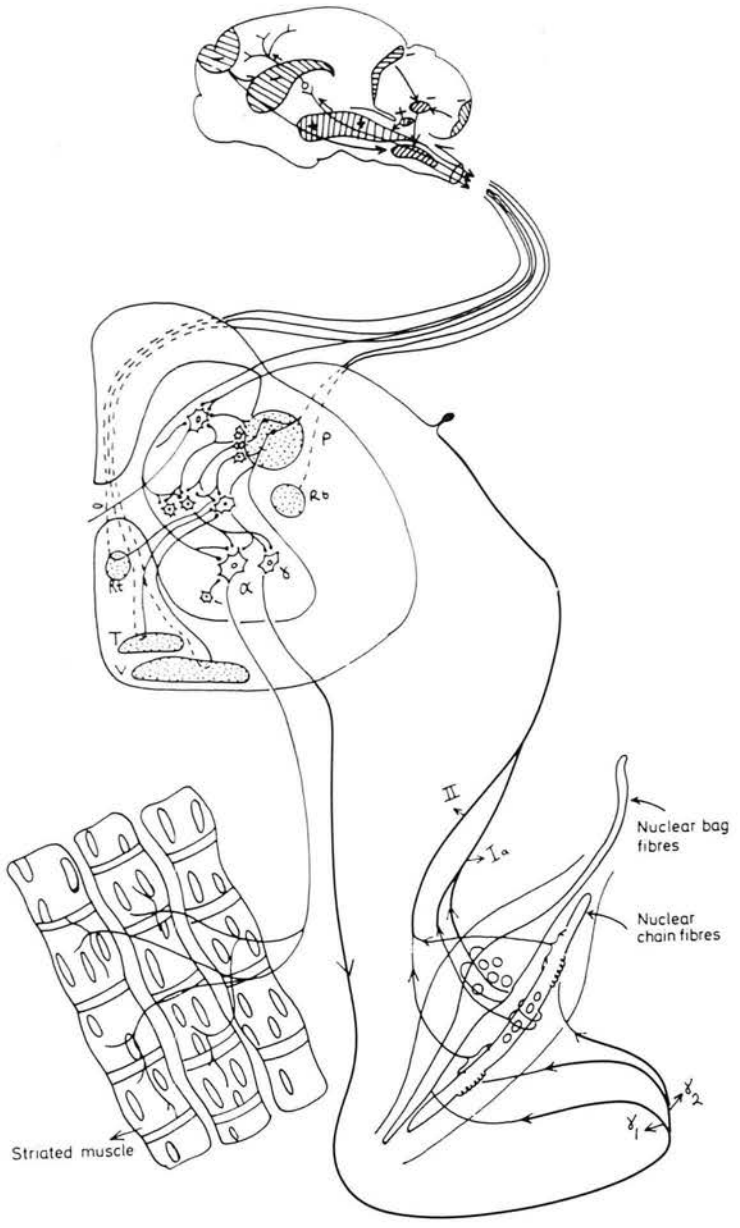
P
Ro
α
γ
T
II
Ia
Nuclear bag fibres
Nuclear chain fibres
γ2
γ1
Striated muscle

Fig. 1:1

Afferent nerves of muscle spindle

We know from the work of Cooper and Daniel (1963) and Boyd (1962) that the sensory afferents from the spindle are also of two kinds: primary (annulospiral) and secondary ("Flower-spray") endings. The former coils around the equator of each type of intrafusal fibre and expands into a fairly thick myelinated Ia afferent nerve fibre which projects on to an alpha-motor-neuron. The secondary ending continues beyond the capsular boundary as a thin myelinated fibre, the II afferent fibre which reaches the flexor motorneurons indirectly via the spinal interneurons (Hunt 1954).

Function

If the spindle is tense relative to the surrounding muscle, its firing rate is increased and its reflex effects tend to cause contraction of the surrounding muscle which thus attains the resting state at a shorter length. If the spindle is slack as compared with surrounding muscle, its firing rate decreases, and its reflex effects tend to produce relaxation of surrounding muscle, thus restoring the resting state at a greater length. The function of a spindle receptor, therefore, is to monitor the ratio of spindle to muscle length and the gamma afferent bias plays a part in determining the final length of the muscle fibres surrounding the spindle (Merton 1953).

The non-contractile equatorial region of an intrafusal fibre makes it a very suitable organ for registering changes in length. Stretching of the primary receptor generates an electrical potential and, in turn, reflex activation of the homonymous alpha-motorneurons occurs. The spindle contraction which occurs in

response to the alpha-discharge counteracts the stretch, thus keeping the length of the muscle roughly constant, and the locomotion effective. The control of highly complicated movements, however, requires that the velocity at which the muscle length is changing should also be sensed and proper correction applied. Muscle spindles are, in fact, sensitive to both the length and its rate of change (Granit 1975).

Engineers explain that a stable servomechanical system must possess both a length-error detector and a velocity detector in order to damp out oscillations in the "equilibrium" length - in this case, of the muscle (Bayliss 1966). The spindle fulfills both of these functions.

Neurophysiological studies (Matthews 1962, 1964, Jansen and Matthews 1962) have shown that primary sensory fibres show two types of response to stretch; the first is particularly sensitive to the rate of change of intrafusal length during stretching (dynamic response) and the second responds to the intrafusal fibre length itself (static response). The terms "dynamic" and "static" are readily understandable as applied to stretch and, similarly, the sensitivity of the muscle spindle to the same stimulus may be regarded as both dynamic and static.

The electrical activity of a muscle spindle afferent is determined not only by the stretching of the muscle but also by the gamma-efferent activity. Matthews (1964) showed that there are two types of fusiform fibre, one of which mainly intensifies the dynamic reaction of the Ia afferents, (dynamic gamma-fibres) while the other chiefly intensifies the static reaction of the Ia as has also been shown recently to be the case with the II afferents (static gamma-fibres) (Appelberg et al. 1966). The

effect of secondary afferents on the motorneurons is not yet known; it may be that their most important function is to pass information on static length to higher levels particularly the cerebellum (Granit and Kellerth 1967).

Following intercollicular decerebration, spontaneous fusimotor activity, both static and dynamic, increases in the extensor muscles (Alnaes et al. 1965, Matthews 1964). In spinal animals, such hyperactivity is confined to the dynamic system of the flexors (Alnaes et al. 1965, Bergmans and Grillner 1967, Jansen 1965).

SUPRASPINAL CONTROL OF THE STRETCH REFLEX

The condition of decerebrate rigidity demonstrates most dramatically that the stretch and other spinal reflexes are subject to powerful supraspinal control.

From observation of patients with brain lesions, Hughlings Jackson (1931-32) developed the concept of a hierarchy of functional levels in the nervous system: when the function of a higher centre was abolished, a lower became hyperactive and this sequence could be repeated. In particular, he postulated that, because spinal activity was subject to opposing influences from the cerebrum and cerebellum, the rigidity and hyper-reflexia of hemiplegia were evidence of unopposed cerebellar activity.

What Jackson developed on theoretical grounds, Sherrington established experimentally by showing that the decerebrate rigidity produced by sectioning the brain stem anywhere between the caudal diencephalon and the level of the eighth cranial

nerves was a "release" from the influence of inhibitory centres located rostral to the diencephalon. Luciani (1891, cited by Dow and Morruzi 1958) attributed decerebrate rigidity to local irritation but this seems unlikely in view of its persistance for four days, or in the hands of Bazet and Penfield (1922) for two to three weeks.

Recent work by Magoun and his collaborators (Magoun and Rhines 1946, Lindsley et al. 1949, Magoun 1950) has demonstrated, however, that decerebrate rigidity and spasticity are due not only to the removal of inhibitory influences acting on the spinal stretch reflex but also to the sustained activity ("influx") of supraspinal influences which facilitate these reflexes. By analogy with a jack-in-the-box, Magoun and Rhines (1948) described the twofold central mechanism of spinal motorneuron excitability as one in which "Jack's hyperactivity depends on the removal of the lid which holds him down and on the spring inside the box, which is the actual factor responsible for pushing him up".

FACILITATORY SYSTEM

Facilitation of the stretch reflex via the vestibulospinal pathways

1) Anatomical note

The chief vestibulospinal projection derives exclusively from the lateral vestibular nucleus of Deiters and descends in the homolateral ventrolateral funiculus of the spinal cord as the lateral vestibulospinal tract (Pompeiano and Brodal 1957) which can be traced throughout the cord in cats, monkeys and man (Nathan and Smith 1955). Schimert (1938) showed that its fibres establish direct contact with the ventral horn cells and have

an excitatory action on these.

Vestibulospinal fibres arising from the medial and inferior vestibular nuclei form the less important medial vestibulospinal tract.

2) Physiological note

Vestibulospinal reflex activity can be modified by somatic activity, possibly by the dual influence of somatic and labyrinthine activity on spinal projection neurons in the lateral vestibular nucleus (Wilson and Peterson 1978). Excitatory activity from cutaneous, joint and muscle receptors reaches this nucleus via the fastigial nuclei and the anterior lobe of the cerebellar cortex (Wilson et al. 1967, Allen et al. 1972). Excitation reaches the anterior lobe by both mossy and climbing fibres and the inhibitory cortical output (of Purkinje cell axons) is distributed mainly to the lateral vestibular nucleus (Ito and Yoshida 1966, Ito et al. 1968).

The inhibition of vestibulospinal neurons by the anterior lobe Purkinje cells not only modifies the response to somatosensory input but also exerts a controlling action on labyrinth-evoked activity. Decerebrate-decerebellate cats exhibit strong opisthotonos, which is not seen in animals which are merely decerebrate (Pollock and Davis 1927). The opisthotonos must be due to tonic vestibular reflexes, because it disappears when the labyrinth is destroyed. We can assume, therefore, that it is caused by pathways relaying in the vestibular nuclei which are under cerebellar inhibitory control since their action is enhanced by cerebellectomy.

As might be expected from the well-known observation that stimulation of the lateral vestibulospinal tract enhances activity

of the extensor musculature (Brodal et al. 1962), stimulation of the lateral nucleus evokes excitatory postsynaptic potentials in extensor motorneurons innervating neck, back, forelimb and hindlimb of the cat (Lund and Pompeiano 1968, Wilson and Yoshida 1969, Grillner et al. 1970). The short latency of these potentials as regards the neck, some back extensor muscles and some hindlimb motorneurons at the knee and ankle identified these as monosynaptic whereas connections with the forelimb and hindlimb were mainly polysynaptic (Wilson and Yoshida 1969). A di-synaptic reciprocal inhibition of flexor motorneurons has been reported (Grillner et al. 1970).

The vestibulospinal system is well developed in carnivores and lower primates (Kuypers 1964) and most investigators have regarded it as the most important single influence on the maintainance of tonic postural contractions. In the chimpanzee and man, however, the tract is quite vestigial and the accumulated physiologic and clinical data have relegated it to a role of least importance in the maintainance of postural tone (Schoen1964). Bucy (1938) severed the vestibulospinal tract in patients suffering from spastic paraplegia; he achieved only a temporary relief of spasticity and concluded that although the vestibulo-spinal system contributed to the maintainance of extensor rigidity in this condition, there were possibly other pathways fully capable of maintaining it at its full intensity.

From the work of Sherrington (1897-98, 1909), Thiele (1905), Brown (1914), Bazet and Penfield (1922), Ranson and Hinsey (1929), it was evident that the decerebrate rigidity produced by transection of the brain stem was maximum when the section was at the inter-collicular level; it persisted until further transections passed

through the level of the eighth cranial nerves and the calamus scriptorius was reached. Whether rigidity was unilateral or bilateral, division of one half of the spinal cord or of the anterolateral funiculus alone abolished rigidity homolaterally in carnivores. This was taken to mean that rigidity was due to impulses descending through the uncrossed vestibulospinal tract, a view which was reinforced by the experiments of Fulton et al. (1930) who destroyed the vestibulospinal tract by a localised lesion in Deiters' nucleus; subsequent decerebration of the animal failed to produce rigidity on the side of the lesion although rigidity and hyper-reflexia appeared in the contralateral, uninjured side. These findings were confirmed by Bach and Magoun (1947).

In the cat or dog removal of the sulcus cruciatus and area frontalis results in contralateral extensor rigidity, homolateral flaccid paralysis and hyperactive tendon reflexes (Olmsted and Logan 1925, Bard 1933, Woolsey 1933). Bach and Magoun (loc.cit.) showed that destruction of the vestibular nuclei had very little effect on the rigidity; this was slightly reduced but the reflexes remained. When in a pericruciate decorticate animal the anterior lobe of the cerebellum was also removed, greater enhancement of the antigravity posture and rigidity ensued than was produced by mesencephalic transection alone and tendon reflexes were very much hyperactive. Schreiner et al. (1949) destroyed both Deiters' nuclei but this had virtually no effect whereas a lesion of the mesencephalic tegmentum abolished rigidity and the stretch reflex was depressed to vanishing point. This is explained by the existence of the reticulospinal facilitatory system; as long as this continues

to discharge on to the anterior horn cells the rigidity is maintained. In the animals of Bach and Magoun (1947) in which decerebrate rigidity had been produced by low decerebration and, therefore, this facilitatory reticulospinal mechanism was impaired, subsequent vestibular destruction rendered the animals flaccid.

Facilitation of the stretch reflex via reticulospinal pathways

The reticular formation is an aggregation of morphologically diverse neurons which extends from medulla to thalamus and although it does not form a distinct, recognisable nucleus it possesses a remarkable functional unity. Its thalamic and mesencephalic portions project diffusely into the cerebral cortex and are concerned with arousal responses for the maintainance of consciousness; the pontine and medullary portions project both facilitatory and inhibitory influences on to the motor neurons of the spinal cord (via the reticulospinal tracts) (Magoun and Rhines 1947). Arousal of the organism via the upstream projections is achieved at the same time as the down-stream projections set the stage for activity. Respiration and vasomotor reactions are controlled by the reticular formation but the extent of this control is uncertain.

Amongst descending fibre systems the reticulospinal appears to play a dominant role in influencing the stretch reflex and therefore muscle tone. From the experimental studies on cats by Torvik and Brodal (1957) reticulospinal fibres have two main origins, from pons and from medulla; fibres from the former descend uncrossed and from the latter both uncrossed and crossed. Physiological studies indicate that fibres originating from the pons are largely facilitatory whereas

those from the medulla are inhibitory (Niemer and Magoun 1947, Magoun and Rhines 1946). Reticulospinal fibres descend in the ventrolateral funiculus of the cord but anatomical identification of their termination is lacking and in cats (Torvik and Brodal 1957) and monkeys (Bodian 1946) they have not been traced below the thoracic level.

McCulloch et al. (1946) traced by strychnine stimulation a descending connection from the 4-S cortical region which diverged from the corticospinal tract at the level of the pons and ended in the medullary reticular formation to establish a direct cortico-bulbo-reticular pathway, impulses of which are relayed to the cord and produce relaxation. The cortico-bulbo-reticular and the reticulo-spinal tracts together constitute a central inhibitory pathway (Magoun and Rhines 1946, 1947); they discovered this inhibitory mechanism by stimulating the bulbar reticular area in decerebrate rigid animals - extensor tone was abolished, limbs became flaccid to manipulation and tendon reflexes could not be elicited.

In its descent from the cortex the projection gives off collaterals which end in the caudate nucleus, as seen from degeneration studies following isolated lesions of this cortical area. Capsular hemiplegia in man results in more severe spasticity than if the lesion were in the cortex alone, evidence that striatal mechanisms are responsible for intensification of the rigidity. In primates with striatal ablations, subsequent 4-S cortical lesions augmented the rigidity and homolateral hyper-reflexia and increased resistance to manipulation were observed (Mettler 1945); this was indicative of a striatal pathway via the basal ganglia, providing inhibition in addition to that of the direct pathway from the cortical 4-S area.

Cerebellar control of the spinal mechanisms is even more complex and is also mediated through the reticular formation. Stimulation of the cerebellar cortex reduces muscle tone and inhibits decerebrate rigidity while ablation leads to extensor hypertonus and other symptoms. Ablation of the pericruciate areas of both cerebral hemispheres and the anterior lobe of the cerebellum leads to an intensely exaggerated, so-called "pillar-like" rigidity in all four limbs (Snider and Woolsey 1941).

The discovery of the brain stem facilitatory system and its effect in augmenting the myotatic reflex raised the possibility that this system might be important in the production and maintenance of rigidity and spasticity.

Bach and Magoun (1947) showed that destruction of the vestibulospinal system greatly facilitated cortically or reflexly induced movements during stimulation of the facilitatory area - the diencephalon, the mesencephalic tegmentum and the rostral end of the pons. When the caudal portion of the facilitatory system was destroyed, stimulation of its rostral portion had no facilitatory effect.

Sprague et al. (1948) demonstrated that in cats with decerebrate rigidity their myotatic reflexes and rigidity were exaggerated bilaterally when the facilitatory area of the reticular formation which had been left intact at operation was directly stimulated.

In summary: The experimental evidence presented above strongly indicates that decerebrate rigidity and spasticity result from excitation of spinal stretch reflexes by impulses originating from a brain stem facilitatory mechanism.

Facilitation of the stretch reflex via other descending systems

1) Pyramidal tracts

The pyramidal tract is regarded as a very important pathway for the performance of fine and skilled movements but its role, if any, in the phenomenon of decerebrate rigidity is as yet unclear.

In the cat the projection of the pyramidal tract on to the anterior horn neurons is polysynaptic but it is now known that in monkey and man the synapse is monosynaptic in order to establish precise cortical control over skilled movements (Phillips 1967). At all levels of the neuraxis except for the pyramids, the tracts are so closely intermingled with other descending systems that it is impossible to produce a pure pyramidal lesion.

Sherrington (1897-98, 1939) showed that section of the pyramids had no effect on decerebrate rigidity. It has been reported, however, (Lance 1970) that pyramidotomy produced only slight rigidity, not the definite spasticity of a cortical lesion, when the animal (cat) was suspended in air. Stimulation of the pyramidal tracts produced transient facilitation of muscle spindle activity from both sides of the body (Granit and Kaada 1952) while Laursen and Wiesendanger (1966) and Kato et al. (1964) showed increased tone of the flexor muscles as a result of the simultaneous activation of both alpha- and gamma-motorneurons. Gernandt and Gilman (1960) demonstrated that in the cat repetitive cortical motor stimulation temporarily enhanced motor neuron activation, an effect which was quickly followed by a profound and lasting depression, which persisted even after pyramidotomy, suggesting

that it was mediated by collaterals passing to the reticular formation.

Cortical motor stimulation produced relaxation of the extensor muscle tone whether or not the pyramid was severed (Tower 1935, 1940, 1949). He emphasised that the pyramidal tracts have no inhibitory effect on spinal stretch reflexes and that cerebral inhibition is mediated by way of extrapyramidal pathways; the rigidity or spasticity, therefore, which accompanies paralysis of voluntary movements is of extrapyramidal origin.

2) Rubrospinal tracts

It appears that, in the cat, the rubrospinal tract is highly specialised and makes monosynaptic connection with both alpha- and gamma-motorneurons of the distal but not of the proximal muscle groups of the hind limbs. Both extensor and flexor toe muscles receive monosynaptic excitatory impulses and the amplitude of the potential evoked in the flexors is greater than that in the extensors (Shapovalov et al. 1971, Shapovalov 1975). In primates, however, the tract seems to be poorly developed and its very existence in man is still debatable (Nathan and Smith 1955, Schoen 1964).

Rademaker (1926, cited by Ranson and Hinsey 1929) concluded from experiments on cats and rabbits that the red nucleus was the centre which regulated muscle tone. Removal of the red nuclei, section of the rubrospinal tracts and section of the decussation of Forel each caused an increase in extensor tone even if the pyramidal tract and the rest of the brain were intact. He considered, from a review of the literature and a study of human pathology that injury to the red nucleus was responsible

for the appearance of decerebrate rigidity in man. This view, however, was short-lived, since sections of the brain stem which left this nucleus intact also resulted in decerebrate rigidity (Bazet and Penfield 1922, Ranson and Hinsey 1929). Mussen (1927) stereotactically destroyed both red nuclei; the consequent bilaterally symmetrical degeneration of the rubrospinal tracts caused only slight, transient unsteadiness. These results were confirmed by Ingram and Ranson (1932).

3) Tectospinal tracts

These originate from the superior colliculi, cross and descend in the anterior funiculi of the cord, their fibres intermingled with those of the medial vestibulospinal tract. They are held to be responsible for rotatory movements of the head and trunk in response to visual stimuli (Nyberg-Hansen 1966, cited by Lance 1970) and to play some role in the development and maintenance of decerebrate rigidity (Eyzaguirre and Fidone 1975).

INHIBITORY SYSTEM

The demonstration of a powerful, central inhibitory mechanism in the medulla (Magoun and Rhines 1946) has considerably amplified our knowledge of the central control of muscle tone. It is located in the ventrolateral part of the medullary reticular formation and appears to extend as far rostrally as the trapezoid body. Its efferent fibres descend in the ventral funiculus of the spinal cord. Its threshold is so low that, even in cat or monkey, weak

stimulation completely abolishes not only cortically induced movements but also all types of spinal reflex. In the decerebrate animal such stimulation "caused extensor tone to be lost, the legs became flaccid and collapsed, were flail-like to manipulation, and reflexes could not be elicited". When stimulation was discontinued, extensor tone and other reflex activity returned to their previous state. Unilateral stimulation abolished tone and reflexes completely in all legs except for the contralateral foreleg, in which the effect was partial. Niemer and Magoun (1947) showed that the spinal inhibitory effects of this centre were mediated through the reticulospinal tracts. Direct destruction of the centre has not been attempted, because of the proximity of respiratory, cardiovascular and facilitatory centres.

In summary: It is now widely accepted that the medullary inhibitory centre is the focus of action of most or all of the inhibitory areas located in cerebral hemispheres, striatum and cerebellum. The function of this centre is dependent on the inflow from these higher centres so that elimination of these, as by high decerebration or decerebellation, shuts it off. This allows the facilitatory system, now unopposed, to increase the level of motorneurone activity, the end result being decerebrate rigidity or spasticity.

Decerebrate rigidity, therefore, may be regarded as the clinical manifestation of an imbalance between the activities of two systems which exert opposite effects upon spinal motor-neurons (Ward 1947).

CHAPTER 2

INTRACRANIAL PRESSURE

DEFINITION

"Intracranial pressure (ICP)" is a term rather loosely used to designate the pressure inside the cranial cavity.

In a hydraulic system with freely communicating compartments forces are equally distributed and the hydrostatic pressure at the bottom of a column of liquid depends on its height and density, not its area or volume. The cerebrospinal fluid (CSF) system is hydraulic and the craniospinal compartments are in free communication; thus, when a patient is lying flat, the same pressure is recorded in the ventricle, cerebral and spinal subarachnoid space provided that the reference point is the same.

The intracranial CSF pressure (CSFP) is the resultant of the interaction of two systems. The first is the CSF, whose production and absorption rates are in a state of dynamic equilibrium which is proportional to the ICP (Cutler et al. 1968). The second comprises the brain tissue, its coverings and blood vessels and possesses viscoelastic properties which tend towards the uneven distribution of forces; an applied pressure distorts the system and decreases these properties.

Under normal conditions the ICP as measured outside the CSF system is considered to closely approximate to the CSFP (Langfitt et al. 1964).

THE MONRO-KELLIE DOCTRINE

Alexander Monro Secundus (1783) argued from anatomical and clinical observations that, since the skull was a rigid box and the brain virtually incompressible, the intracranial blood

volume must remain constant. Monro lacked the experimental evidence to support this concept but his pupil, Kellie, was able to provide it; he reported in 1824, on the basis of autopsy findings and some animal experiments, that no fluid could, in fact, be withdrawn from within the cranium without its simultaneous replacement by another - the Monro-Kellie doctrine.

Some doubt was cast on the doctrine at the end of the 19th century when Hill's hypothesis (1896) - that the cerebral vessels were rigid tubes and that the cerebral circulation was a function of the arterial and venous pressures - briefly held the field. The experimental evidence for the existence of independent cerebral vasomotor tone (Roy and Sherrington 1890) was overlooked.

Acceptance of the doctrine was helped by the re-discovery of the CSF by Magendie (1827, cited by Clark and O'Malley 1968). Burrows (1846) (who, in fact, opposed the doctrine) realised the importance of this fluid and its relationship to the craniospinal venous system: that changes in brain volume could occur at the expense of other fluids was the crux of the matter, not that the brain was incompressible.

Monro and Kellie, being ignorant of the existence of CSF and the variability of the intracranial volume, had strictly limited their doctrine to the cranium. It was soon realised, however, that the bony and membranous coverings of the skull and spinal cord were not as rigid as had been thought. In particular the spinal dura was much less closely related to bone than the cranial and the considerable epidural "space" which therefore existed contained an extensive venous plexus and fatty areolar tissue the plasticity (elastance) of which is

even now not known with certainty but is unlikely to be negligible.

It is known (Magendie 1836, cited by Weed 1929) that there is a lack of rigidity in the region of the atlanto-occipital ligament where pulsations may be seen, just as in the case of the anterior fontanelle in infants. This phenomenon led Blackfan et al. (1927) to argue whether the doctrine could be applied in its entirety or whether some limitation was required. Consideration has also to be given to the possible escape of CSF along the perineural channels which were demonstrated by Key and Retzius (1876, cited by Clark and O'Malley 1968) and later by Weed (1914), and whose physiological role is still unknown. Another factor limiting the applicability of the doctrine is the existence of the subarachnoid venous plexus, whose valveless, thin-walled veins can collapse and empty into the incollapsible venous sinuses. All those factors which ensure a smooth blood-flow, protect the brain against sudden alterations in pressure (as a result of postural changes) and facilitate the transmission of CSF to the venous sinuses also tend to restrict the applicability of the doctrine. There is experimental evidence for a linear relationship between the jugular and CSF pressure over a wide range above and below the atmospheric pressure (Williams and Lennox 1939, Kety and Schmidt 1948).

These factors were critically reviewed by Weed and Hughston (1921, 1921a, 1921b) and Weed (1929) who concluded that they were of insufficient importance to invalidate the concept of the bony investment of the CNS as a closed container. "All these potentially active factors seemed to be of theoretical rather than any practical significance under the physiological limits of our

observations. From the point of view of intracranial physiology, as a basis for experimental or surgical procedures, the doctrine holds and its importance is great in any clinical procedure" (Weed 1929).

These rather ill-defined factors may impose certain limitations on the Monro-Kellie doctrine. Although they may not disqualify it, they do cast certain doubts on the universal validity of the concept of rigid container and incompressible brain; changes in the intracranial volume certainly can and do occur. Recent experiments have conclusively shown that the pressure starts to rise only after an appreciable increase in volume has occurred, whether by CSF infusion or the inflation of a balloon (Langfitt et al. 1965, Miller and Garibi 1972, Löfgren et al. 1973). Such brain volume changes are limited by the concomitant changes in intracranial pressure which will be described later.

PATHOPHYSIOLOGY OF INTRACRANIAL PRESSURE

CEREBROSPINAL FLUID

Historical note

Cotungo (1764, cited by Clarke and O'Malley 1968) made the first adequate description of the ventricular and spinal subarachnoid fluids and demonstrated their continuity, pointing out that this fluid had not been identified previously because of inappropriate dissection techniques (Cushing 1926, Woolam 1957, Brisman 1970). This important discovery was, however, overlooked until Magendie (1825, cited by Clarke and O'Malley 1968) rediscovered and named it "cerebrospinal fluid", demonstrated its normal occurrence in mammals and by injection techniques

confirmed the free communication between the cerebral and spinal subarachnoid spaces and the ventricular system to its absorption by the arachnoid granulations (Key and Retzius 1855, cited by Woolam 1957). Luschka (1855, cited by Clarke and O'Malley 1968) provided evidence that the fluid was formed by the choroid plexuses and circulated. The introduction of lumbar puncture by Quinke (1891) made the fluid readily available for detailed study of its clinical pathology.

Further development came about because of the neurosurgeon's need to understand the pathology of the CSF pathways and the development of the techniques necessary for delicate operations on animal brains. The most outstanding achievement was that of Dandy, who with Blackfan (1913) produced hydrocephalus by blocking the aqueduct, thus establishing that the CSF was produced in the ventricles. Dandy (1955, cited by Wilson 1955) used phenolsulphophthalein as a marker to study possible routes of CSF absorption and concluded that this took place rather diffusely throughout the subarachnoid space as well as through the granulations. New data have resulted from recent work, mainly by Davson (1956), Milhorat (1972) and Bowsher and Kugelmass (1961) but conclusive evidence for many aspects of CSF production, circulation and absorption is still lacking.

Formation

As proposed by Weed (1914), Cushing (1914) and Dandy (1929) it is generally accepted that under normal conditions almost all of the CSF is formed by the choroid plexuses of the four ventricles, whence the fluid passes into the cerebral subarachnoid

space to be absorbed into the lateral lacunae via the arachnoid granulations. In the last decade, however, this concept has been strongly challenged; Polley and Curl (1967) perfused the aqueduct with an artificial CSF containing inulin and showed some dilution of the inulin which they attributed to fluid derived from the surrounding brain parenchyma. Milhorat (1969) managed to produce hydrocephalus by occluding the aqueduct with a balloon, even in plexectomised monkeys; these results were criticised by Davson (1972) who argued that the fluid formed was not CSF but a plasma exudate due to operative trauma. Davson and Segal (1970) provided evidence, based on a study of inhibitor agents, for a fundamental difference between the rate of turn-over of sodium in CSF and in extracellular fluid.

Lorenzo et al. (1970) observed that the rate of CSF formation in a hydrocephalic patient with aqueduct stenosis perfused from one lateral ventricle to the other was the same as in those perfused from ventricle to subarachnoid space, suggesting that the CSF was formed mostly within the ventricles. The mean rate of formation in adults is 0.4 ml/min (Rubin et al. 1966), and in children 0.35 ml/min (Cutler et al. 1968). Recently in a mixed group of children and adults the mean rate was 0.3 ml/min (Lorenzo et al. loc. cit.).

Experiments on normal dogs in which the CSFP was varied between +280 and -100 mmH_2O (Heisey et al. 1962) showed no significant correlation between the production rate and pressure. Sahar (1972) ingeniously enclosed the plexus <u>in situ</u> in a small, fluid-filled chamber and measured the rate of secretion. He found that the rate was reduced by increasing the pressure until secretion ceased at +150 mmH_2O. This was attributed

to a reduction of blood flow through the plexus as a result of the raised pressure.

Absorption

Weed's concept of the CSF being returned to the general circulation through the arachnoid granulations is generally accepted. These act as one-way valves between the subarachnoid space and the lacunae of the dural sinus; fluid transfer occurs as a result of either the difference in the colloid osmotic pressure of blood and CSF (Weed 1935), the existence of direct channels opening at a "critical pressure" (Welch and Friedman 1960) or by phagocytosis (Shabo and Maxwell 1968). The critical opening pressure in man is claimed to be 68 mmH_2O (5 mmHg) (Lorenzo et al. loc.cit.). Other sites of absorption have been suggested, i.e. from the spinal subarachnoid space into the large spinal veins (Brierley and Field 1948, Pollay and Welch 1962).

The absorption of CSF is pressure-dependent, increasing with elevated ICP (Welch and Pollay 1961). In hydrocephalus this relationship is linear, over the range of CSF pressure from 68 - 360 mmH_2O (Lorenzo et al. loc.cit.). When high perfusion pressures (and consequently high CSF pressures) were used in <u>in vitro</u> preparations of dural sinus the CSF flow through the granulations was diminished presumably because of mechanical distortion (Welch and Friedman 1960).

It is likely that adaptations to obstruction which would result in a normal CSFP may occur in either the clinical or experimental situation but to what extent these involve reduced secretion or the opening up of new drainage pathways remains to be seen.

Volume

The CSF volume constitutes 10% of the total intracranial volume and in the human adult has been estimated at approximately 140 ml (range 100 - 160 ml); in children it varies between 60 - 120 ml. Its major portion (75%) is within the cerebrospinal subarachnoid space and the remaining 25% is in the ventricular system (Lups and Haan 1954). If we accept a daily secretion of 576 ml, the volume is completely replaced several times in 24 hours. Production and absorption are in dynamic equilibrium.

Pressure

Masserman (1934) found the CSFP to be 148 $\pm$ 2 mmH_2O in the lumbar theca in 300 normal subjects, lying in the lateral recumbent position. Similarly positioned, approximately 1000 normal subjects were found to have a lumbar CSFP of 150 mmH_2O, upper limit 180 mmH_2O (Merritt and Fremont-Smith 1937). Spina-France 1963 (cited by Davson 1967) found the average cisternal CSFP to be 119 mmH_2O (ranging between 47 - 197), whereas the lumbar pressure was 167 mmH_2O. Gilland (1965) found the average lumbar CSFP to be 144 mmH_2O. A recent important study is that of Cutler et al. (1968) who used a perfusion technique in children and found that absorption ceased when the CSFP was less than 68 mmH_2O and the patient was lying horizontally; the pressure at which secretion and absorption were in dynamic equilibrium was of the order of 112 mmH_2O, which, they concluded, must represent the average CSFP in the ventricle with the patient in this position.

Similar pressures have been found in cats: 110 mmH_2O (Flexner and Winters 1932) and 82-150 mmH_2O (6-11 mmHg) (Beks 1973).

The position of the patient and site of CSF measurement are known to be important. Loman (1934) showed that, with the subject sitting the CSFP at the lumbar level was 375-565 mmH_2O whilst in the cisterna magna it varied between 40 and 80 mmH_2O; the difference equalled the height of the CSF column between the two levels. Masserman (loc.cit.), however, showed that from a CSFP of 150 mmH_2O when the patient was horizontal, it rose to only 280 mmH_2O whereas the actual increase in the hydrostatic column was 675 mmH_2O; i.e. only 40% of the theoretically anticipated rise occurred. Similar discrepancies were found in animals (Weed et al. 1932).

There is, therefore, some factor in CSF hydrodynamics which prevents the column from exerting its full weight, an elastic factor which modifies what otherwise would be a large alteration in CSFP with postural changes. This will be considered in detail when discussing brain elastance.

The CSFP trace from either the ventricle or the lumbar sac exhibits two superimposed frequency patterns; one of high frequency which is related to the cardiac pulsations (Bering 1955, Dunbar et al. 1966) and a second of lower frequency, related to the respiratory excursions (Davson 1967, Bradley 1970). The cardiac waves are more evident when the CSF pressure is increased, because the damping effect of the arterial wall is diminished and the CSF pulse more closely resembles the cardiac (Bering 1955). Cameron and Rossen (1941) have shown that the respiratory fluctuations are, in fact, due to transient venous impulses. The CSFP rises because of such venous volume increases as occur during abdominal compression, coughing or straining (Quinke 1891). Batson (1940, 1942, 1944)

has shown that when the abdomen is compressed, blood which normally returns to the heart via the inferior vena cava is diverted into the v ertebral venous plexuses. He has repeatedly emphasised that the subarachnoid venous system communicates with the spinal extradural system of longitudinal vertebral veins, which in turn connect through the intervertebral foramina with the azygos and hemiazygos veins in the thorax and at the abdominal level (Bowsher 1954). The connections between the cranial sinuses and the spinal vertebral venous plexuses via the inferior petrosal and occipital sinuses are well known. The spinal subarachnoid and the cephalic venous systems drain all the subarachnoid venous blood into the superior vena cava; this is important because changes in the venous volume brought about by respiration, coughing, straining etc. are transmitted in phase throughout the subarachnoid system. The CSF respiratory pulse and changes in the subarachnoid venous blood volume are brought about by events in the thoracic cavity, so that when the intrathoracic pressure is increased (as in expiration, coughing etc.) venous blood flow through the azygos system is reversed and the subarachnoid veins fill. This has been demonstrated by Bowsher and Kugelmass (1961), who measured the variations in CSFP in cats with the chest open and the chest closed (respiration in both cases was artificially maintained). When the chest was open and the intrathoracic pressure changes abolished, the CSF respiratory pulsations virtually disappeared.

As a model of the subarachnoid space and its veins, Bowsher (1953) used a glass cylinder, closed at each end by a perforated bung and having a side opening by which it communicated with a U-tube manometer. An elastic rubber tube was threaded through

the cylinder from end to end. The manometer and glass cylinder were filled with water. If the rubber tube were then distended, the level rose in the manometer tube to a level independent of the bore of the tube. Whatever the pressure changes which accompany the displacement, we are primarily concerned with a volumetric displacement phenomenon when the abdomen is compressed, there is a rise in the intrathoracic pressure or CSF respiratory fluctuations occur. The speed at which these changes occur precludes the possibility that the increase in CSF pressure results from an increase in its volume brought about by impairment of absorption (by an increase in venous pressure) while secretion continues; at the known rate of production of CSF, two minutes of total failure of absorption would be necessary to produce the volumetric changes recorded. That increases in CSF pressure are unequivocally a dislocation phenomenon due to an increase in the venous volume was shown by Bowsher and Kugelmass (1961). They compressed the inferior vena cava while injecting saline into the iliac or azygos vein; CSF was displaced from the lumbar sac into a manometer and when the caval pressure was released the CSFP returned to its previous level.

BRAIN TISSUE

The brain substance is relatively incompressible but exhibits the property of "plastic creep"; i.e. if subjected to persisting tension it grows longer and when the tension is withdrawn the stressed portion does not regain its previous length and shape. The brain yields at the site of maximum stress and in order to distribute the stress uniformly it is necessary that the deformed substance should flow into the less stressed

areas (Holborn 1943). This phenomenon, evaluated by Holborn on experimental models, has been widely applied to the case of a brain forced to herniate by a raised supratentorial ICP. Inflation of a balloon in the supratentorial space produces transtentorial herniation which may be temporarily reversed by lumbar saline infusion but since saline promptly flows above the tentorium the herniation recurs, is aggravated and becomes permanent (Langfitt et al. 1964).

Brain volume increases as a result of oedema or tumour. Traumatic brain oedema may be focal or spread centrifugally throughout the white matter from the site of tissue disruption where the blood brain barrier (BBB) has been damaged. This may explain symptoms of dysfunction at a distance from the focal lesion (Bakay 1965).

Brain oedema has been defined as an increase in the water content (Klatzo 1967). Usually it is accompanied by transudation of serum proteins across an abnormally permeable BBB and for this reason it has been called "vasogenic cerebral oedema" (Klatzo 1967). This is the commonest type of oedema and occurs in head injuries, cerebrovascular accidents, inflammatory and neoplastic conditions (Rinder and Olsson 1968). It is characterised by its intercellular location in the white matter and the accumulation of serum proteins, sodium and chloride in the oedematous tissue. This type of oedema differs from the "cytotoxic oedema" of acute anoxia, in which the fluid accumulation is in the grey matter and is intracytoplasmic (Klatzo 1967). Another condition must also be recognised, that which Elliot and Jasper (1949) originally described as "brain inflation"; in this there is a dramatic increase in

brain volume, presumably as a result of vascular dilatation since there is no abnormal accumulation of fluid in the brain, extra or intracellular. This acute vascular dilatation occurs when vasomotor tone is impaired - the "vasomotor paralysis" of Langfitt et al. (1965).

As the brain increases in volume it is deformed and displaced. A gradient of 10 mmHg in CSF between the supratentorial and infratentorial compartments is enough to produce severe and irreversible herniation at the tentorium (Kaufmann and Clark 1970). If the volume of one cerebral hemisphere increases so rapidly as to allow no time for compensation, herniation of the cingulate gyrus into the opposite supratentorial compartment may occur and lead to compression of one or both anterior cerebral arteries (Jennett and Stern 1960, Adams and Graham 1976). Commoner and more important are herniation of the hippo-campal gyrus of the temporal lobe through the tentorial incisura i.e. uncal, tentorial or transtentorial herniation, and herniation of cerebellar tonsils through the foramen magnum, i.e. tonsillar herniation (Jefferson 1938, Finney and Walker 1962, Adams and Graham 1976). All of these herniae may co-exist. Tentorial herniation leads to disturbances of the level of consciousness, pupillary dilatation, pyramidal signs and decerebrate rigidity with or without respiratory and cardiovascular complications. The syndrome of tonsillar herniation is less clearly defined and clinical diagnosis may be difficult; the commonly attributable signs are neck rigidity, paraesthesiae in the upper extremities, evidence of vagal stimulation (bradycardia, hiccough) and sudden respiratory arrest without premonitory disturbances of the level of consciousness (Zülch 1959, Tönnis 1959, both cited by Heiskanen 1964).

The symptoms of tentorial herniation are considered to be due to local compression and its vascular sequelae. The latter are of two kinds:

a) displacement of the brain stem and temporal lobe results in local venous stasis and rupture of the small branches of the basilar artery to midbrain and pons and

b) large arteries may also be compressed, resulting in ischaemia in their distribution territories (Jefferson and Sheldon 1956, Tomlinson 1959).

The vascular lesions are dependent on the rate of increase of the ICP and not on the pressure actually attained. Whether the brain stem haemorrhages are due to arterial rupture (Tomlinson 1959, Johnson and Yates 1956) or venous stasis (Evans and Scheinker 1943) is still hotly disputed.

CEREBRAL BLOOD VOLUME

The major portion of the cerebral blood volume (CBV) is in the capacitance veins, as in other somatic vascular beds, and is regulated by the same mechanisms as are involved in cerebral blood flow (CBF) regulation, i.e. arterial pCO_2, pO_2 and local hydrogen ion concentration (H^+). The CBV and CBF are related by the formula

$$CBV = CBF \times \bar{t}$$

where $\bar{t}$ is the mean transit (circulation) time. This equation embodies the "Stewart-Hamilton principle" which, though used originally for the measurement of cardiac output (Stewart 1921, Moore et al. 1929), has been adapted for the measurement of CBF (Nylin et al. 1961). The relationship between circulation time and CBF is complex and closely depends upon the CBV among other factors. Normally the relationship is reciprocal; the

relationship was lost if 5% carbon dioxide was administered (Fieschi et al. 1966). Harper et al. (1968) showed inthe monkey that, under conditions of constant blood flow, there was a linear relationship between the circulation time and CBF which was unaffected by either vasoconstriction or vasodilatation (hyperventilation or carbon dioxide administration respectively). When the CBF was increased, however, the CSFP, which was being used as an index of CBV, also increased, and the relationship was no longer linear. Under normal circumstances in young healthy subjects, Risberg and Ingvar (1968) studied changes in CBV during mental exercise, and found no satisfactory correlation between CBV and CBF; the functioning areas (frontal and temporal) showed an increase in CBV, which was attributed to selective localised vasodilatation, while in the parietal and occipital there was a decrease in CBV. If either of the other intracranial components (brain tissue or CSF) were now to increase in volume this could only be at the expense of the CBV but the CBF would not change.

The CBF normally remains constant over the range of mean blood pressure from 50 to 150 mmHg (Shapiro 1974, Lassen and Christensen 1976). The CBF is better maintained by increasing cerebral perfusion pressure (CPP) (i.e. the difference between ICP and aortic pressure, (Zwetnow 1970)) by raising the ICP than by lowering the arterial pressure (Miller et al. 1972). This effect is attributed to a sympathetic effect on the large intracranial vessels, a suggestion which is reinforced by the finding of a normal CBF in severe hypotension and in shock (Reivich et al. 1973). The ability of the cerebrovascular bed to maintain a constant flow during wide changes of CPP is called

"autoregulation". The mechanism of this effect is still hotly disputed. Bayliss (1902) originally postulated that the mechanism was probably the transmural pressure at the arterial end of the capillary bed ("myogenic hypothesis") (Folkow 1964). Changes in the transmural pressure across the arterioles results in a reciprocal alteration of their resistance, thus keeping the CBF constant despite the dropping of CPP. There are upper and lower limits to the CPP changes beyond which the CBF becomes a function of the arterial pressure. That brain damage may affect cerebral autoregulation globally or locally has been demonstrated in head injuries and subarachnoid haemorrhage (Bruce et al. 1973, Hajedimos et al. 1973, Paulson et al. 1970). Defective vasomotor tone results in a reduction in CPP when the ICP is elevated and in turn this leads to a reduction in CBF, either locally or globally. When vasomotor tone is locally defective although there may be no change in either the global CBF and CPP yet local reductions in CBF may cause local ischaemia and oedema.

The CBF is directly proportional to the pCO_2, which exerts its maximum effect on CBF at subnormal levels.

Doubling the pCO_2 (say, from 20 to 40 mmHg) doubles the CBF by arterial dilatation and results in a proportional increase of the CBV (Phelps et al. 1973, Reivich 1964), the amount of which depends also on the elastance of the system. This effect of pCO_2 is exerted only between 20 and 100 mmHg; beyond these limits there is no further change in the CBF. Care is taken not to exceed the lower limit when hyperventilation is used therapeutically.

The CBF is reduced when the pO_2 is reduced to about 50 mmHg

(Johansson and Siesjo 1975). If the level is further reduced to 15 mmHg it leads to a 4-fold increase in CBF (Cohen et al. 1967, Johansson and Siesjo 1975, McDowell 1966). The use of hyperbaric oxygen leads to vasoconstriction and reduction in CBF (Purves 1972).

The effects of both carbon dioxide and oxygen are considered to be mediated by the influence of the H^+ of peri-arteriolar extracellular fluid (Severinghaus et al. 1966, Lassen 1968, Wahl et al. 1970) on the tone of the arteriolar smooth muscle. An increase, therefore, in local metabolism would increase the CBF without changing the CPP.

Under normal circumstances, when the CPP falls below 50 mmHg the CBF starts to fall also. Only when it has fallen to approximately 40-60% of normal is the cerebral metabolic rate slightly reduced, as judged by the EEG changes, oxygen and glucose consumption, but no ischaemia occurs (Bruce et al. 1975). A 50% CBF represents a CPP of the order of 20-25 mmHg. This would explain why when the ICP was experimentally raised in volunteers by Evans (1956) their only complaint was of slight headache; similarly, cases with greatly raised intracranial pressure (80-90 mmHg) as in pseudotumour cerebri are virtually free from symptoms. In comatose patients, when cerebral metabolism is reduced, a reduction in the CBF is indicative of preservation of metabolic autoregulation. If the latter is lost, however, globally or locally, the accumulation of metabolites leads to an increase in CBF, CBV and ICP. The rise in the capillary pressure would lead to the development or aggravation of an already existing oedema.

When cerebral autoregulation is lost ("vasomotor paralysis"

Langfitt loc.cit.) vasodilator stimuli which, in the normal brain would increase CBF, now paradoxically decrease the CBF, locally or globally, the so called "steal" effect. The contrary effect is now seen after vasoconstrictor stimulation; whereas these stimuli reduce the CBF in normals, they now produce a paradoxical increase, the "inverse steal" effect (Lassen 1966, Lassen and Christensen 1976).

When autoregulation is defective the relationship between CPP and CBF becomes unpredictable and useless in clinical management.

In summary, therefore, under normal conditions the CBF must be halved before the first signs of cerebral ischaemia appear. In the damaged brain with impaired metabolism a much smaller reduction might be critical. The observation of a low CBF in a severely injured patient may be evidence of well preserved metabolic vasomotor control whereas an apparently advantageous increase in CBF means, in fact, potentially disasterous hyperaemia and oedema due to failure of that control.

EFFECTS OF A PROGRESSIVE RISE IN INTRACRANIAL PRESSURE

An understanding of the normal dynamics of CSF and blood circulation is fundamental to the effective treatment of intracranial hypertension. The effect of progressive supratentorial elevation of the ICP on CSF and blood dynamics is illustrated in Fig. 2:1 a-b-c. The cranial contents are enclosed in a semi-closed rigid containor and any change in the volume of one component is reflected in a reciprocal change in one or both of the others in order to keep the pressure constant (Monro-Kellie doctrine).

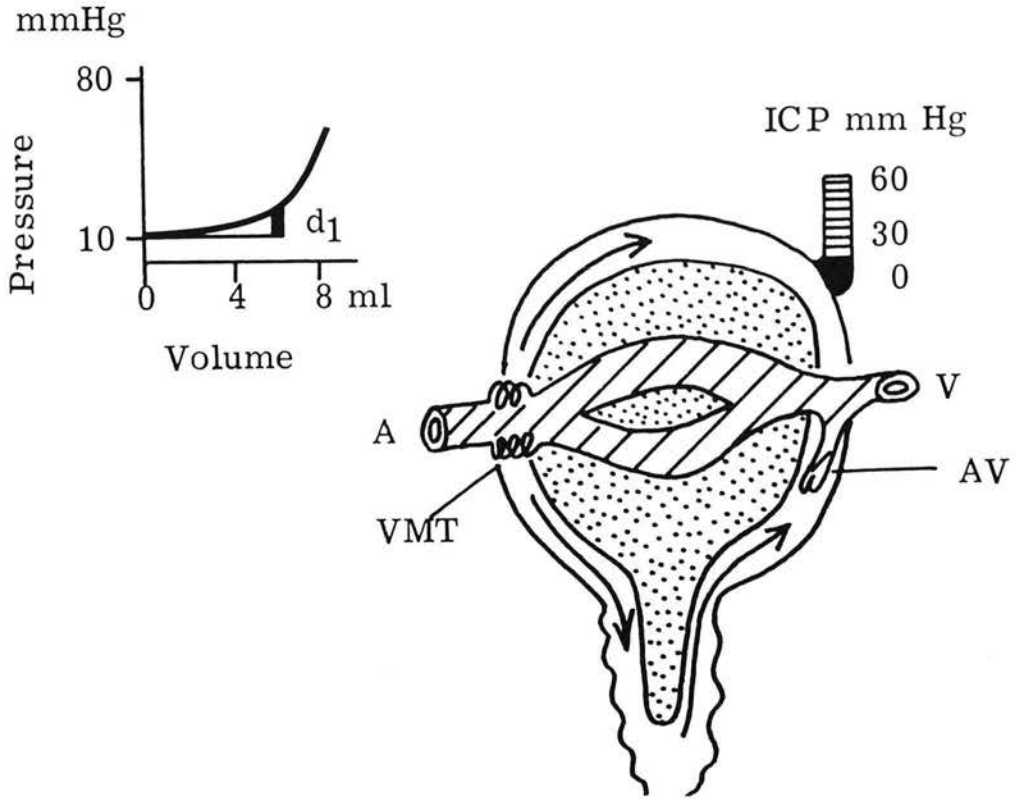

Fig. 2:1a

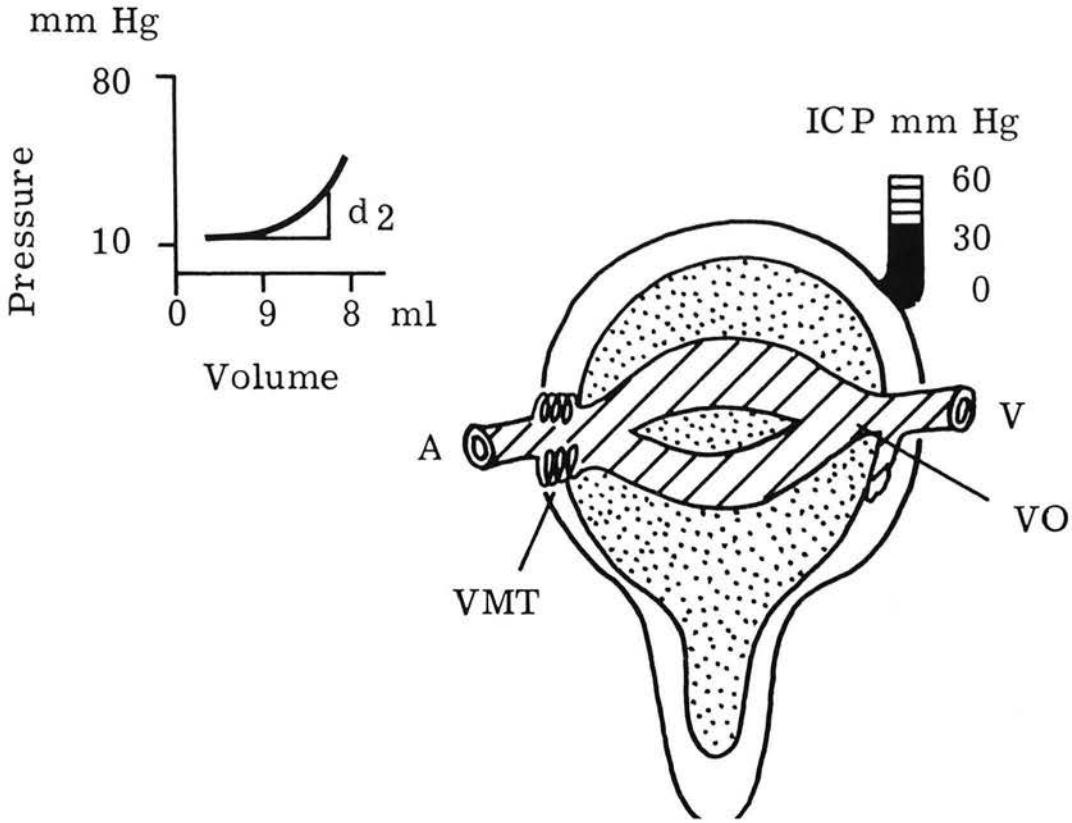

Fig. 2:1b

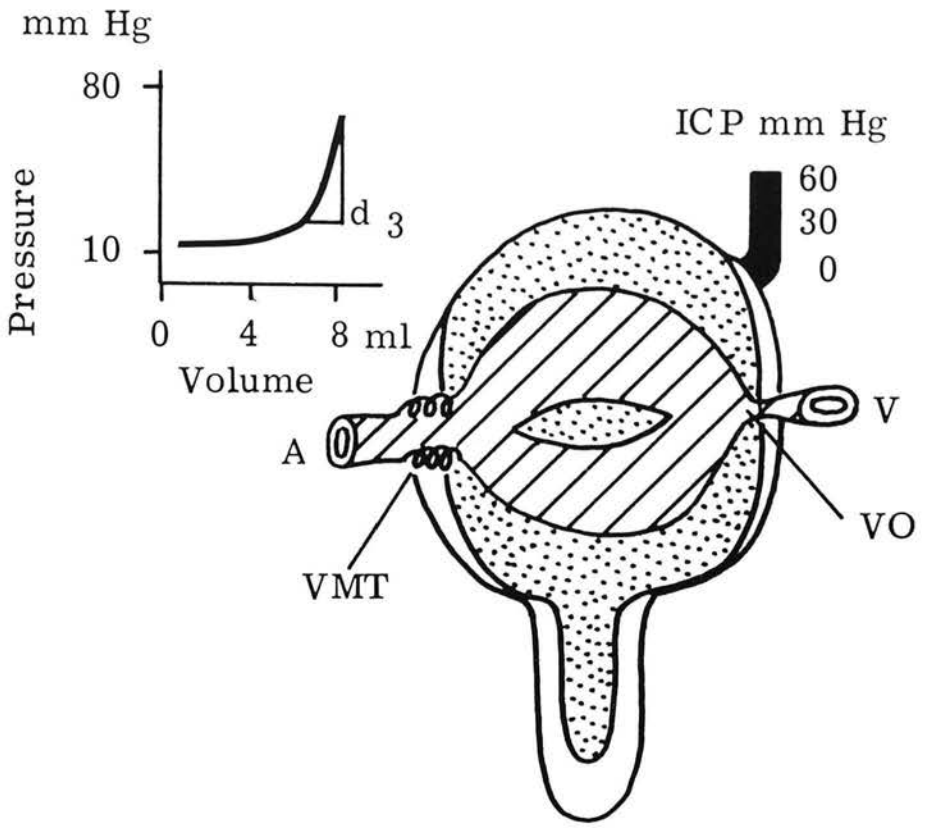

Fig: 2:1c

The development of a small space-occupying lesion (clot, oedema, tumour) results in displacement of a small volume of CSF from the ventricles into the spinal subarachnoid space, which, under normal circumstances, can accommodate this increase in volume and no pressure increase occurs (Fig. 2:1a). If the volume of the lesion continues to increase, the CSFP then starts to rise. CSF production and absorption increase since these are pressure-dependent so long as the CSFP does not exceed 387 mmH_2O. At higher pressures, mechanical collapse of the granulations results in total cessation of absorption. There must come a point when production must be slowed so as to reduce the total CSF volume within the craniospinal system (Shapiro 1974). Since the most effective buffer against raised ICP has been expended, further buffering can be provided only by alterations in the CBV and especially that portion of it contained in the low pressure venous system. The cerebral veins are normally elliptical in section but when the CSFP increases their section approximates to the circular (Bowsher 1953). Progressive enlargement of the intracranial mass eventually distorts and blocks the CSF pathways (Fig. 2:1b), collapses the basal cisterns, isolates the cranial from the spinal components of the CSF volume and compresses the arachnoid granulations. The cortical veins draining into the sagittal sinus collapse and when this is complete the venous resistance is increased, thus creating a back pressure in the related capillary bed. The CBF is maintained by an increase in CPP brought about primarily by an increase in the mean arterial pressure, but a decrease in the arteriolar resistance also helps maintain an effective CBF when the venous resistance is increased (Langfitt et al. 1965).

A CPP of 50 mmHg is necessary to maintain the CBF (Zwetnow 1970, Rowan et al. 1970). Both workers agree that this is a manifestation of some kind of autoregulation, similar to the well-known one which maintains the CBF in the face of changes in arterial pressure (Langfitt et al. 1965, Harper 1966). Miller et al. (1970, 1972) showed conclusively that CBF could be maintained in the presence of a rising ICP only for as long as the CBF could be increased by raising the mean arterial pressure. A decreased arteriolar resistance would lead to further regional or global CBV augmentation, (Fig. 2:1c) especially if associated with reflex arterial hypertension (so called "Cushing response") induced by either ischaemia (Cushing 1902) or direct mechanical compression (Rowan and Teasdale 1977) of the vasomotor centres of the brain stem. Reduction in both arterial and venous resistance eventually leads to elevated capillary pressure and predisposes to cerebral oedema (Klatzo 1967).

Finally, when the volume of the intracranial mass has reached the point at which no further compensation is possible by displacement of blood, the swollen brain herniates through the tentorial incisure and the foramen magnum, with the clinical and pathological effects already described.

In summary, a progressive rise in intracranial pressure affects cerebral function by reducing the blood flow and by producing irreversible, lethal displacements.

BRAIN ELASTANCE

DEFINITION

The relationship between pressure and volume was first studied by Weed et al. (1932) and Flexner et al. (1932) who

performed a series of experiments in which dogs were abruptly tilted from the horizontal to the vertical head-down or tail-down position. They presented evidence for the existence of an important relationship between the displacement of CSF and its pressure. They found that, in any one animal, the volume of fluid displaced bore a fairly constant relationship to the change in pressure; this relationship - "the coefficent of elasticity" - was expressed as the quotient dV/dP, the average value of which was 0.17. The formula which had been used for the determination of the elasticity coefficient of solids, fluids and gases could now be applied profitably to the cranio-spinal system.

Ryder et al. (1952, 1953) by the fractional withdrawal and injection of lumbar CSF demonstrated that the CSF Pressure/Volume relationship was non-linear and it was appropriately defined by the pressure/volume curve, the form of which was described as hyperbolic. They also showed that the dP/dV coefficient had its minimal value when the fluid pressure approximated to the systemic venous pressure.

Langfitt et al. (1965) in rhesus monkeys expanded a supra-tentorial balloon at the rate of 1ml/hour and found that a significant rise in ICP was obtained only when the volume had reached 5 ml. The compliance curve (dV/dP) had a horizontal portion, called "spatial compensation", which they postulated was due to the expression of approximately 1 ml of either CSF or blood from the intracranial space in response to each ml of fluid added to the balloon. An exponential rise in ICP occurred when the volume of fluid available for displacement was less than the volume added to the balloon. Langfitt's measurements

represent the steady state of ICP (static compliance) and take no account of the elastic properties of the craniospinal system. These are taken into consideration when elastance is determined by the dynamic techniques of Miller and Garibi (1972), Shulman and Marmarou (1971) (dynamic elastance) who found an exponential relationship between the response of the ventricular fluid pressure and changes in fluid volume over a wide range of pressures in man and in animals.

The terms elastance (dP/dV) or its inverse, compliance (dV/dP), are used depending on whether changes in pressure (elastance) or in volume (compliance) are to be emphasised.

MEASUREMENT

Two methods are available:

1) Miller and Garibi (1972) proposed the simplest method, the so called "volume/pressure response". Over a period of one second, 1 ml of sterile saline is added to or 1 ml of CSF is withdrawn from the ventricle and the ratio dV/dP or dP/dV is calculated. Miller and Leech (1975) showed a linear relationship between the V/P response, the ICP and the intracranial volume (Leech and Miller 1974); i.e. the "tighter" the brain the greater the V/P response. Miller et al. (1973) and Miller and Leech (1975) found an increase in pressure of more than 2 mmHg following the injection of 1 ml saline into the ventricles to be statistically significant. Miller et al. (1973, Miller and Pickard (1974) stated that the patient should cope well clinically with a V/P response less than 2 mmHg whereas a value greater than 5 mmHg indicated that decompression was urgently needed. Miller and Leech (1975) showed that the administration of either

mannitol or dexamethasone reduced the V/P response significantly more than it reduced the ICP and that in cases where neither was effective in this, they nevertheless reduced the V/P response.

2) Shulman and Marmarou (1971) used a slightly different method in hydrocephalic children which permitted the calculation of outflow resistance and the rate of CSF formation as well as elastance.

Clinical estimates of the elastance can be obtained by observing the ICP elevation in response to endotracheal suction or small changes in pCO_2, central venous or arterial pressure. This is a strictly qualitative measure of elastance and Shapiro (1975) assessed it by bilateral manual compression of the internal jugular veins as traditionally used for the diagnosis of a subarachnoid block.

CLINICAL SIGNIFICANCE

The continuous measurement of ICP provides a record of fluctuations of ICP as they occur, but this alone is of no predictive value. It is more important to know the response of the ICP, under controlled conditions, to an increase of intracranial volume as might be caused subsequently by hypercapnia, hypoxia or other factors. The ICP recording from the ventricle then assumes a new dimension of great importance.

The findings of McDowall et al. (1966 and Jennett et al. (1969) strikingly illustrate this. In patients with normal CSF pathways the administration of halothane or trichloethylene caused a small increase in CSFP of 3-14 mmHg, whereas in patients with intracranial space-occupying lesions, these same agents caused significantly greater increases in ICP, more than 50 mmHg in

some of them, even when the resting ICP was normal.

A measure of intracranial elasticity and the shape of its curve depends on the rate of volume expansion and on the systemic arterial and venous pressures (Löfgren et al. 1973). This author analysed the separate contributions of the cranial and spinal CSF compartments to the P/V curve in dogs, and found that 70% of the variation in volume within the system was related to the spinal compartment and 30% to the cranial (Löfgren and Zwetnow 1973).

An increase in the mean arterial pressure from 25 to 230 mmHg produces an approximately 5-fold increase in the elastance, whereas the elastance curve is not appreciably affected by arterial pCO_2 changes; the latter observation was confirmed by Leech and Miller (1974). Hyperventilation has no effect on the curve.

Increasing the central venous pressure (Löfgren et al. 1973) by mechanical ventilation displaces the curve upwards parallel to the ordinate (pressure axis): the converse occurs when the pressure is reduced.

PART TWO

METHODOLOGY

CHAPTER 3

INTRACRANIAL PRESSURE

REVIEW OF METHODS FOR MEASURING INTRACRANIAL PRESSURE

MEASUREMENT OF THE CEREBROSPINAL FLUID PRESSURE

Development of technique

Since the early methods of measuring the ICP are of only historical interest and are neither used in clinical practice nor have any bearing on this work only a few are briefly reviewed. A detailed review of them is that of Lagergen (1937).

CSF is hardly mentioned in the classical literature. It was interest in the pulsation of the brain which appears to have led eventually to the study of the CSF. Magendie (1839, cited by Leyden 1866) attributed these movements to the cardiac pulse and respiration and attempted to measure the CSF pressure in mmH_2O but failed since the dura had to be punctured and the CSF run out freely. Leyden (1866) was the first to obtain valid measurements of CSFP (10-11 cmH_2O) in dogs using straight or U-shaped open-ended manometers. His results were complicated by the fact that the CSF ran into the tube and when he forestalled this occurrence by filling the manometer with saline this was quickly absorbed from the tissue.

Cerebral pulsations were recorded in dogs as poorly detailed tracings by Leyden. Mosso (1881, cited by Purves 1972) estimated changes in volume of the human intracranial contents by watching or feeling the movements of the fibrous membrane covering a skull defect. Roy and Sherrington (1890) using a plethysmograph connected to a membranous drum ("oncometer") and Bayliss et al. (1895) using a metal membrane, recorded brain volume changes in dogs: this was a precursor of the epidural method of ICP recording. Becker (1922, cited by Lundberg 1960) obtained

reasonable curves of ICP fluctuations from the open fontanelle by means of a Marey capsule.

Reliable CSF pressure measurements were only obtained when lumbar puncture was introduced (Quinke 1891) and the normal levels of CSFP were studied (Merritt and Fremont-Smith 1937, Massermann loc. cit.). Combined cisternal and lumbar CSFP measurements were first used by Thurzo and Piroth (1932, cited by Lagergen 1937) for the diagnosis of spinal subarachnoid blocks. The fact that it was now possible to measure the lumbar CSFP stimulated clinical research into the effect upon it of anaesthetics (Taarnhoj 1949) and dehydrating agents, such as urea, (Javid and Settlage 1956); the effects of these were also studied under conditions of artificially altered CSFP (Ecker 1955, Shenkin and Finneson 1958).

The continuous measurement of lumbar CSFP was attempted by Carmichael et al. (1937) who used an optical system to simultaneously record the pulsations of the CSF, arterial, venous and respiratory pressures in man. Lagergen (1937) developed an electromanometer for measuring the cisternal and lumbar CSFP for the diagnosis of spinal blocks. Ryder et al. (1952) studied the relationship between CSF pressure and cerebral blood flow and the influence of abnormally raised ICP on cerebral function. Gilland (1962, 1965) applied a capacitance transducer to the continuous graphic recording of CSFP, mainly for the detection of spinal blocks; he also determined the volume elasticity coefficient curve of the spinal compartment with and without a block (i.e. spinal elastance curve). Magnes (1976, 1976a) measured the lumbar and ventricular CSF and arterial pressures by means of strain gauge transducers while

a patient moved from the lying to the sitting position and found that the pressure waves induced in the CSF by such movements were either "transient" or "stationary waves", the latter resembling the plateau waves of Lundberg (1960)(q.v.). Lumbar CSFP recording has been widely employed during ventriculo-ventricular and ventriculo-lumbar perfusion studies of CSF inflow-outflow relationship (Cutler et al. 1968, Lorenzo et al. 1970, Ekstedt 1977).

Simultaneous recordings of ventricular and lumbar CSF pressure were used by Blackfan et al. (1929) in the differential diagnosis of communicating and non-communicating hydrocephalus in children. Bering (1951) devised an electronic technique for the simultaneous measurement of the VFP, the lumbar CSFP, the jugular and arterial pressures and studied both the mechanism of the change in CSFP which followed an induced change in the volume and the derivation of the CSF pulsations. All of these techniques could be used for only a limited period of time (up to 48-72 hours) and complications such as infection were common.

Guillaume and Janny (1951) pioneered an electromagnetic method with which they made the first reliable recordings of variations in CSFP and correlated these with clinical events. They also showed that recording of the ventricular fluid pressure was not only very informative but was also safe enough to be used clinically.

Lundberg's (1960) monumental work firmly established the place of continuous VFP recording in neurosurgical practice and triggered an enormous amount of fruitful research into intracranial dynamics. His method is the one now universally

used and his analysis of the pressure waves and their relationship to pathological conditions is fundamental to contemporary ICP studies.

Disadvantages of ventricular fluid pressure recording

1) Infection: This is admittedly a potential danger which, however, has been exaggerated because of the considerable infection rates reported during the early development of the technique and indeed are a complication of continuous ventricular fluid drainage alone.

Sundbärg et al. (1972) reported that out of approximately 1000 patients studied by this technique between 1956-68, without prophylactic antibiotics there were 11 cases with definite and 35 with suspected leptomeningitis as judged from CSF cell-counts and regular bacterial cultures. From 1969-71 there was only one case of infection in 283 cases (0.4%); there were no deaths from this cause. Jennett (1973) reported that of his series of 300 patients who had their ICP monitored for 2-5 days, only one developed intracranial infection and he recovered completely. In our department none of the 86 patients studied has become infected.

2) Ventricular catheterisation: In some head injuries complicated by brain swelling and compression of the lateral ventricle it is difficult to cannulate the ventricle; success increases with experience.

3) Blockage of the ventricular catheter: This may be by clot, brain or choroid plexus. It is easily overcome by carefully withdrawing or injecting 0.5 - 1.0 ml of saline.

Advantages of ventricular fluid pressure recording

1) It is the easiest procedure and has the fewest complications.

2) The external transducers (strain gauges) used are much more rigid, reliable and cheaper than those implanted and they may be re-zeroed as often as necessary.

3) One knows exactly what is being measured, i.e. the CSF pressure, whereas with the implantable devices there is room for doubt on this point.

4) The most important advantage of all, however, is that it provides access to the CSF compartment:

a) The withdrawal of a few mls of CSF is the most effective way of reducing an abnormally raised ICP, much more effective than any dehydrating agent. Particularly in cases of acute hydrocephalus and raised ICP resulting from blockage of arachnoid granulations by subarachnoid haemorrhage, traumatic or otherwise, the presence of a ventricular catheter for CSF drainage has been found by most neurosurgeons to be a lifesaving procedure.

b) Intraventricular haemorrhage can, on occasion, be washed out through the catheter.

c) If the need arises for ventriculography the facility is already available.

d) CSF is readily accessible for biochemical examination.

e) Access to the ventricle makes it possible to <u>measure</u> the craniospinal elastance. This is feasible with none of the other known methods and opens up an entirely new dimension in human ICP studies.

MEASUREMENT OF ICP BY SUBDURAL DEVICES (*)

Most of the techniques used for ventricular fluid pressure (VFP) monitoring require ventricular cannulation and fluid continuity of the tubing from the ventricle to the externally sited strain-gauge transducer but this is difficult or impossible if the ventricular system is compressed by a space-occupying lesion, such as haemorrhage, oedema or tumour, or the fluid-filled tubing system is obstructed by tissue or clot.

To overcome these difficulties, Hoppenstein (1965) recorded the ICP and its pulsations by means of a fluid-filled latex tambour which was connected to an external iso-volumetric strain-gauge by a polyethylene tube, the tambour being located in either the subdural or the subarachnoid space. The structure of its walls had an unfortunate damping effect and recordings of as little as 60% of the true values were obtained.

Numoto et al. (1966) used a small, air-filled, manually operated switch device, but this allowed neither graphic nor continuous recording of the ICP.

Hulme and Cooper (1966) described a small pressure transducer which was implanted in the subdural space and claimed that it was reliable for long-term monitoring. There was, however, no clinical evaluation of the method.

Jacobson and Rothballer (1967) presented a miniature strain-gauge connected by wires to an external potentiometer. It offered more stability than the previous subdural devices but was very sensitive to thermal and barometric changes,

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(*) Although these are loosely regarded as located in the subdural space, their accurate placement is, in fact, not possible; in any one case it may be located in the subdural or subarachnoid space.

was not clinically evaluated and was very expensive.

Coe et al. (1967) placed a small transducer in the subdural space and discussed the cause of the higher values which they obtained as compared with those from the ventricle. They attributed them to the superimposition of the "wedge pressure" (to which the transducer's probe was subjected by virtue of its contact with subdural structures) upon the actual VFP. Considerable problems arose during this clinical trial from serious variations of pressure due to temperature and barometric changes, leakage of CSF through the dural incision and lack of calibration in situ.

Eversden (1970) modified a miniature pressure transducer so that it could be calibrated in situ.

Gosch and Kindt (1972) reported a method which was simplicity itself for long-term monitoring of the subdural pressure. He plugged a three-way stopcock firmly into a twist-drill hole of appropriate size in the skull and connected it with tubing to a fluid-filled spinal manometer which was supported at the level of the ventricle. The height of the column was the subdural pressure, which could be graphically recorded by means of a strain gauge. The main problem was damping of the pressure waves and tissue growth in the skull defect.

These criticisms also apply to the variant of this method developed by Vries et al. (1973) in which a hollow screw is inserted into the skull with its tip in the subarachnoid space and its outer end connected to an extracranial pressure transducer. This device, called a "subarachnoid bolt" is now often used in cases of Reye's encephalopathy, in which severe brain swelling

compresses the lateral ventricles (James et al. 1975, Bruce et al. 1977).

Such implanted miniature subdural transducers have certain disadvantages:

i) Base line instability due to changes in temperature and atmospheric pressure: a 20% error can be caused by a temperature change of 1°C (Jacobson and Rothballer 1967).

ii) Alteration of the intracranial dynamics by leakage of CSF through the dural incision.

iii) There is some risk of infection since the dura remains open for long periods.

iv) With the exception of Eversden's none of them can be calibrated in situ.

v) Removal of the transducer requires a second operation.

vi) The pressure recorded has always been found to be higher than the VFP.

vii) In the long term, wires emerging from the scalp are uncomfortable to the patient.

viii) The devices are expensive.

Kindt's and Vries' methods are admirable in their simplicity but in a severe head injury compression of the subdural and subarachnoid spaces makes the recording of the ICP impossible because the fluid continuity they require in the tubing system cannot be achieved.

EPIDURAL MEASUREMENT OF ICP

Measurement of the ICP through an intact dura minimises the risk of infection and alterations of the intracranial dynamics

due to leakage of CSF.

Nornes and Serk-Hanssen (1970) developed a miniature pressure transducer whose sensitive element was a diaphragm. The probe could be implanted in the epidural or subdural space or in a tumour cavity. Variations due to changes in atmospheric pressure were eliminated by venting the submembranous chamber to the atmosphere. Serious disadvantages of the method were lack of in vivo calibration and zero-line drift which was always positive and was attributed to "creep" of the membrane.

Mackay et al. (1960) successfully applied the "coplanar principle"* to the measurement of the intraocular pressure. Scettini et al. (1971) applied it to the monitoring of brain surface pressure. Their transducer measured membrane pressure from the centre of a sensitive area, while the tensile forces which resulted from stretching of the dura were absorbed by the insensitive coplanar periphery. The transducer was claimed to have a better frequency response than a Statham strain gauge and although in vivo calibration was possible it was sensitive to temperature and water vapour. Simultaneous recordings from the epidural space and cisterna magna showed the former pressure to be considerably higher under normal circumstances. This difference was enhanced by hyperventilation.

Dorsch et al. (1971) reported their clinical experience

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*Coplanar principle: When a small area of the wall of any cavity (e.g. a blood vessel, an eye) is flattened by an externally applied force so that the two surfaces are in coplanar approximation, then the pressure within the cavity equals that applied. If we know the contact area and measure the force the absolute intracavital pressure can be derived, since the forces resulting from the elastic properties of the cavity wall are largely absorbed by the insensitive annular surround of the coplanar area (Mackay et al. 1960).

with an epidural device and discussed the methodological factors which might be responsible for the difference between the EDP and VFP.

Gobiet et al. (1972) and Jørgensen and Riishede (1972) confirmed in long-term comparative studies that the epidural was always higher than the VFP. The value of their results was reduced by continuous, significant zero-line drift, the device proved highly sensitive to temperature changes, was impossible to calibrate in vivo, was rather fragile and the covering of the transducer could be torn by the very high pressures which were sometimes attained. Sundbärg and Nornes (1972) demonstrated that although the VFP/EPD ratio was linear under standard conditions, the ratio varied from one patient to another. The EDP was invariably higher than the VFP and the difference increased with rising intracranial pressure.

Coroneos et al. (1972) found a lack of correlation between EDP and VFP in post-operative cases. They also demonstrated that the EDP was 10 mmHg when the VFP was zero and that this difference increased to more than 20 mmHg under disturbed physiological conditions.

Donaghy and Numoto (1972) developed an instrument based on a pressure switch for monitoring the ICP. This was a silastic balloon, implanted in the epidural space and connected through the scalp by a semirigid vinyl tube to an external pressure transducer. It had a poor frequency response but it was claimed to have good stability and to be easily implanted.

Gobiet et al. (1974) refined their original (loc.cit.) technique by adding the facility of in vivo calibration and managed to reduce the EDP/VFP difference to a few mmHg at

levels of VFP up to 50 mmHg; above this level the difference between the EDP and VFP increased.

The monitoring of the ICP from the epidural space has disadvantages as regards both the instrumentation and the site itself:

i) Zero-line instability, which increases with time and differs from one transducer to another.

ii) Sensitivity to temperature, atmospheric pressure and water vapour.

iii) Frequent unavailability of in vivo calibration; this has been remedied in more recent devices. Calibration presents no difficulty between 10 and 80 mmHg but pressures below ... and above these can be a problem (Dorsch et al. loc.cit.).

iv) The measured EDP is always higher than the VFP, by an amount which varies from one patient to another. Differences of 30 mmHg in humans and 20 mmHg in animals have been reported (Coroneos et al. loc.cit.). It seems, therefore, that measurement of the EDP alone is neither accurate nor reliable.

The recent coplanar devices have improved the linearity of the EDP/VFP ratio and although at pressures up to 50 mmHg the difference may be as little as 5 mmHg, at higher levels it still increases considerably (Jørgensen and Riishede loc.cit.). One likely explanation of the difference is imperfect coplanarity due to either the transducer lying at an angle to the dura, unduly firm attachment of the dura or blood pooling between the dura and skull (Dorsch et al. loc.cit.). Whatever the reason(s), the divergence of EDP and VFP at the extremes of the pressure range casts grave doubts on the validity of EDP measurements.

v) The devices are too fragile for routine clinical use.

vi) Long-term implantation leads to local scalp cellulitis.

vii) A second operation is required to remove the transducer.

viii) Long-term monitoring is uncomfortable for the patient because of the wires emerging from the scalp and, to a less extent, the implanted transducer itself.

Measurement of the ICP through the intact dura is highly desirable and this method, which is based upon a very sophisticated principle, has undoubted merits but the validity of the results obtained are still debatable. The major criticism is that the dura is a tough, inelastic membrane which resists transmission of the ICP: what, then, is really being measured from the epidural space?

The term intracranial pressure is rather indiscriminately used to mean the CSF pressure, or the cerebrovascular pressure or the brain tissue pressure. Scettini et al. (loc.cit.) claimed that in fact surface tissue pressure was being measured, because at the site of the transducer the CSF space was collapsed. This does not, however, preclude the existence of some relationship between the epidural and the CSF pressure, since we are still dealing with a closed cavity. The contribution of the cerebrovascular pressure to the recordings is, as yet, unknown.

MEASUREMENT OF BRAIN TISSUE PRESSURE BY "WICK CATHETERS"

Brock and his co-workers (1972) postulated that the brain oedema which follows arterial occlusion could generate gradients in the local brain tissue pressure which would influence its propagation. In furtherance of this argument they measured

the "tissue" or "interstitial fluid" pressure of the brain by the "wick method".

Earlier workers had applied various techniques to the measurement of interstitial fluid pressure. McMaster (1946) inserted a fine needle into the tissue. Guyton (1963) chronically implanted perforated plastic capsules in the subcutaneous tissue and skeletal muscle of dogs. The intracapsular fluid was claimed to be in continuity with the interstitial fluid. At the end of a month he measured the intracapsular pressure through a hypodermic needle and found it to be negative. In oedematous tissue the pressure was always positive. He conceded that his results did not necessarily imply that tissue pressure was negative in such normal tissues as the central nervous system and encapsulated parenchymatous organs. He attributed the negative pressure to the fact that the mean capillary hydrostatic pressure was lower than the plasma colloid osmotic pressure.

Scholander et al. (1968) described a rapid and easy technique for measuring the interstitial fluid pressure of different tissues in various animals; they were concerned with dehydration and oedema and in general confirmed Guyton's observations. They used a polyethylene capillary tube with a cotton-wool wick projecting about 0.5 cm from the central end. The outer end was connected through a glass capillary tube to a manometric recorder. The entire system was filled with 0.9% saline. The end of the wick was sterilised by boiling which also eliminated air bubbles. Satisfactory operation required liquid continuity between the interstitial space and the manometer.

The use of a wick provided both fluid continuity and wide contact with the surrounding tissue, thereby accelerating pressure equilibration. It also prevented blocking of the capillary, which would make the measurement meaningless and gave more accurate and sensitive measurements than a simple capillary tube.

Strømme et al. (1969) elaborated and clinically evaluated Scholander's wick technique.

The wick method is claimed to measure the hydrostatic pressure of the interstitial fluid. Snashall et al. (1971) have shown, however, that the pressure measured cannot be hydrostatic, since the interstitial fluid is minimal, but depends on osmotic forces. They slightly modified the technique for clinical application in patients with disorders of fluid balance by connecting the wick catheter to a semiconductor strain-gauge and used heparinised isotonic saline as the conductive medium. The system had a good amplification response and had no hysteresis, but suffered from zero-line instability (changes in temperature and atmospheric pressure gave considerable drift), had inadequate linearity over the important range of -20 to +20 cmH_2O and was difficult to zero.

Brock et al. (1972) found that under normal conditions there was no significant difference between the brain tissue pressure as measured by a wick catheter and the CSFP as measured by a needle.

Brodersen et al. (1972), using a similar method, argued that a subatmospheric (i.e. negative) pressure in the brain substance was artifactual and was caused by either leakage of fluid, displacement of the catheter after implantation,

inappropriate calibration or various combinations of these.

The contradictions in these findings could be attributed to technical differences and difficulties. It is known that the brain herniates through any defect in dura or skull: this alone would suggest that the brain tissue pressure exceeds atmospheric.

The clinical application of the wick technique presents the problem of unjustifiable tissue damage and has no advantages over other methods for measuring the ICP. It is likely, therefore, to remain an experimental tool, although Brock et al. (1973) have suggested its use in tumour cavities for post-operative monitoring of the ICP.

MEASUREMENT OF THE ICP BY RADIOTELEMETRIC METHODS

Mackay (1968) first suggested the use of radiotelemetric methods for the long-term measurement of ICP.

The development of active pressure endoradiosondes* (Mackay 1960) has made possible various studies of pressure fluctuations in man, e.g. in the gastrointertinal tract (Farrar and Bernstein 1958), urinary bladder (Gleason and Lattimer 1962) and uterus (Hindson et al. 1965). The use of such devices is limited by their relatively large size and the short life of their batteries.

In an attempt to overcome the latter problem, rechargable dry cells of various types have been used, some of which

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* Active pressure telemetering endoradiosondes or active transensors are so-called because their power source is an external battery, most commonly a Mallory mercury cell.

(nickel-cadmium cells) can be recharged in the body by an external oscillator (Olsen et al. 1968). A biological power source has also been used to energise the transmitters.

Collins (1967) described a miniature passive pressure transensor * for the measurement of the intraocular and other physiological pressures. It had two tremendous advantages over the active transmitters: its small size and a theoretically unlimited life, since no internal battery was necessary.

Atkinson et al. (1967) were the first to employ passive telemetric methods in the human for the measurement of the epidural or subdural pressure.

These early passive devices, however, brought their own complications:

i) Unacceptable drift of the zero-line in long-term recording because all sensor diaphragms were of plastic which was semi-permeable and susceptible to "creep" deformation.

ii) Tissue reaction might be excessive and meningeal scarring then damped the input to the transensor diaphragm (Atkinson et al. 1967).

iii) Rupture of a diaphragm exposed copper to tissue fluids and its ionization then caused excessive tissue reaction (Atkinson et al. 1967).

Shulman and Marmarou (1968) sought to minimise the tissue reaction to their passive sensor by making it of noble metals which they coated with paraffin. Glass transensors were also

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*Passive transensor is one which contains no power source, but is energised from an external radiofrequency power source.

developed which were biologically inert and compatible with animal tissue, had good zero stability, a good frequency response and caused no loss of CSF.

Brock and Diefenthäler (1972) added the facility of *in vivo* calibration but even this did not greatly add to the usefulness of the technique.

In summary, passive radiotelemetry offers no advantage for the *short term measurement* of the ICP. On the contrary, it is unreliable and its application to either human or animal studies has presented problems over and above those of the conventional techniques:

i) Short transmission range

ii) Instability of the zero-line due to semipermeability and creep of the diaphragm

iii) Hysteresis

iv) Temperature sensitivity. Air trapped under the diaphragm exerts an additional pressure on it which is proportional to the temperature

v) Sensitivity to barometric changes

vi) Unreliability and the need for repeated *in vivo* calibration

vii) Tissue reaction

viii) Doubtful sensitivity because of the possible damping effect of meningeal scarring

ix) Difficulty in quantification

For *long term monitoring* of the ICP there is an evident need for a method which requires neither wires nor cannulae and causes minimal discomfort. There requirements are met by passive telemetry. Although considerable problems remain to be solved and the method needs refinement, telemetric monitoring of the ICP in chronic hydrocephalus and in glaucoma appears to hold much promise.

THE FUTURE OF INTRACRANIAL PRESSURE MEASUREMENT

It is generally agreed that measurement of the VFP is the most reliable index of the ICP (Beks and Weeme 1967, Miller 1978). It remains the most popular and widely used technique despite subsequent developments. In a recent survey of the use of ICP monitoring techniques it emerged (Saunders 1978) that of the 100 neurosurgeons in 76 centres in the U.S.A. who answered, the methods used were as in Table 3:1.

The subarachnoid screw (so-called bolt) is favoured in children with Reye's syndrome in which due to swelling the ventricles are small and extremely difficult to tap; cortical haemorrhage, however, has been observed as a result of trauma by the device.

As to the future evolution of ICP monitoring devices, Miller (1978) indicated the need for a sturdy, reliable and accurate telemetric device capable of being externally calibrated, but considered that, because of its many advantages the use of the ventricular catheter would undoubtedly continue.

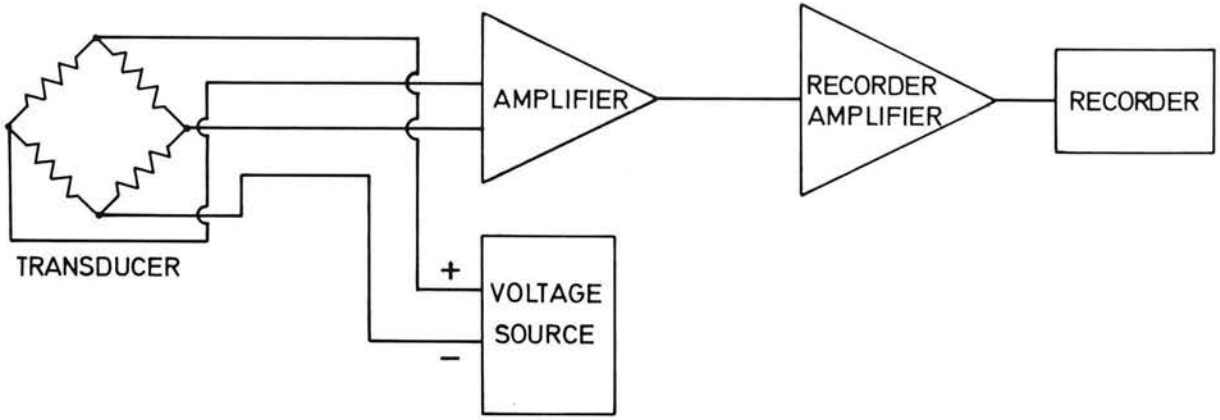
METHODS OF MONITORING INTRACRANIAL PRESSURE IN ANIMALS AND MAN

Any apparatus designed for continuous monitoring of pressure parameters within the body cavities requires three major components (Fig. 3:1):

1) A physiological pressure transducer which may be internal or external.
2) An amplifier with a bridge balance supply.
3) Some form of constant display, such as a cathode ray oscilloscope but preferably a paper chart recorder.

Monitoring Methods	
Ventricular catheter	18
As well as subdural balloon	1
Cranial Screw (subdural or subarachnoid)	8
Ventricular catheter and cranial screw	
Catheter more often	13
Screw more often	8
Both with equal frequency	7
Both in addition to fibreoptic sensor	1
Extradural fibreoptic sensor; Numoto extradural switch	6
Subdural device	4
"Telemetric" experimental device	1
No monitoring techniques utilised	9
Total responses	76

Table 3:1



BLOCK DIAGRAM OF INTRACRANIAL
PRESSURE RECORDING UNIT

Fig. 3:1

MEASUREMENT OF THE ICP BY A MILLAR MICRO-TIP TRANSDUCER

Transducer

Initially we favoured the use of an internal rather than an external transducer for the monitoring of intracranial pressure in our patients. This was a Millar micro-tip catheter pressure transducer (size: 7F, model: PC 470) designed specifically for use in cardioangiography.

Structure: Macroscopic (Fig. 3:2)

The transducer has its sensor mounted at the tip of a woven Dacron catheter (120 cm long, 2.33 outside diameter). The lumen (0.66 mm diameter) opens immediately proximal to the sensor and at the other end is a female Luer fitting. The lumen may be used for cerebrospinal fluid sampling, external pressure monitoring or the injection of drugs or dyes into the ventricle.

Structure: Microscopic - Functional principle

When two silicon wafers are bonded to opposite sites of a thin metal beam and the beam is flexed, the wafer on the convexity is stretched, while that on the concavity is compressed. The electrical resistance of the wafer under compression is decreased and vice versa.

This principle has been combined with a Wheatstone bridge to produce a difference in voltage which is proportional to the deflecting force. To our knowledge, all pressure transducers available for ICP monitoring at the present time, with the exception of Gilland's (Gilland 1965) and Brock's (Brock and Diefenthäler 1972) capacitance transducer*, are composed of

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* The capacitance transducer is part of an oscillating tuned circuit. A change in capacity will cause a change in oscillation frequency. This change is used as a means of registering a change in pressure. At a particular frequency increased capacity would decrease frequency.

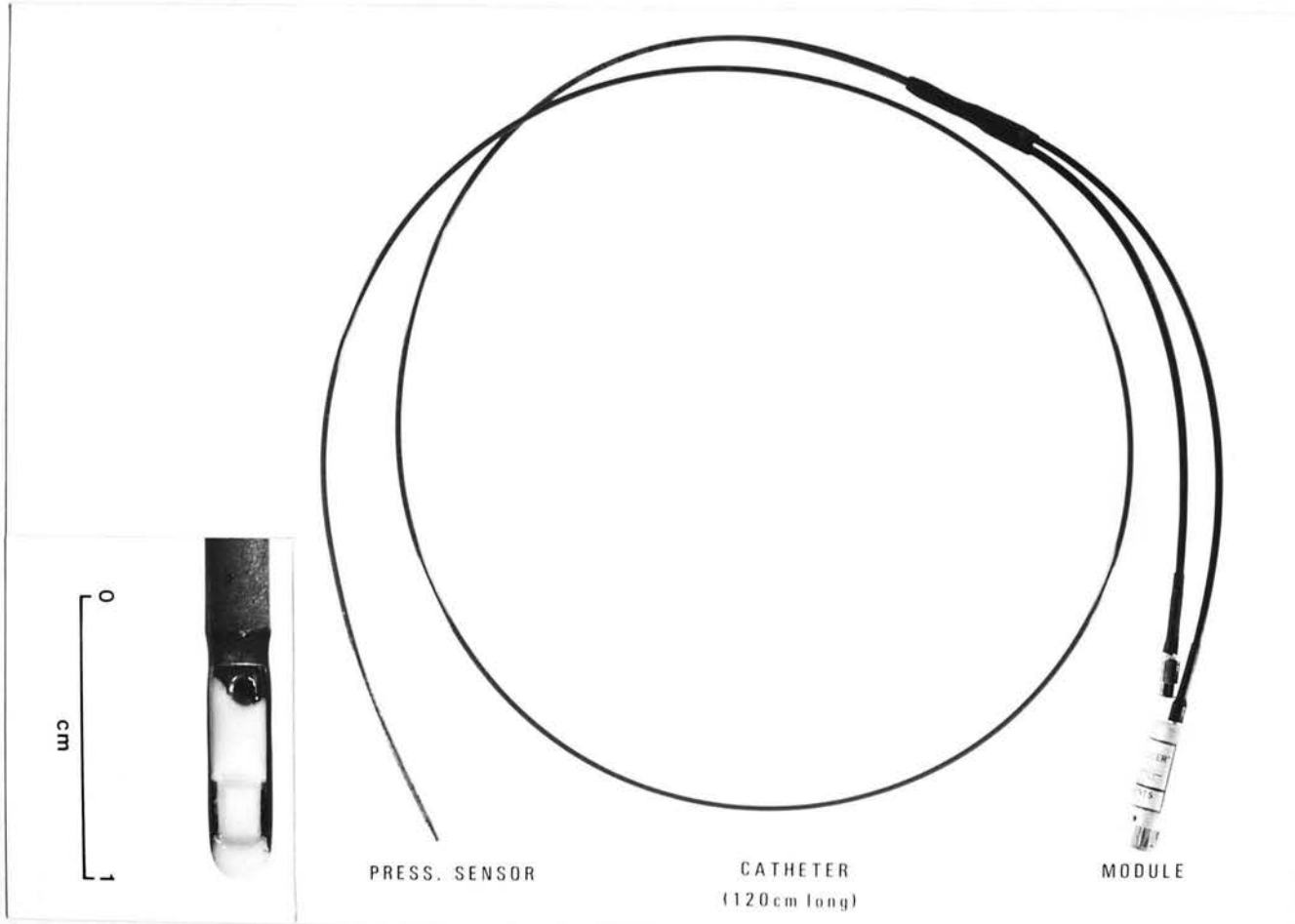


Fig. 3:2

A Millar micro-tip transducer. On the left a magnified view of the pressure sensor.

either a half (two arms) or full (four arms) Wheatstone bridge network of resistors, the change in balance of which is pressure-dependent.

The Millar transducer works on this principle with half of the bridge within the transducer's head (R_3, R_4) and half within the module at the proximal end of the catheter (R_1, R_2) (Fig. 3:3). The wires are embedded in the wall of the catheter.

The manufacturer balances the bridge so that when no pressure is applied to the sensor diaphragm there is no output. Pressure on the diaphragm deforms the silicon semiconductor gauge and changes (dR) the resistance (R_3, R_4).

When an excitation voltage (U_{in}) is applied, a differential output voltage (U_{out}) results:

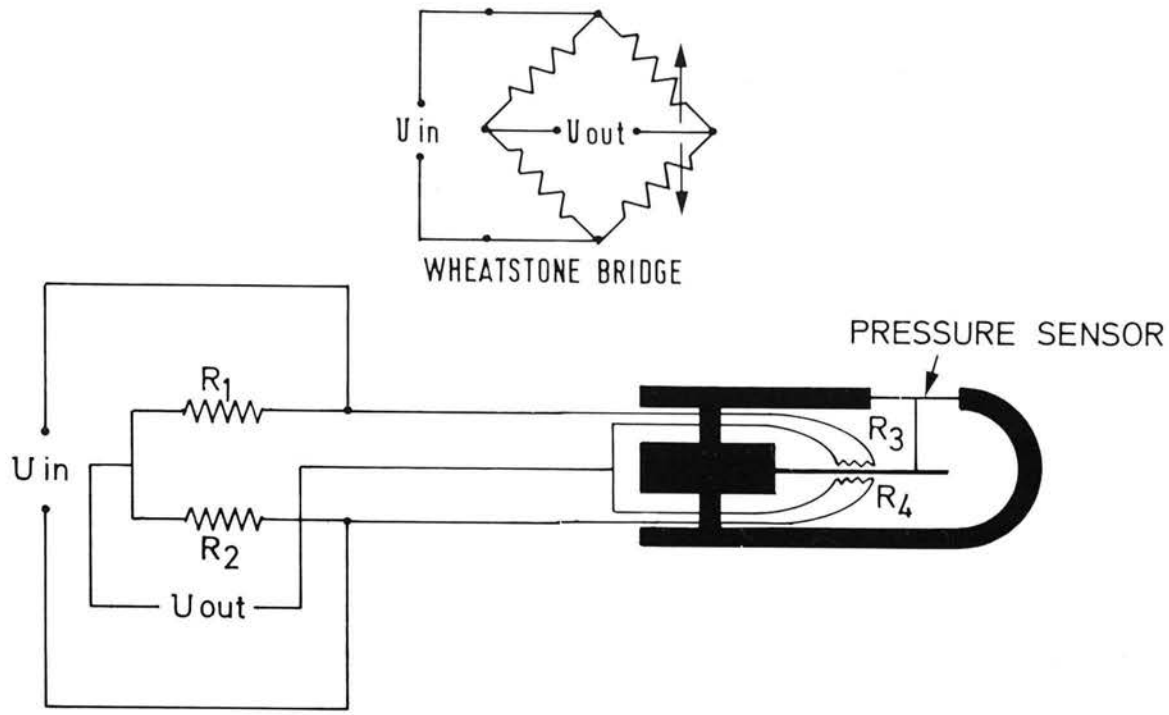
$$U_{out} = U_{in} \frac{d\,R}{d\,R}$$

This change of voltage is proportional to the applied voltage (U_{in}) and to the effective resistance ($= \frac{d\,R}{d\,R}$), which in turn is linearly proportional to the applied pressure.

This change is of the order of only a few millivolts (mV) and therefore requires amplification before it is fed to the recorder. The amplitude of the recording trace can be calibrated to register the pressure on the transducer diaphragm.

The transducer's gauge chamber is vented to atmosphere via a separate lumen in the catheter. Changes of atmospheric pressure, therefore, do not disturb the bridge balance and baseline drift does not occur due to barometric changes alone.

Although the manufacturers recommend up to 10 volts of either DC or AC for excitation, we found that the transducer



BASIC DIAGRAM OF A MILLAR TRANSDUCER

Fig. 3:3

gave the most stable results at 3 volts.

This type of transducer has both advantages and disadvantages as compared with an extracranial device.

Advantages

1) It does not require re-zeroing following changes in the position of the head in space, since the sensor is within the cranial cavity.

2) It does not depend on successful ventricular cannulation, because the transducer gives a perfectly adequate recording when implanted in the substance of the frontal lobe.

3) There is no fluid-filled tube to get kinked or blocked.

4) Its high frequency response gives an excellent pressure waveform.

Disadvantages

1) The device cannot be calibrated in situ.

2) Base line instability due to changes in temperature, especially in long-term recording of the ICP.

In our experience excellent quantitative and qualitative recordings could be obtained for the first twelve hours after implantation of the transducer. After this time the drift from the zero-line was variable and depended mainly on the duration of the recording; over a period of five days there was a drift of about 20 mmHg in one of our patients. Surprisingly, the drift was always in a negative direction. This, we suggest, is evidence that the temperature around the sensor area was elevated; if the temperature is set to zero at 37.5°C and the sensor then plunged into water the zero drift is seen to be positive in cold water and negative in warm. The small

increase in temperature necessary to account for the drift seen could be either in the brain tissue immediately adjacent to the sensor or, more likely, could derive from the resistive elements within the head of the transducer. The morphology of the ICP waveform remained unchanged until the end of the monitoring period.

3) It is EXPENSIVE and EXTREMELY FRAGILE

4) When the micro-tip was in the brain parenchyma, the pressure recorded was always higher than the ventricular fluid pressure as measured simultaneously by an extracranial transducer. The ventricular fluid pressure and brain tissue pressure were simultaneously recorded on three patients, two of whom had developed hydrocephalus following a subarachnoid haemorrhage while the third had suffered a head injury.

We suggest that this was because the weight of brain tissue overlying the sensing area was superimposed upon the true ICP reading; differences of as much as 10 mmHg might occur (Fig. 3:4) but were minimised (less than 3 ± 1 mmHg) when the transducer was implanted perpendicular to the skull surface.

Amplifier

The amplifier (Fenlow Transducer amplifier ZA 2) was designed for use with resistance strain-gauges, composed of either two or four active elements. It provided facilities for bridge balancing, checking zero and setting of calibration (Fig. 3:5).

Recorder

The recorder was one of Bryans Southern Instruments, Ltd., (2800 series) with disposable fibre-tip pens. The built-in

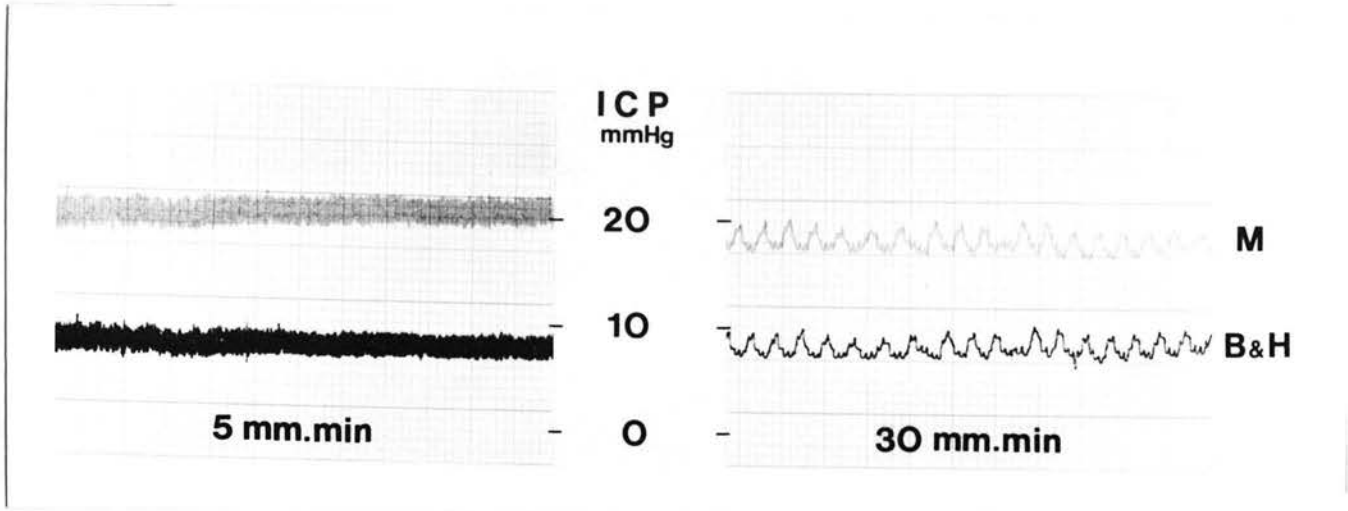
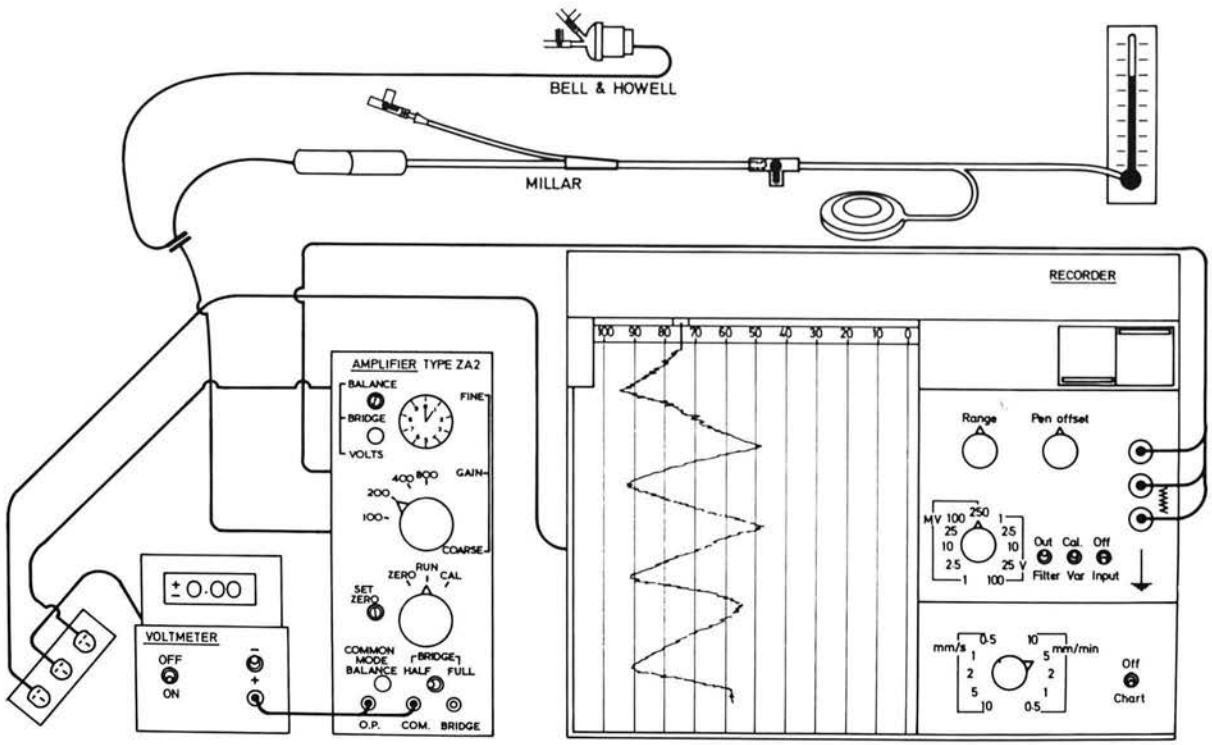


Fig. 3:4

Simultaneous record of the ICP by a Millar transducer (M) and an extracranial one (Bell and Howell : B-H) at two speeds. The difference in the absolute value is approximately 10 mmHg although the ventricular catheter was in the ventricle of the hemisphere in the frontal lobe of which the Millar catheter had been implanted.



ARRANGEMENT OF APPARATUS USED FOR MONITORING OF ICP.

Fig. 3:5

amplifiers of the recorder were bypassed because their range was inadequate.

As a refinement we included a Fenlow digital Voltmeter to give immediate read-out of the intracranial pressure (Fig. 3:5).

Calibration

The layout of the apparatus is seen in Fig. 3:5.

Preparation

1. The transducer module was connected up to the amplifier recorder and voltmeter, switched on and left to warm up and stabilise for an hour during which the zero conductance of the amplifier and the constancy of the voltage supplied to it were checked.

2. The tip of the catheter bearing the transducer was inserted into one channel of a three-way stop-cock, the other of which was connected to a mercury manometer. The proximal (Luer) end of the catheter was fitted with a similar stop-cock so that the intraluminal pressure could be increased by pumping up the manometer.

3. With the mercury manometer reading zero, the voltmeter needle was brought to zero by adjusting the "Balance" screw on the amplifier.

4. The pen of the chart recorder was then brought to its zero position by adjustment of the "Pen Offset" knob on the recorder.

Calibration

When the air or atmospheric zero had been set, the mercury manometer was pumped up to 50-60 mmHg and the pressure held at this level by clamping the exit tube. The recorder pen then indicated the same pressure as the mercury manometer. If it

did not, the pre-amplifier was adjusted by means of a vernier scale knob until the pen did indicate the same pressure reading as the mercury manometer. This procedure might need to be repeated several times.

Paper Chart Speed

A paper chart speed of 2 or 5 mm/min was selected when quantitative measurements of the mean intracranial pressure were to be recorded. When we were interested in clarifying details of the pressure waveforms, i.e. in studying the qualitative characteristics of the tracings, the paper speed was increased to 30 or 60 mm/min (this is 0.5 or 1 mm/sec on the recorder's scale).

Sites of ICP Measurement

The optimal position of the pressure sensor was in a lateral ventricle and preferably the right anterior horn. In very severe brain injuries, however, where the ventricular system was compressed by haemorrhage and swollen brain, this could be difficult to achieve. On these occasions we had to implant the sensor within the right frontal lobe.

Sterilisation

Following calibration the module was disconnected and the catheter assembly was sterilised with Cidex. The catheter was disconnected at its proximal end, gently curved into a wide arc and placed in a metal or plastic tray. The module (Fig. 3:2) was wrapped in a dry gauze swab and was always kept outside the tray, since it has exposed electrical connections. Recently activated glutaraldehyde (Cidex - Arbrook) was poured into the tray until the transducer was covered. A small,

sterile syringe was filled with the glutaraldehyde and connected to the three way stop-cock at the Luer end of the transducer. Glutaraldehyde was then flushed through and left in the lumen. The device was left in the glutaraldehyde solution for 20 minutes, at the end of which time it was assumed to be sterile. The transducer was then rinsed with sterile normal saline and the catheter flushed through two or three times with more saline to remove traces of glutaraldehyde.

Implantation

A standard right frontal burr hole was made and the ventricle tapped with a standard brain cannula. No CSF was aspirated. The depth of the ventricle from the skin was measured. The ventricular cannula was withdrawn and the transducer inserted down the track to the same depth as the cannula, so that its tip was in the ventricle. Its location can be checked by attempting to aspirate but this should be avoided, if at all possible, since it alters the intracranial dynamics. The safest way to ensure that the transducer's tip was in the ventricle was to fill the lumen of the catheter with sterile saline and plug the Luer end with a three-way stop-cock before insertion. After insertion, by slowly opening the stop-cock to the air the first drop(s) of saline will be expelled only when an equal, very small, volume of CSF has entered the catheter. Pre-filling of the catheter with saline thus avoids either significant loss of CSF or disturbance of intracranial pressure dynamics.

To avoid dislodging the catheter from the ventricle, a stitch was put through the scalp and around the catheter, which

was then kept at right angles to the scalp for the first 3 or 4 cm, after which it could be gently curved. The emerging transducer leads were taped to a crepe bandage round the head. The patient was returned to the ward, the module was connected up and recording started.

Removal from the patient

Removal of the Millar transducer was easy - the scalp stitch was cut and the catheter pulled out. A check of calibration and of baseline drift was always carried out just before removal of the catheter. The transducer was carefully washed in running water and left to dry in air.

MEASUREMENT OF THE ICP BY A BELL AND HOWELL TRANSDUCER

During long-term (more than 1-2 days) monitoring sensitivity to changes in temperature and atmospheric pressure are the main sources of error, because changes in the electrical characteristics of the elements of the sensor offset the bridge balance; this presents as a change in the base line pressure. Because of such changes, implantable devices are thought to have the advantage over extracranial ones. In spite of the good thermal stability claimed by the manufacturers, however, we had considerable problems with baseline drift due to temperature changes. This, together with the impossibility of recalibration in vivo of the zero point made quantitative long term studies so unreliable to be meaningless.

In order to improve the situation as regards in vivo calibration, the transducer was used extracranially. That is, the transducer's micro-tip was connected to the extracranial end of a ventricular catheter through a three-way stop-cock

(Fig. 3:6). Recalibration in vivo could then be performed as often as required. This, however, had the unfortunate effect of destabilising the zero line, despite the fact that the patients were isolated in a room of constant temperature. Because of these findings and the fact that the Millar transducer is a very expensive and a very fragile instrument which requires special care in use, it was decided to change over to an extracranial strain-gauge.

This was a Bell and Howell physiological pressure transducer (type 4-422-0001/2, Devices Instrument Ltd.) designed for arterial blood pressure measurements (Fig. 3:7).

The transducer consists of a pressure diaghragm (A) which is mounted in a cylindrical nickel-chrome case, one end of which is closed by a plexiglass dome (D) through which fluid connections are made while the other carries the electrical leads (B). These are covered, for sterilisation purposes, by a captive metal screw-cap (C). The transparent dome is necessary to ensure that no air is trapped against the face of the diaphragm.

Structure

The heart of the transducer is a four-active-arm unbonded strain-gauge element which operates as a Wheatstone bridge. This sensing element is welded to the back of the diaphragm (Fig. 3:8) by a "force-rod". When fluid pressure is applied, the displacement of the diaphragm is transmitted to the spring element, deformation of which then displaces two centrally pivoted posts so that the ends nearest to the diaphragm are brought closer to each other. A change in the resistance of

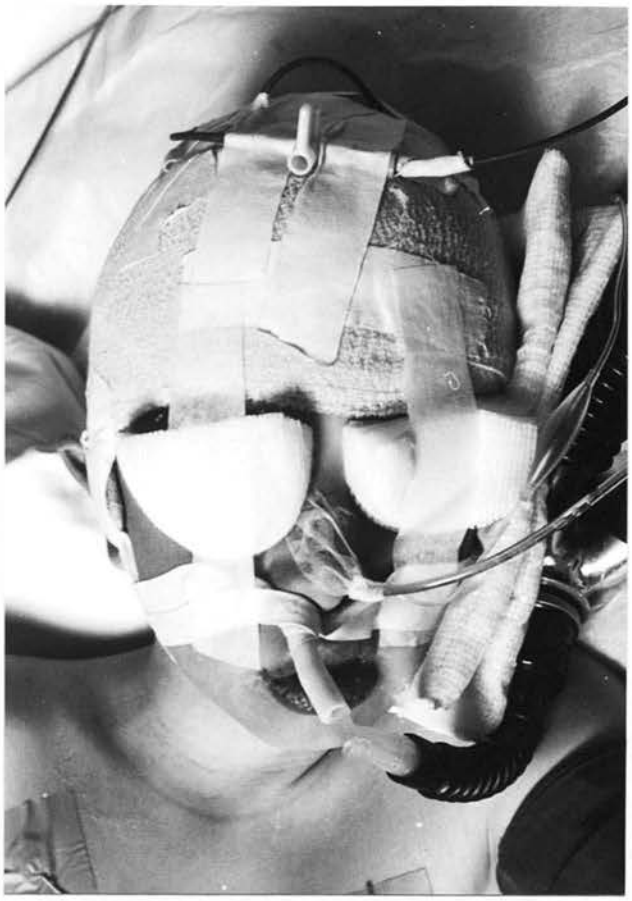


Fig. 3:6

In order to provide the facility of *in vivo* calibration during continuous ICP monitoring, the Millar's micro-tip was connected to the extracranial end of a ventricular catheter through a stop-cock.

Fig. 3:7

A macroscopic view of a Bell and Howell pressure transducer.

(A: pressure diaphragm; B: electrical leads; C: metal screw-cap; D:dome)

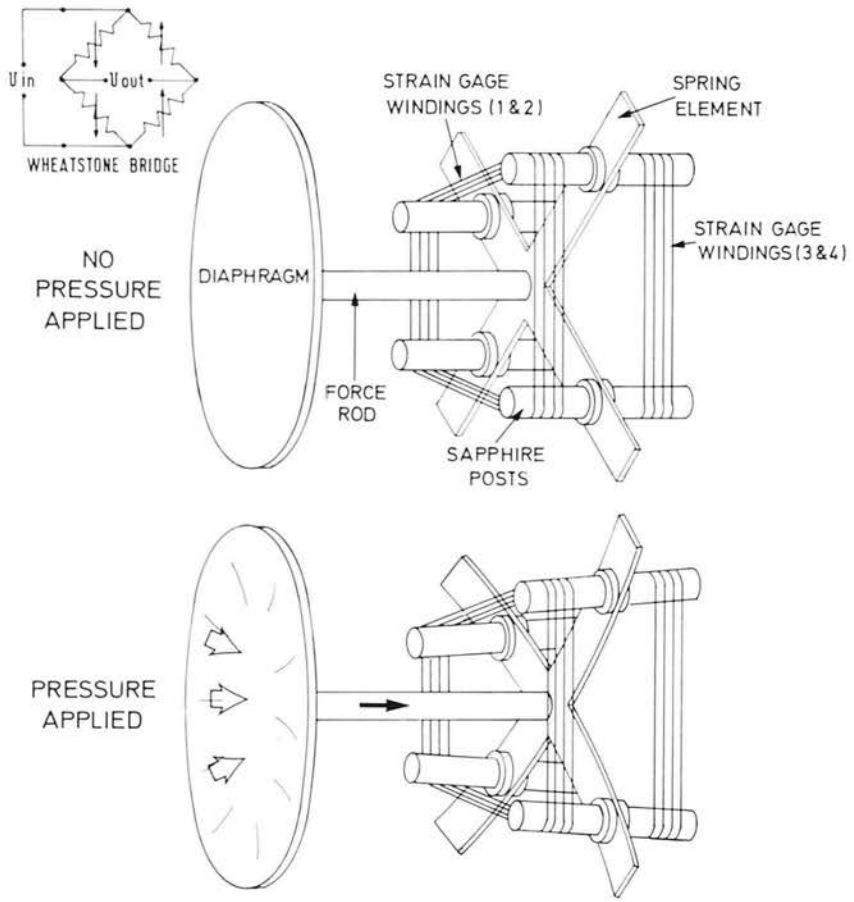


Fig. 3:8

Basic structure of a Bell and Howell pressure transducer

the windings of the Wheatstone bridge is thereby produced. The resulting electrical signal is linearly proportional to the applied pressure and also to the applied excitation voltage (U_{in}) (see Equation 1). The output is amplified and fed to a recorder.

The excitation voltage used was 10 volts.

The amplifier and recorder were those described for use with the Millar transducer.

Site of ICP Measurement

Ventricular cannulation and insertion of a transparent, rigid, polyethylene catheter into the anterior horn of the right lateral ventricle was carried out in the standard manner. This was not always easy, particularly in cases with small ventricles due to compression by haemorrhage and/or swelling of the brain; it proved impossible in two cases.

Because the Millar transducer was out of commission at the time, in these cases an 18 gauge catheter filled with normal saline in the subdural/subarachnoid space was used. A similar method was used by Gosch and Kindt (1972) who plugged a three-way tap through a burrhole into the subarachnoid space and by Vries et al. (1973) whose specially made transducer diaphragm was directly in contact with the CSF of the cerebral subarachnoid space (see Subdural Devices). In the first patient, a boy 6 years old, the CSF and its pulsations could be observed in a 5-7 cm column of fluid in the catheter. After connection with the extracranial transducer, a satisfactory recording was obtained. Unfortunately, this was maintained for only a few hours, because the continuity of the CSF within the tubing was lost and air trapped within it severely damped the

amplitude of the cerebral pulsations and the waveform tracing eventually became an almost straight line. The CSF pulsations and waveform could be restored by injecting saline into the polyethylene tube until the recording became satisfactory, but this had to be repeated so many times that finally we lost confidence in the validity of the measurements. After two days recording, refilling of the tubing no longer improved the VFP tracing and we, therefore, discontinued monitoring. We attributed this late failure to obstruction of the cerebral subarachnoid space by cerebral oedema. In the second patient, a woman 19 years old, with a severe head injury and massive brain swelling it was impossible to record the ICP from the subarachnoid space even after considerable amounts of saline had been injected into the subdural catheter.

Measurement of the subarachnoid CSF pressure in animals using fine (pink Luer) transparent catheters met with very little success. Pulsations were barely distinguishable and the tracing was virtually a straight line. The fact that the catheter was indeed in the subarachnoid space was indicated only by an increase in ICP when the abdomen was compressed. The accurate measurement of cerebral subarachnoid pressure via a catheter seems, for the present, to be impossible.

Method of Measurement

The method used in this study on man is that of Lundberg (1960) as described in his thesis on continuous monitoring of the ICP in neurosurgical practice. The extracranial end of the ventricular catheter is connected via a three-way stop-cock and a rigid, transparent, polyethylene "manometer line"(Portex)

to one of the dome inlets of the transducer. The other inlet is connected to a water manometer fed by an infusion set so that calibration can be checked as often as necessary to compensate for baseline drift. Accurate measurements can only be made if the reference point in the head, the zero level of the manometer and the centre of the transducer are all in the same horizontal plane (Fig. 3:9).

Reference level

Selection of the optimum reference point has been a problem to all investigators who have used this technique. Lundberg concluded that the most practical and valid point would be the frontal cerebral subarachnoid space, which is considered to be located 1.5 - 2.0 cm in from the skin along the track of a ventricular catheter in a standard frontal burrhole. Some workers have used the level of the foramen of Munro.

It is our opinion that the ideal reference point should be located within the ventricular system at the intersection of three mutually perpendicular planes. At this point the zero would be constant irrespective of changes in the position of the head. Guyton and Greganti (1956) attempted to find a physiological reference point for measuring circulatory pressure and positioned dogs until they found axes in all three directions within space that showed no change in CVP with position. Such an ideal reference point, however, even if it could be identified, would then have to be related to surface anatomical landmarks and would of course apply only to normal ventricular systems.

The frontal cerebral subarachnoid space as defined by Lundberg has been used throughout this study.

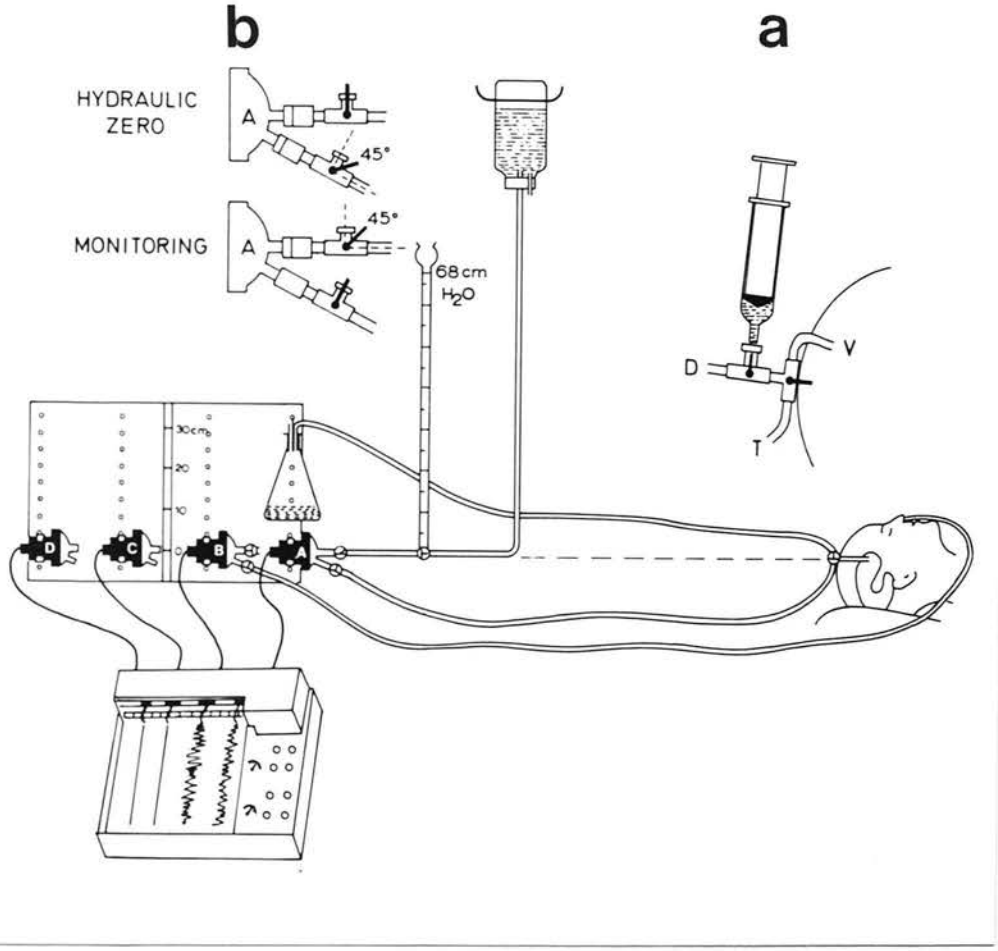


Fig. 3:9

Continuous monitoring of the ventricular fluid pressure (VFP) and the intrathoracic pressure (ITP).

A:transducer measuring VFP
B:transducer measuring ITP
a: arrangement of the recording and drainage tubing system
V: ventricle
D: drainage
b: arrangement of the three-way stop-cocks on the transducer for monitoring, zeroing and calibration.

Fixation of the transducer

The transducer(s) was fixed on a steel plate, which was drilled with four parallel, vertical rows of holes at 1 cm intervals. A 30 cm ruler was attached at the centre of the plate which was vertically movable on a stand bar. Special clamps were screwed through the holes of the plate to hold the transducer(s) and a flask for intermittent CSF drainage at any desired level.

Prophylaxis against infection

Prophylactic administration of antibiotics during VFP monitoring has been used routinely by Lundberg, while other investigators (Sundbärg et al. 1972, Pia 1977) have considered it unnecessary.

In this Department Ampicillin and Sulphadimidine are administered only in cases with compound skull fractures and CSF rhinorrhoea or otorrhoea. CSF samples both from the ventricles and the drainage bottle were cultured once a week and showed no growth of pathogenic micro-organisms. Particular attention was paid to the sterilisation and assembly of the monitoring system under sterile conditions. The non-engaged outlets of the system were plugged with sterile stoppers which were changed daily to prevent secondary contamination by pathogenic or saprophytic micro-organisms.

MEASUREMENT OF CEREBRAL ELASTANCE

The pressure/volume (P/V) ratio of the cerebrospinal fluid, expressed as Elastance (E : mmHg/ml), was calculated at intervals throughout the period of study, by rapidly injecting 1.0 ml

of sterile normal saline or removing 1.0 ml of CSF and recording the subsequent pressure changes on a scale which was sensitive enough to accurately record minimal changes. This was repeated every 10 minutes for 20-50 minutes, the interval being sufficient for stabilisation of the resting level (Miller et al. 1973, Löfgren et al. 1973). The rate of injection or withdrawal was rapid in order to eliminate possible errors due to alteration in the rate of resprption of CSF.

CHAPTER 4

MUSCLE TONE

DEFINITION OF MUSCLE TONE

To formulate a simple definition of muscle tone is difficult because of the several meanings of the word "tone".

Müller (1838, cited by Pollock 1928) appears to have been the first to employ the word "tonus", as meaning the slight contractile tension characteristic of normal skeletal muscle at rest.

Much of what is known about muscle tone derives from the studies of Sherrington and his associates on decerebrate rigidity. Their physiological analysis of postural reactions in vertebrates showed that two major reflex systems are involved in the innervation of skeletal muscle.

One maintains and regulates constant tone, and is the basis of posture ("postural tone"). This tone can be varied to produce changes in posture, by proprioceptive stimuli from the labyrinth and from the muscles themselves, especially those of the neck - the "righting" and "standing" reflexes of Magnus and DeKleijn (cited by Magnus 1925), the centres for which are located within the midbrain and medulla. Liddell and Sherrington (1924) showed that the muscle proprioceptors are stimulated by stretching - the "stretch" reflex. The second reflex system results in short-lived phasic movements and its arc is largely spinal.

The possibility that extraneural factors may be responsible for the maintenance of tone was raised by Pollock (1928). He argued that tension, contractility, elasticity, extensibility, resilience, plasticity, hardness and many other properties of muscles have at times been used synonymously with tone.

What relationship these several properties really bear to tone is unknown; as he put it "none are tone, and all may be part of it".

"Tone" as used by physiologists is a complex concept and frequently appears to bear little relationship to a clinician's use of the word.

The "stretch reflex" is that with which the clinician is concerned and which he calls tone, but his methods of detecting its activity and of determining its departures from normal differ greatly from these employed in the laboratory; he estimates the degree of tension in the muscles by manipulation of the limbs and calls this "tone". It is the active, elastic tension he feels when he passively stretches a muscle.

METHODS PREVIOUSLY USED FOR THE MEASUREMENT OF MUSCLE TONE

The quantitative measurement of muscle tone has long posed problems for clinician and experimentalist alike. None of the numerous and often ingenious traditional methods is entirely satisfactory and to this we may attribute the deficiencies in our knowledge of the harmonious functional relationships of the nervous and skeletal systems.

STATIC METHODS

The earlier methods were "static", the muscle tone being measured on the immobile limbs of living subjects or cadavers.

It is known that there is a relationship between the concomitant neuromuscular activity of an individual and both the

threshold and amplitude of his reflexes. It was Jendrassik's observation on the potentiation of the knee-jerk by clasping the hands which led Lombard (1887) to investigate the external (environmental) factors affecting the reflex and to attempt to measure muscle tension by a study of tendon reflexes and response to electric shock. Courtis (1939) found a close relationship between the pressure exerted on a hand dynamometer and the amplitude of the knee jerk, the "height" of which was used as indirect measure of muscle tension. These parameters, however, varied too widely to be useful.

Braune and Fischer (1889) and Fick (1904) (both cited by McKinley and Berkwitz 1928) studied the forces developed in the elbow in six cadavers selected as being of similar build and musculature. Their data were scanty and insufficient for statistical treatment.

Spiegel (1923) measured the tension in the quadriceps femoris after balancing the leg at different angles with weights and pulleys. This method was open to the criticism that the weight of the extremity distal to the joint had to be counter-balanced.

Jacobson and Carlson (1925) attempted to measure the "height" of the knee jerk which was "reproducibly"elicited by means of a spring-hammer while the subject lay with the knee flexed to an angle of about 70^{o}.

DYNAMIC METHODS

It had been realised, meanwhile, that a limb was a dynamic system and that, therefore, reliable and accurate measurements of its tone could be made only if it were permitted to move

freely. Some of the dynamic methods of measuring muscle tone have reached extraordinary levels of complexity.

Carmichael and Green (1928) graphically recorded the time required for a voluntarily relaxed forearm to fall through an angle of 80^{o} under the influence of gravity; this was an index of the tone of both the biceps and triceps muscles.

Doshay (1938) described a method for determining the "graphic rigidity index" in patients with Parkinsonism. This was essentially a matter of calculating the frequency with which groups of muscles could be voluntarily contracted and relaxed and the rate at which the movement tired. The apparatus was not described.

Smith et al. (1930) applied a similar method to the lower leg which was allowed to fall through 90^{o} of flexion from full extension. The displacement curve which recorded the rate of fall was analysed mathematically to obtain numerical values for muscle tone. This method, however, like the similar static one of Spiegel, necessitates estimation of the weight, the location of the centre of gravity and the moment of inertia of the part; to do this, they employed the data of Braune and Fischer (loc. cit.), compounding the inadequacies of these by using subjects of varying build.

A similar method was described by Grimmer and Langworthy (1941). This was a system of pulleys which recorded on a kymograph the efforts of a Parkinsonian patient to lift a weight vertically by contraction of the muscles at the elbow or wrist. The method was admittedly unsatisfactory, being insensitive to fast movements because of the rebound inherent in the apparatus and consequently it was difficult to demonstrate

slight rigidity.

Timberlake (1964) described a "gravity driven ergograph" for recording the movement at a joint to which a force was applied. It was used in the horizontal plane to eliminate the effect of gravity. Varying weights descending under the influence of gravity supplied a steady, reproducible acceleration which moved the limb and stretched the muscle. The amount of movement in response to the force applied reflected the degree of rigidity.

Erdman and Heather (1964) developed an apparatus which involved two parts: a device to deliver a near-uniform stimulus and a force recorder. The deflection of a beam of light reflected from the sole of the foot to a calibrated ground glass screen was directly proportional to the force supplied by a spring-loaded hammer which could be adjusted to deliver a reproducible force to the Achilles tendon.

The dynamic methods used for the measurement of muscle tone have evolved along two main lines:

a) The measurement of resistance of a passively moved limb combined with EMG recording from the muscle tested and

b) The EMG alone, simple or integrated.

The following methods are all clinically applicable, are based on the definition of tone as resistance to passive stretching and all employ the principle of torque measurement.

Measurement of torque

Filimonoff (1925) described an apparatus to record the resistance to passive movement which was dependent on a patient's ability to produce by hand a constant pull against a recording

tambour. No quantitative analysis was attempted.

Kuznetsov (1925) applied known forces to the patella so that he could measure changes in the resistance to stretch of the quadriceps muscle, paying particular attention to the shortening and lengthening reactions under the pull of a constant weight. The method, however, was applicable to only this particular muscle.

McKinley and Berwitz (1928) used weights to pull a rest to which the forearm was fixed. They defined muscle tone as the torque of the limb and measured it in terms of the angle through which the limb moved before it came to rest. The great advantage of the method was that all calculations were avoided. The validity of their definition of muscle tone is, however, questionable.

Schaltenbrand (1929) used isometric dynamometers to measure muscle resistance to stretch.

La Joie and Gersten (1952) determined the resistance of the spastic arm to extension by measuring the least force required to extend the elbow 1.5^{o}(sic) from an angle of 145^{o} while the EMG activity was recorded. The method could be applied only to cases in which spasticity was already known to exist.

Agate et al. (1956) used a combination of pulleys and strain-gauges to measure the torque of the elbow during extension and tremor.

Wright and Johns (1960) studied those physical properties of a joint (compliance, inertia etc.) which contribute to its stiffness under normal and pathological conditions. A heavy pendulum rotated an index finger through 30^{o} of flexion; at

midposition of the finger the pendulum was at rest. The torque required to impose this motion was recorded from strain-gauges bonded to the lever to which the finger was attached. The amplitude of the swing and the rotational velocity were measured by a potentiometer and a velocity transducer.

In Brumlic and Boshes' (1961) method, the torque developed by a human arm was transmitted to a "tonometer", which consisted of 4 strain-gauges arranged in the form of a Wheatstone bridge. The measurement of tone was the mean of 4 torque readings from each upper limb, taken during repeated extension and flexion of the elbow.

Long et al. (1964) measured the resistance offered by the middle finger to being driven externally by a servo motor running at a constant speed; they thus determined the rheologic properties of muscle (elasticity, viscosity, plasticity) and used these as a measure of muscle tone. The finger was used because it was expected to be less subject to postural contractions than the lower extremity segments. Provision was made for EMG recording.

Leavitt and Beasley (1964) recorded mechanical and electrical muscle variables on a multi-channel system. These were the resistive forces developed in extensor and flexor muscles by passive stretching, tensive forces developed by deep muscle myotatic reflexes elicited by tapping the tendon and the angle of swing in unrestricted active responses of the same type. EMG activity was recorded concurrently with the muscular resistive forces and the angle of motion. The application of the method and results from a single spastic patient were recorded.

Webster (1964, 1966) devised an extremely complicated system of pulleys, a turntable, V-belts and strain-gauges in order to measure the torque, angular velocity, rate of tremor and work output in response to velocity input in normal and in spastic (1964) and in rigid (1966) patients. The limb was passively moved through 100° at varying angular velocities. At high velocities spasms developed which opposed the motion. These muscular reactions, measured as torques, were plotted against displacement and were characteristic for normal, spastic and rigid limbs. This complex plot was simplified by integrating the torque amplitude throughout the range of angular displacement. This torque integral was then a measure of the net work done by the patient's limb in response to the applied passive motion.

Nashold (1966) measured the torque exerted by the rigid biceps or triceps. An attached potentiometer detected the angle of movement of the forearm. The forearm was rotated in the horizontal plane, with the shoulder abducted 15° below the horizontal to eliminate rotation of the humerus. The instrument suffered from inertia and from acceleration of the moving limb.

Martinez (1966), with a strain-gauge "myokinetograph" measured the angular movement of the forearm, which was displaced from extension to flexion and vice versa between $1\text{-}90^{\circ}$ in the horizontal plane. A high angular speed as shown by an increased speed of deflection of the tracing, meant an increase in muscular rigidity and vice versa.

Joyner and Finley (1975) recorded the force exerted by the gastrocnemius muscle. The subject's foot was placed on a

platform supported on two strain-gauges. When he pressed against the plate, the signal was displayed on a polygraph simultaneously with the rectified EMG signal.

Measurement of electromyographic activity

The EMG has been widely used and remains the prime tool for the investigation of human neuromuscular disease. It has been indispensible for the measurement of muscle tone in animals. None of the methods which measure the resistance to displacement by a known force could be applied to a conscious animal; if fully conscious the animal would inevitably struggle and anaesthetics or relaxants would be necessary, the administration of which would abolish the parameter under test.

Hoefer and Putman (1940) studied the action potentials arising from the muscles of subjects with motor disorders. Direct ipsi- and contralateral responses to proprioceptive stimulation and spontaneous activity in patients with spasticity and clonus were studied.

A number of patients with Parkinsonian rigidity and one case of decerebrate rigidity and tremor were studied by EMG tracings from the extensor and flexor muscles of the arms and legs. The effect of curare and scopolamine on tremor, clonus and voluntary power was investigated in a few of these patients (Hoefer and Putman 1940a).

Records from normal subjects made under comparable conditions were used as controls (Hoefer and Putman 1939).

Feldman and Sahrmann (1971) did an EMG analysis of postural reflex phenomena on two decerebrate patients and a few normal controls. In both groups stereotyped extensor

posturing occurred, especially of the upper limbs; this posturing in response to proprioceptive stimuli was transient, inconstant and more obvious in the decerebrate patients.

Tursky (1964), because of the great difficulty he found in quantifying gross muscle spasm from the raw clinical EMG record, revolutionised its evaluation by the application of a number of integration procedures. Such techniques had first been used by psychologists primarily interested in correlating muscle tension with psychological and behavioural variables (David 1942).

Levine et al. (1964) developed a method for remote monitoring of the EMG and integration of raw EMG data into graphic form. Telephone telemetry (so called "telemedography"), for recording EMG, ECG and EEG data from immobile patients in their homes, was also described.

SPECIAL METHODS

Tonic vibration reflex (TVR)

This is a tonic contraction evoked by muscle vibration. Hagbarth and Eklund (1968) showed that, whereas in normal man this stimulus evokes a slowly increasing tonic contraction, in the spastic limb and the decerebrate cat a rapid contraction occurs. They also reported that in the upper limb of a spastic patient the TVR increased as the vibrated muscle was stretched.

Ashby and Burke (1971) confirmed this finding, and showed that the behaviour of the TVR parallelled that of the stretch reflex. Burke et al. (1972) showed significant differences between the TVR of spastic patients on the one hand and that of normal and Parkinsonian patients on the other. In the former

the TVR rapidly developed to its peak level within 2-4 seconds whereas in the latter the peak level was reached only after 20-60 seconds.

H-Reflex

A single electrical shock to a peripheral motor nerve evokes two distinct muscle potentials; the first (M) results from direct stimulation of motor nerve fibres and the second (H) is the expression of a monosynaptic reflex, both the afferent and efferent pathways of which are located within the same muscle (Magladery et al. 1951). As no internuncial neuron is involved the amplitude of H provides a measure of spinal motorneuron excitability (Granit 1950).

Since the monosynaptic stretch reflex is exaggerated in spastic muscles, the H reflex might be expected to provide useful data for its measurement. Magladery et al. (1952) tried, therefore, to evaluate the H reflex as an index of spasticity. They showed distinct differences in recovery of excitability after activation and in some patients with spinal cord or lower brain stem lesions they elicited H reflexes in certain muscle groups which were never detectable in normal subjects. These differences, however, were inconstant and it became evident that the threshold of the H reflex was not a reliable measure of spasticity; the same was shown to hold for the magnitude of the reflex, which was affected by such factors as electrode placement and skin thickness.

In an attempt to obtain more information Angel and Hoffman (1963) plotted the stimulus/response curve and from this calculated the H/M ratio. There were slight differences between the threshold values of spastic and normal limbs,

the H/M ratio being much higher in the spastic than in the unaffected limb. The ratio varied so greatly, however, that it could not alone be used to diagnose spasticity. Many of their recordings had to be discarded for technical reasons and they could not compare the results for their normal and spastic groups in respect of each of the various experimental manoeuvres.

All of these techniques are, in theory, clinically applicable. Their evolution, however, has been at the hands of the physiologist and the parameters they measure are not those apparent to the clinician nor, indeed, do they relate to anything of which the patient complains. Their place is in the laboratory, for the present at least, and it does not seem likely that they could easily be translated to the bedside.

SPECIAL TECHNIQUES FOR CLINICAL ASSESSMENT OF MUSCLE TONE

Special manipulations and techniques have been used for the clinical assessment of muscle tone.

Wartenberg (1951) demonstrated a number of manoeuvres in Parkinsonian patients: passive to-and-fro swinging of the shoulders, knee swinging and the head drop test or neck swing ("Wartenberg's tests"). Their systematic study by Schwab (1964), however, showed that not only do they require considerable co-operation and understanding on the part of the patient, but also the examiner must be thoroughly familiar with the "feel" of the normal joint. For these reasons they were difficult to quantify. The great merit of the subjective, clinical assessment of rigidity, in Parkinsonism in particular, is that it can distinguish between spasticity and rigidity, something of which no electronic or mechanical device is capable.

METHODS OF MEASURING MUSCLE TONE IN ANIMALS AND MAN

MEASUREMENT OF MUSCLE TONE IN ANIMALS

Muscle tone in animals was measured from the amplitude and frequency of the electromyographic activity as recorded by an Officine Galileo Electroencephalogram (Model E 8a) using 16 monopolar steel needles (orange Luer - G 24) implanted in the biceps and triceps muscles of the forelegs and in the gastrocnemius and tibialis anterior muscles of the hindlegs. Before insertion of the needles the skin was shaved to make identification of the muscles easier. The electrodes were so wired that the four pairs on each side of the body recorded simultaneously and the opposite set could be displayed by the operation of a single switch. The animal lay face down on a flat base with the head fixed in the Narishige frame (q.v.) and the legs hanging free.

MEASUREMENT OF MUSCLE TONE IN MAN

The application of an appropriate force for the study of muscle tone has been the major problem, and those techniques which have involved the use of weights and springs have proved to be relatively cumbersome and restricting. The availability of a printed circuit motor has allowed the development of a powerful and versatile instrument with very important properties.

The printed motor's armature is a formation of many flat copper wires connected together in a pancake configuration and embedded in heat resistant plastic to form a disc (Evans 1972). Brushes which deliver the supply power to the motor press against one side of the disc and run on the flat surface of the

protruding copper wires thereby acting as a commutator for the system (Fig. 4:1). The inductance of the armature is trivial because there is no iron in its circuitry and this allows the rapid generation of forces. The armature has low inertia and so minimally affects the mechanical properties of the limb. The arrangement of the copper wires allows the printed motor to run smoothly at all speeds, thus eliminating cogging effects. The torque generated by the motor is directly proportional to the current applied to it by a transistorised power amplifier.

Since precise control of the force generated is required, a feedback loop was used so that errors in the force were compensated automatically by adjusting the current supplied to the motor. Sine, square or triangular waves can be supplied by an appropriate waveform generator; a variety of torque patterns can thus be provided.

A conductive plastic potentiometer was coupled to one end of the motor spindle while the other end was coupled to the limb under examination by a metal splint; the limb was strapped firmly to avoid losses of motion. The motion of the joint was in the horizontal plane. The hand was attached to the spindle so that the wrist joint and the printed motor were co-axial (Fig. 4:2). The potentiometer recorded the angular position of the limb and the velocity was registered by means of an operational amplifier.

Surface electromyographic recordings were made using suction-cup rubber electrodes filled with jelly and attached over the flexor and extensor muscles of the forearm, two over each

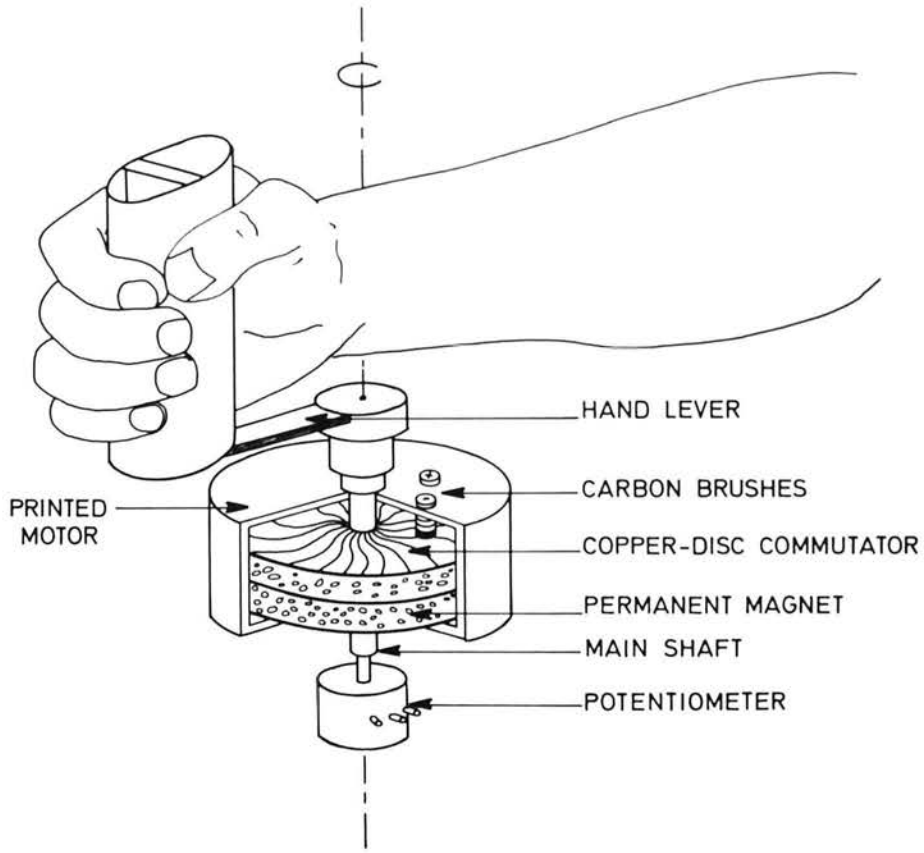


Fig. 4:1

A schemiatic cut-away view of a torque generator and arrangement for testing muscle tone of the right wrist.

Fig. 4:2

Arrangements for testing muscle tone of left wrist of a patient with decerebrate rigidity. Patient is lying supine and slightly turned to the left. Wrist is firmly bandaged to a splint and attached co-axially with the torque generator. Motion is in the horizontal plane. EMG electrodes are placed over the flexor and extensor muscles of the forearm.

muscle group, 50 mm apart.

The torque, position, velocity and EMG data were all graphically displayed by means of a Mingograph ink-jet recorder. The method has been described in more detail by Walsh (1974) under the name of torque-induced motion analysis.

CHAPTER 5

OTHER METHODS

INTRATHORACIC PRESSURE

STEREOTACTIC METHOD

INTRODUCTION

The oesophageal pressure (OP) being widely accepted as reflecting the mean intrapleural pressure its measurement is a convenient technique for the study of pulmonary dynamics, i.e. the volume/pressure relationship (compliance) of the lungs and the thoracic cage.

FACTORS AFFECTING ITS MEASUREMENT

The work of Petit and Milic-Emili (1958), Ferris et al. (1959), Knowles et al. (1959) and Milic-Emili et al. (1964, 1964a) showed that the OP in normal volunteers was affected by:

a) the body posture

b) the location of the oesophageal balloon

c) the physical characteristics of the balloon.

BODY POSTURE

In each subject the OP was highest in the supine position and lowest in the upright position and lower in the lateral than in the prone position. OPs in the lateral and prone positions were similar to those in the upright position. This has been attributed to the pressure exerted on the oesophagus by other mediastinal structures. In the supine position the oesophagus is compressed by the weight of the heart and great vessels; as the subject changed to the lateral, prone or upright position gravity would force these structures to fall away and minimise their effect on the OP.

LOCATION OF THE OESOPHAGEAL BALLOON

Upper third of the oesophagus

Changes in mouth pressure, head posture and external pressure on the trachea produced alterations in OP which were unrelated to changes in intrapleural pressure and were attributed to traction on, or compression of, the oesophagus by the trachea. These artifacts were absent in the lower two-thirds of the oesophagus.

Lower third of the oesophagus

OPs were found to vary greatly and were markedly affected by the body posture.

Middle third of the oesophagus

OPs were relatively uniform, were unaffected by body posture and were considered to closely reflect local pleural pressures, identifying this as the most appropriate level for the measurement of OP.

PHYSICAL CHARACTERISTICS OF THE OESOPHAGEAL BALLOON

Circumference

Petit and Milic-Emili (1958) and Milic-Emili et al. (1964) showed a direct relationship between this and the difference between the true OP and the pressure as measured by an oesophageal balloon. The error was least when the circumference was between 2.5 - 3.5 cm and ranged from 1 - 24%.

Length

The same workers demonstrated that the error introduced by identifying OP with intrathoracic pressure (ITP) was greater

the shorter the balloon used (usually 3.0 - 5.0 cm). Because of the variation in the OP along the length of the oesophagus, if the balloon is longer than 15 - 20 cm it extends into the upper third of the oesophagus where the OP is less and therefore false pressures may be recorded. Accordingly a short balloon, i.e. 10 - 12 cm, was considered to be the most suitable for the measurement of OP.

Volume

Measurements made with balloons of large volume gave falsely high values. With lungs of average volume this difference was relatively small, whereas, at the extremes of vital capacity a large balloon volume might introduce significant distortions, appreciably more positive than the pressures obtained by extrapolation to zero balloon volume. A close approximation to the extrapolated pressure was obtained with a balloon containing 0.2 ml of air (Milic-Emili et al. 1964).

MEASUREMENT OF THE INTRATHORACIC PRESSURE IN MAN

All patients used in the study were paralysed with pancuronium bromide to permit intermittent positive pressure ventilation (IPPV); none of them had any apparent major chest injury or disease.

A rubber balloon, (a so-called "oesophageal catheter" Morgan Ltd, Kent) 10 cm in length and 3.5 cm in circumference attached to a polyethylene catheter 100 cm in length and 1 mm internal diameter was used (Fig. 5:1). With the patient supine the balloon was passed through a naso-pharyngeal catheter (No. 5 Portex) into the oesophagus until the tip entered the

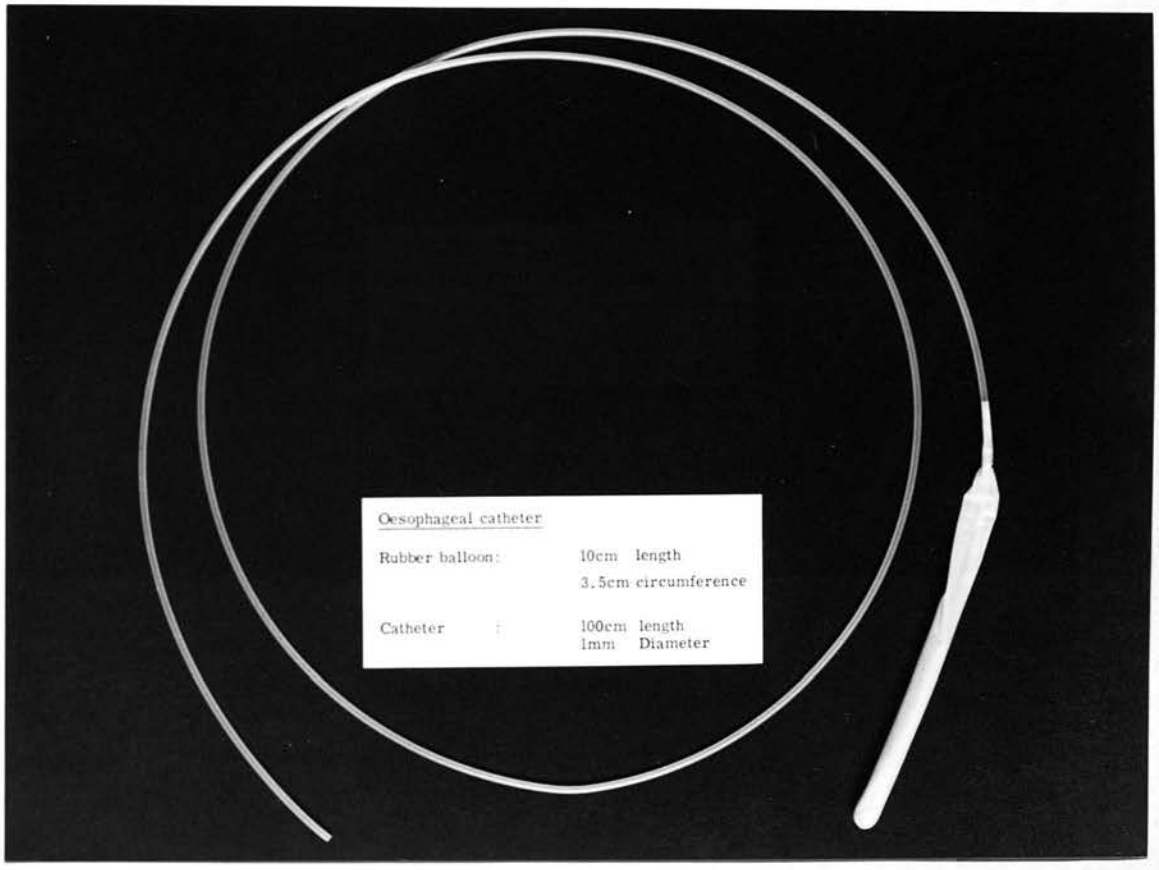


Fig. 5:1

An oesophageal catheter

stomach at 50 cm from the nostril. The nasopharyngeal tube was removed and a three-way stop-cock, connected to the proximal end of the catheter. A Bell and Howell pressure transducer (type 4-422-0001/2) was connected up to one inlet and 0.2 ml of air was injected into the catheter which was then slowly withdrawn and with each 5 cm advance up the oesophagus the pressure was read off. The lowest pressure reading was taken as the location at which there would be least distortion due to oesophageal tone and the balloon secured at this level by taping the proximal end of the catheter to the nose. The transducer was at the level of the sternum but this was really immaterial since air does not create hydrostatic problems (Fig. 3:9).

MEASUREMENT OF THE INTRATHORACIC AND INTRA-ABDOMINAL PRESSURES IN CATS

A catheter with a balloon length of 3-5 cm was used in the cats (Petit and Milic-Emili 1958). The catheter was passed through the mouth into the oesophagus using a laryngoscope and local suction to identify the oesophageal opening. The cardiac end of the oesophagus lies at approximately 18 cm from the incisor teeth (Crouch and Lackey 1969). For the OP the procedure was as in man and for the measurement of the intra-abdominal pressure the tip was advanced to approximately 23-25 cm from the incisor teeth.

STEREOTACTIC METHOD

APPLICATION OF STEREOTACTIC CO-ORDINATES

The position of a point in space is known if its perpendicular distance from each of three mutually perpendicular planes is known.

To apply this principle one plane must first be established; the other two planes more or less automatically follow. In the Narishige frame (Figs. 5:2, 5:3, 5:4 & 5:5) the base plane passes through the long axis of the ear bars and the palatal bar; and therefore lies parallel to the horizontal bed of the frame. A second, coronal plane also passes through the long axis of the ear bars, at right angles to the bed and is itself intersected by a third vertical plane which passes through a point midway between the tips of the ear bars and through the axis of the post of the palatal bar. Any point in the animal brain may thus be designated by reference to its distance in millimetres above or below the horizontal plane, anterior or posterior to the coronal (interaural) plane (which is also the intercollicular plane) and to right or left of the midline. The horizontal reference plane used in practice lies 10 mm above that described. The "address" of a point is given in the form:

$$A_x L/R_y H_z$$

If, for example, the position of an electrode tip is given as $A_1 R_1 H_5$ it is located 1 mm anterior to the coronal interaural plane, 1 mm to the right of the midline and 5 mm above the horizontal plane. The form $A_1 L/R_1 H_{-5}$ indicates the presence of bilaterally symmetrical lesions, 1 mm to right and left of the midsagittal plane.

PICTORIAL VIEW OF A NARISHIGE STEREOTACTIC FRAME

See Figs: 5:2, 5:3, 5:4 and 5:5

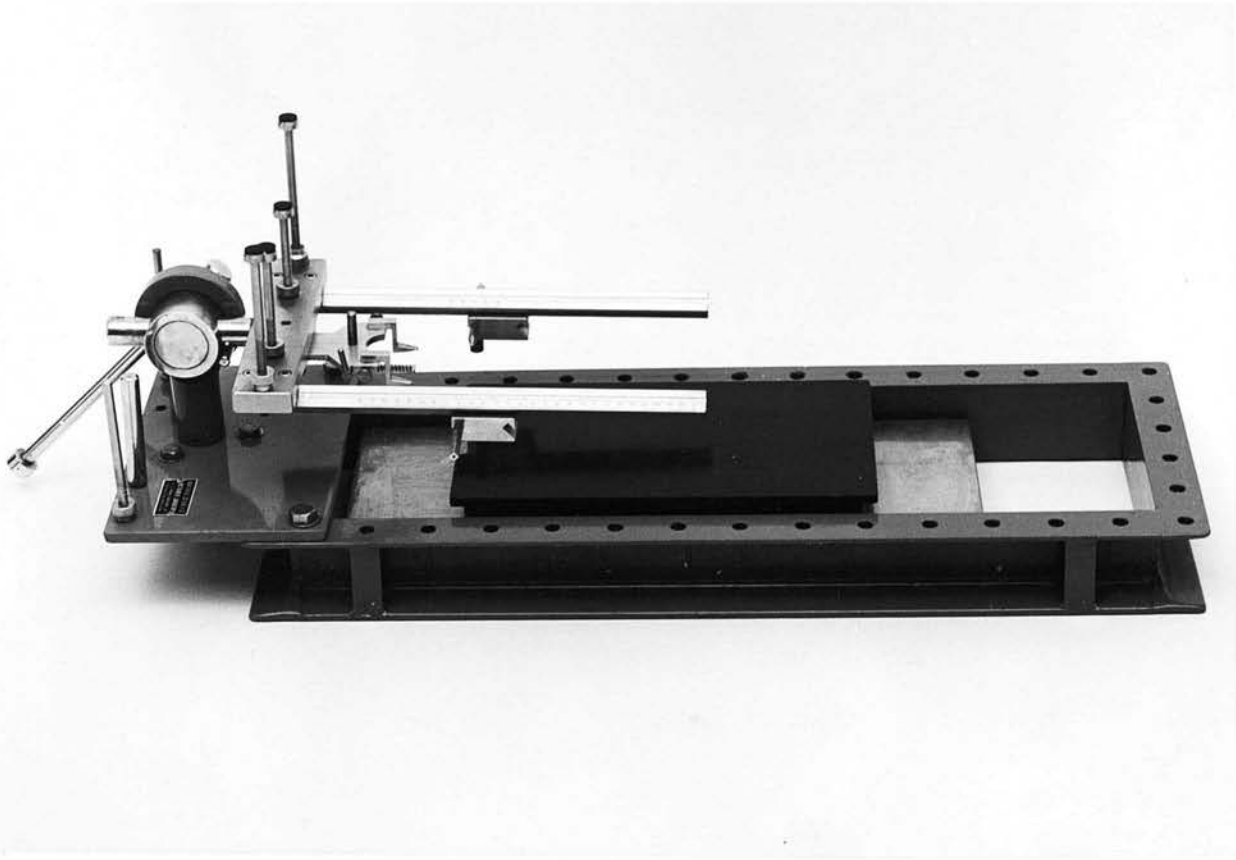


Fig. 5:2

A Narishige (SN-2) stereotactic frame

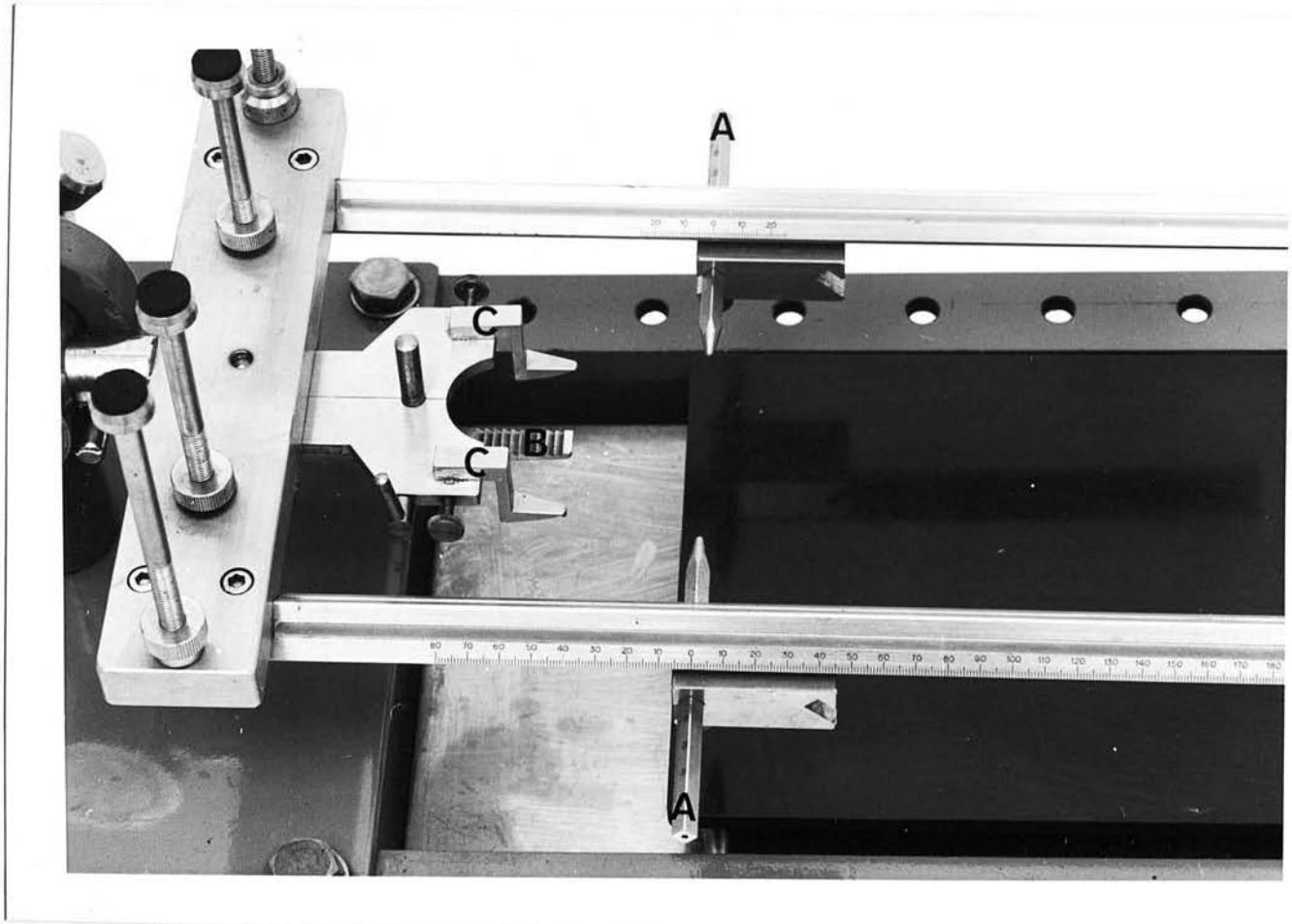


Fig. 5:3

Details of a Narishige frame.

A: Ear bars, B: Mouth-piece, C: Maxillar clamps

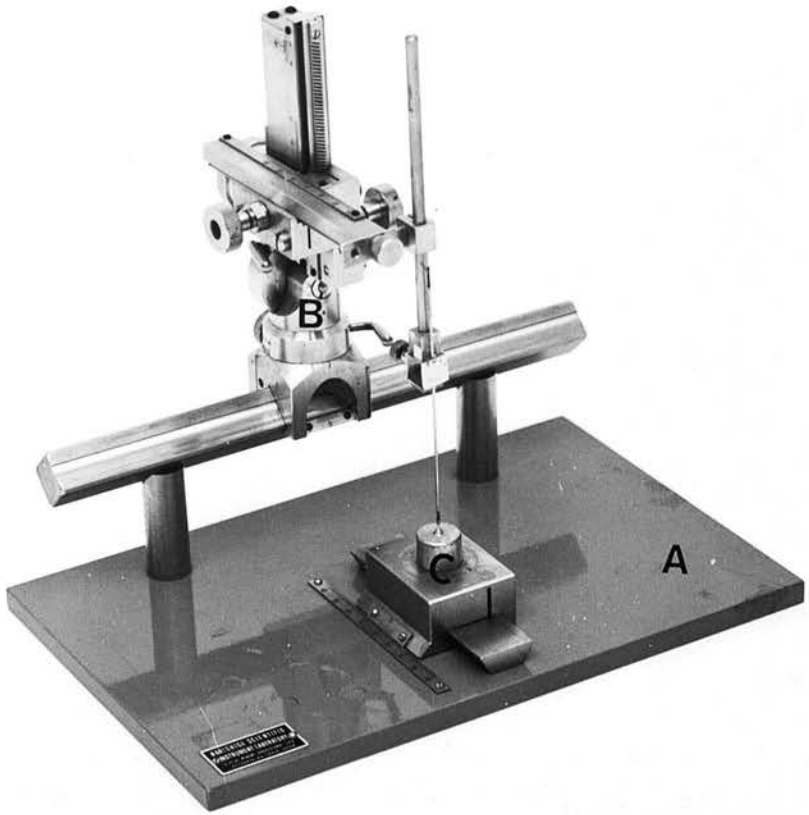


Fig. 5:4

Details of a Narishige frame.

A: Calibrating table, B: Electrode carrier, C: Zeroing the lesion electrode.

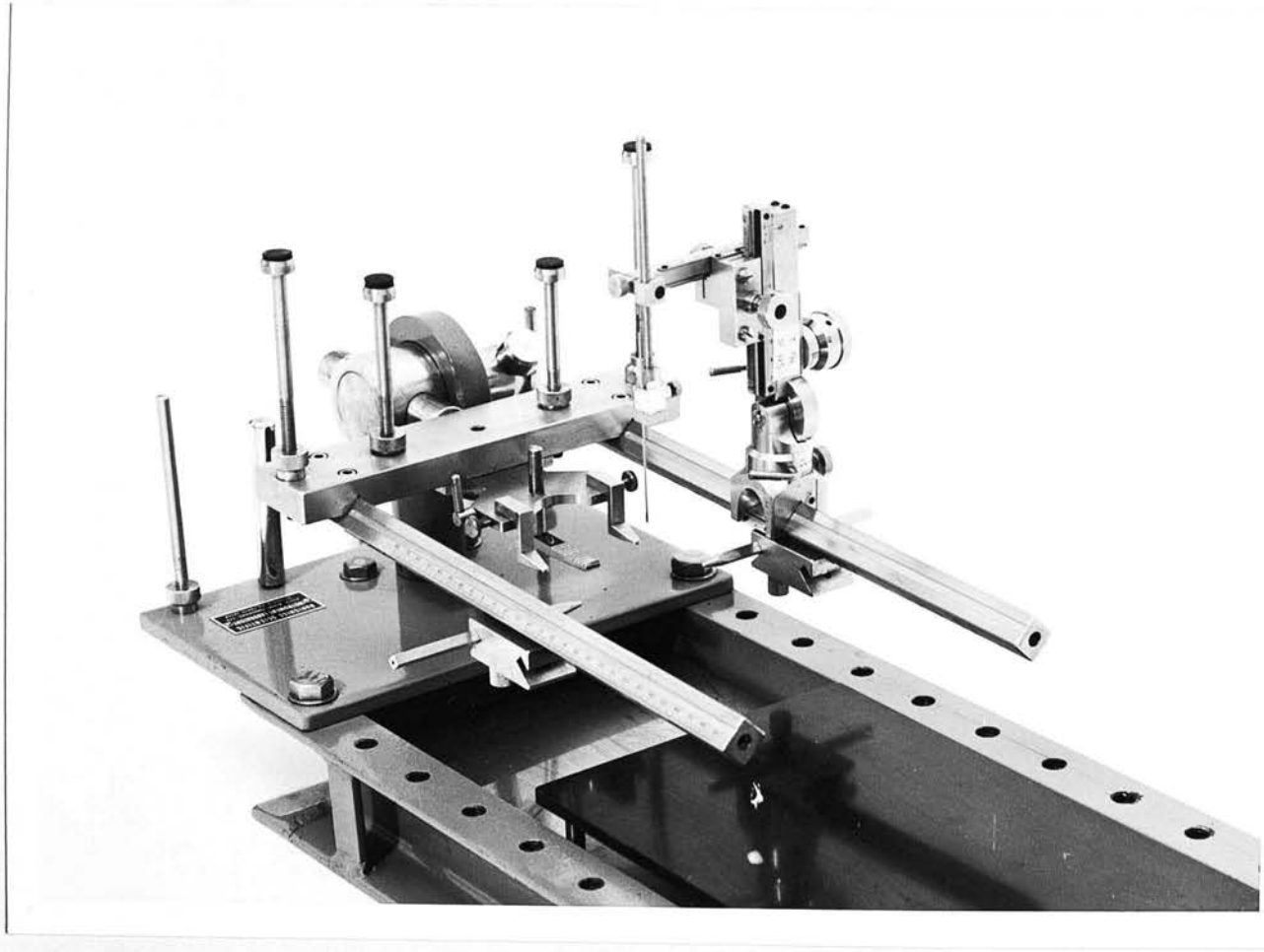


Fig. 5:5

Close-up of a Narishige frame. The electrode carrier with the zeroed lesion electrode mounted.

FIXATION OF THE ANIMAL AND PROCEDURE OF STEREOTACTIC TECHNIQUE

Care was taken to fix the head of each animal similarly. Proper fixation of the ear bars was the crux of the procedure. Once the external auditory meatus had been identified (at times it was necessary to incise the tragus) the bars were inserted one at a time and fixation of the head tested by rotating the head through 90-180 degrees flexion/extension and pressing it downwards. The mouth piece was inserted to press against the hard palate and anchored with the orbital and maxillary clamps.

When the target had been chosen for either depth recording, stimulation or "lesioning" the appropriate electrode was fixed on its carrier which was placed on the zeroing table (the so-called "electrode angle calibrator") so that the tip of the probe was zeroed with regard to the three mutually perpendicular planes. The electrode and its carrier were transferred to the frame, where the actual zero points of each of the planes was applied and the target co-ordinates set. Each time the electrode was used it had to be re-calibrated in order to ensure precise reinsertion.

ELECTRODES

DEPTH MICRO-RECORDING ELECTRODE

This was made from a 15 cm length of tungsten wire sharpened to a tip diameter of 5-10 μ and insulated with Araldite resin (Appendix 1). (Fig. 5:6 a & b).

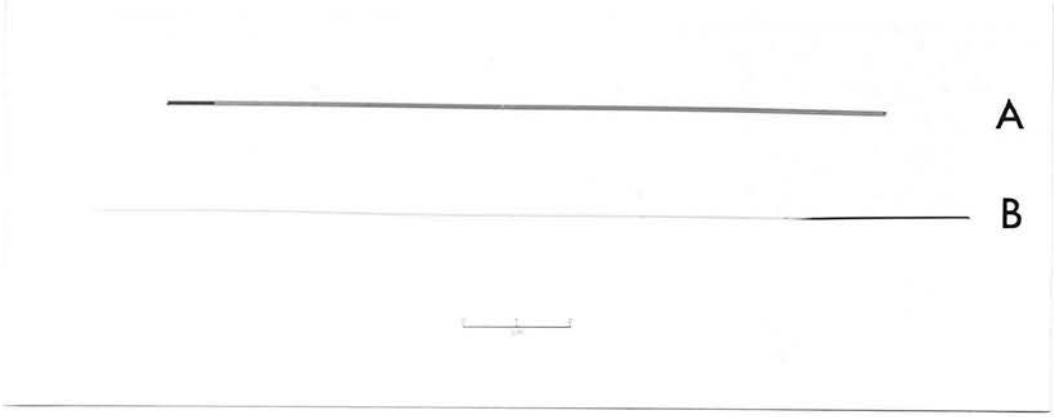


Fig. 5:6a

Stimulation (A) and depth recording microelectrode (B)

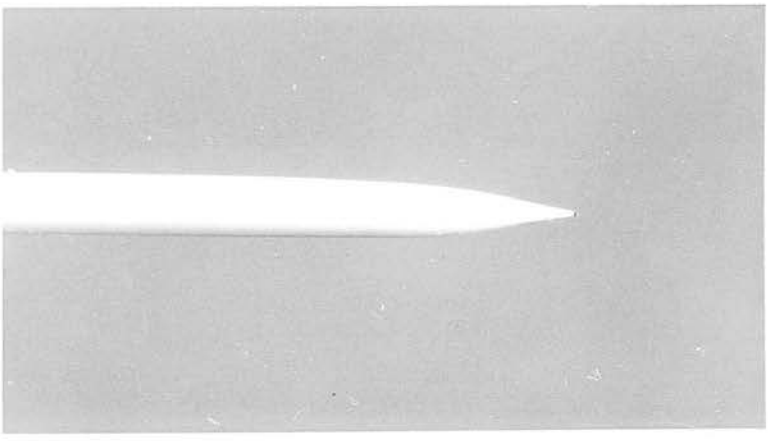


Fig. 5:6b

A close-up of depth recording microelectrode (mag. x 15)

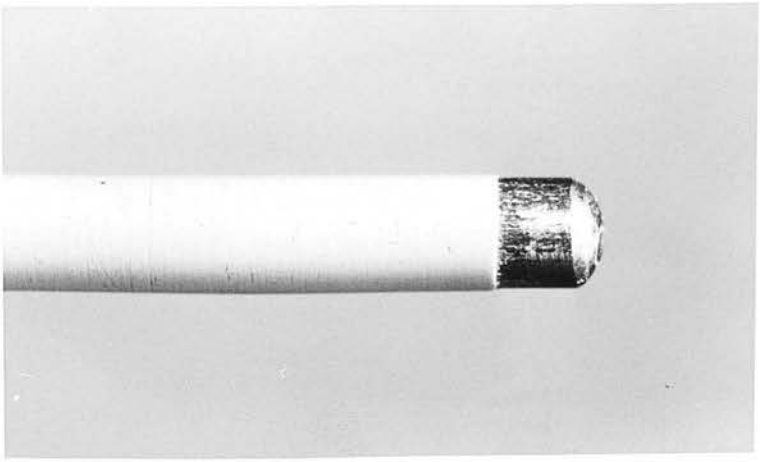


Fig. 5:6c

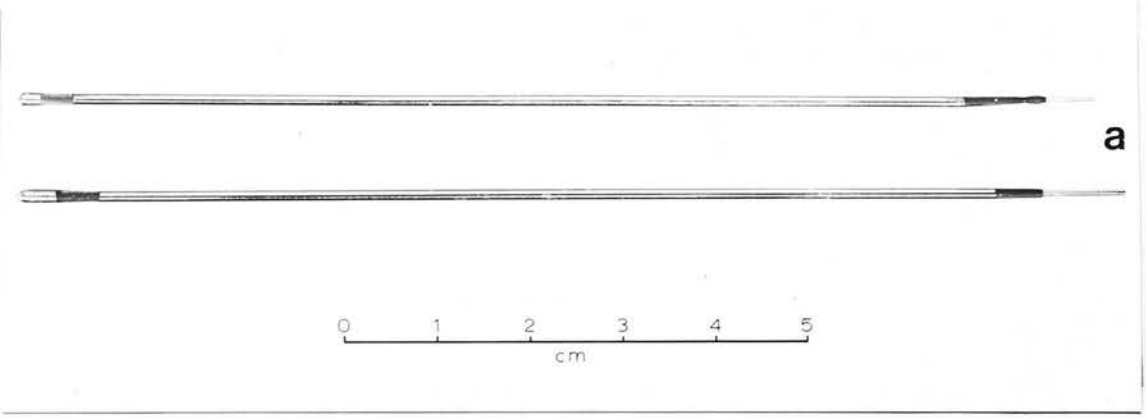
A close-up of stimulation electrode (mag. x 15)

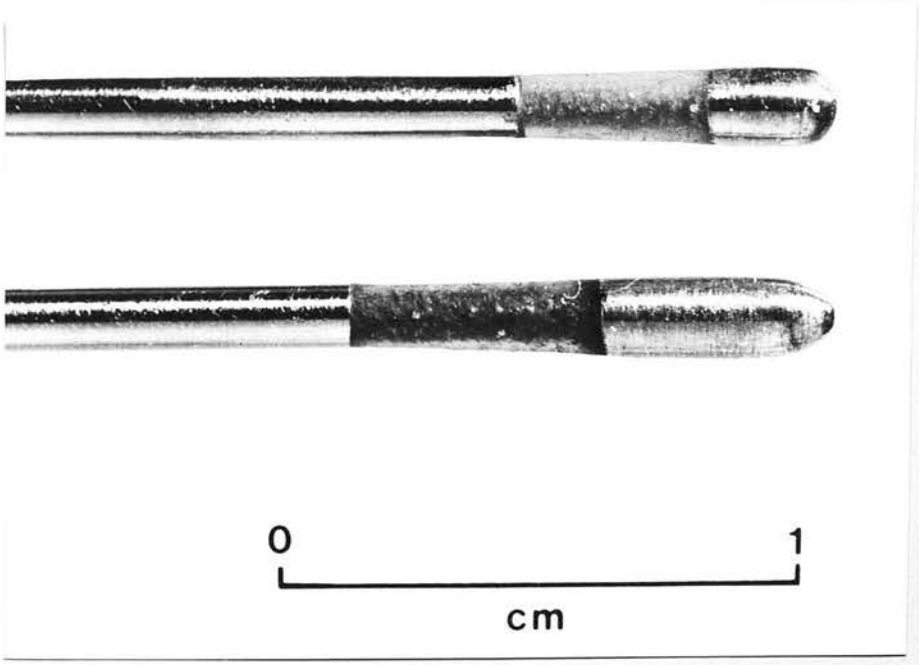
STIMULATION ELECTRODE

A silver electrode 15 cm long with a 1 mm bare tip was used, also insulated with Araldite. (Fig. 5:6 a & c).

LESION-MAKING ELECTRODE

The electrode used for making a lesion was a 15 cm long steel rod (0.5 mm diameter) with a gold plated tip (2.5 x 1.2 mm) soldered to one end (Fig. 5:7 a & b). The rod was stiffened by being inserted into a stainless steel tube (135 mm long x 1.0 mm diameter) from which it was insulated by a layer of Araldite; this insulation extended to the base of the gold plated tip and to within 1.5 - 2.0 cm of the other end which was thus left bare for making the electrical connection. The scalp or temporal muscle was used as the earth of the circuit.





Figs. 5:7 a & b

(a) Two lesion electrodes

(b) A close-up view of the two lesion electrodes

PART THREE

ANIMAL WORK

CHAPTER 6

RADIOFREQUENCY LESIONS IN THE GUINEA PIG BRAIN

Relationship between duration and intensity of current, tissue impedance and size of lesion.

INTRODUCTION

The development of the first stereotactic apparatus by Horsley and Clark (1908) made it possible to place small, accurately localised lesions in deep-seated brain structures. It was early apparent that meaningful analysis of the anatomic and physiologic consequences of such lesions demanded that their location, size, morphology and possibly their histologic characteristics should be adequately controlled.

Several means of producing such lesions have been employed: Chemicals, such as zinc or aluminium chloride, diffused rapidly and produced large, irregular, necrotic areas which often resulted in convulsions, excitability and pain (Brown and Henry 1934, Kopeloff et al. 1950).

Electrolytic lesions were made by the passage of a direct current by Horsley and Clark (1908) who reported that unipolar anode lesions were smaller and less irregular in shape than unipolar cathode lesions. They attributed this to the greater amount of steam formed at the tip of the cathode. Bipolar lesions were even larger and more irregular than unipolar ones. This method of producing localised lesions in the brain has been widely used but all investigators are agreed on the great variation in size and morphology of the lesions (Carpenter and Whittier 1952). Similar results were obtained by the use of high frequency alternating current. Glees et al. (1947) noted that tissue destruction was not confined to the region of the electrode tip; the size of the lesion was unpredictable and seemed to vary with the amount of steam formed at the point of coagulation.

Tissue was mechanically disrupted by Clark and Henderson (1920) who described specially designed lesion makers (cyclotome,

spherotome, orthotome) and Glees et al. (1947) who used a rotating knife. Both claimed the production of well-defined and suitably sized lesions. The photomicrographs, however, of Papez (1930) disclosed wide variations in their size and morphology.

Ultrasound. Exposure of the animal brain to either focused or unfocused high-density ultrasound waves through the intact cranium results in superficial pyramidal areas of necrosis (Lynn and Putman 1944). Various workers, however, have succeeded in producing discrete lesions deep within the brain (Barnard et al. 1956) by the use of multiple, intersecting, relatively narrow beams of high-density ultrasound. The method has also been used in humans, mainly for the relief of intractable pain due to metastatic tumour; the frontal lobes were irradiated and the procedure was effective for various lengths of time. The necrosis and oedema which are seen are considered to be thermal or cavitation effects (Nelson et al. 1959).

Radioactivity. Short-lived beta-emitting radon seeds implanted in the medulla of dogs resulted in well localised tissue destruction (Borison and Wang 1951). The use of beta- or alpha-emitting material for the destruction of the adenohypophysis was introduced by Rasmussen et al. (1954) and has been widely used therapeutically. The method is slow and unsuitable for acute experimental or clinical lesion making.

Cryogenic lesions. The earliest systematic study of freezing the brain for purposes of physiologic investigation was that of Openchowski (1883, cited by Cooper 1962). Subsequent reports suggested that cold might be used both for its inhibitory physiologic effects and the production of localised anatomical

lesions in the brain. Hass and Taylor (1948) produced discrete, circumscribed and reproducible lesions by freezing. Cryogenic techniques have been elaborated and used in tumour surgery (Rowbotham et al. 1959), in physiologic experiments, inhibition and for the creation of stereotactic lesions (Cooper 1962, Siegfried 1962). Miyasaki (1962, cited by Cooper 1962), however, reported that the lesions produced by cooling showed considerable variation in size; this was exacerbated by prolonging the cooling and haemorrhage also occurred, whose extent was directly proportional to the rate of cooling.

Radiofrequency current has been used in controlled experimental and clinical studies. Sweet et al. (1960) produced well-demarcated, small and "controlled" lesions in cats and in the human medulla in an attempt to interrupt the crossed pain tracts. These initially empirical uses of radiofrequency current were supplemented by the same groups' detailed study of the biophysical effects of radiofrequency current (Aronow 1960).

Brodkey et al. (1964) used low-power radiofrequency current to make reversible, physiologic, thermal "lesions" in cats and in two patients. In the latter this was done to determine the final location of an electrode before a permanent lesion was made in the target area.

The ease with which radiofrequency power can be produced and delivered, the good understanding of its destructive action and, most important, the small, well-demarcated, non-haemorrhagic lesions it can make have made the technique widely accepted and it is used today in surgery for pain relief, behavioural disorders and epilepsy.

We, therefore, used radiofrequency current to produce lesions in animals and in a preliminary study investigated the relationship between intensity and duration of current, the size of the lesion and its impedance before and after destruction. It was hoped to be able to use the data thus acquired as a guide to the production of small, reproducible, non-haemorrhagic lesions in cats.

MATERIAL AND METHODS

Twelve guinea pigs of both sexes weighing between 0.7 - 1.0Kg were used. The anaesthetic was a proprietary mixture of diallylbarbituric acid and urethane (Dial Compound), 0.35 ml/Kg intraperitoneally for both intubation and maintenance of anaesthesia. The animals were fixed on a Narishige (SN-2) stereotactic frame (Fig. 6:1). A midline scalp incision, approximately 6 cm long gave good exposure of the coronal and longitudinal sutures and the parietal bones. Using a dental burr, a 2-3 mm diameter hole was made in each parietal bone, 8 mm posterior to the coronal suture and 4 mm lateral to the longitudinal suture. Since there is no guinea pig stereotactic atlas, the depth of the basal ganglia was obtained from a dead animal fixed on the frame with its forebrain removed; they were entered 3.5 mm from the outer table. This neural structure had been selected because of its similarity to the midbrain, each containing a mixed population of grey and white matter.

The radiofrequency electrode to be used in the main study on cats was used here. When this had been implanted and before a lesion had been made the impedance of the target was measured by means of an ohmeter (Model IM-1, Radionics) (Fig. 6:1,A).

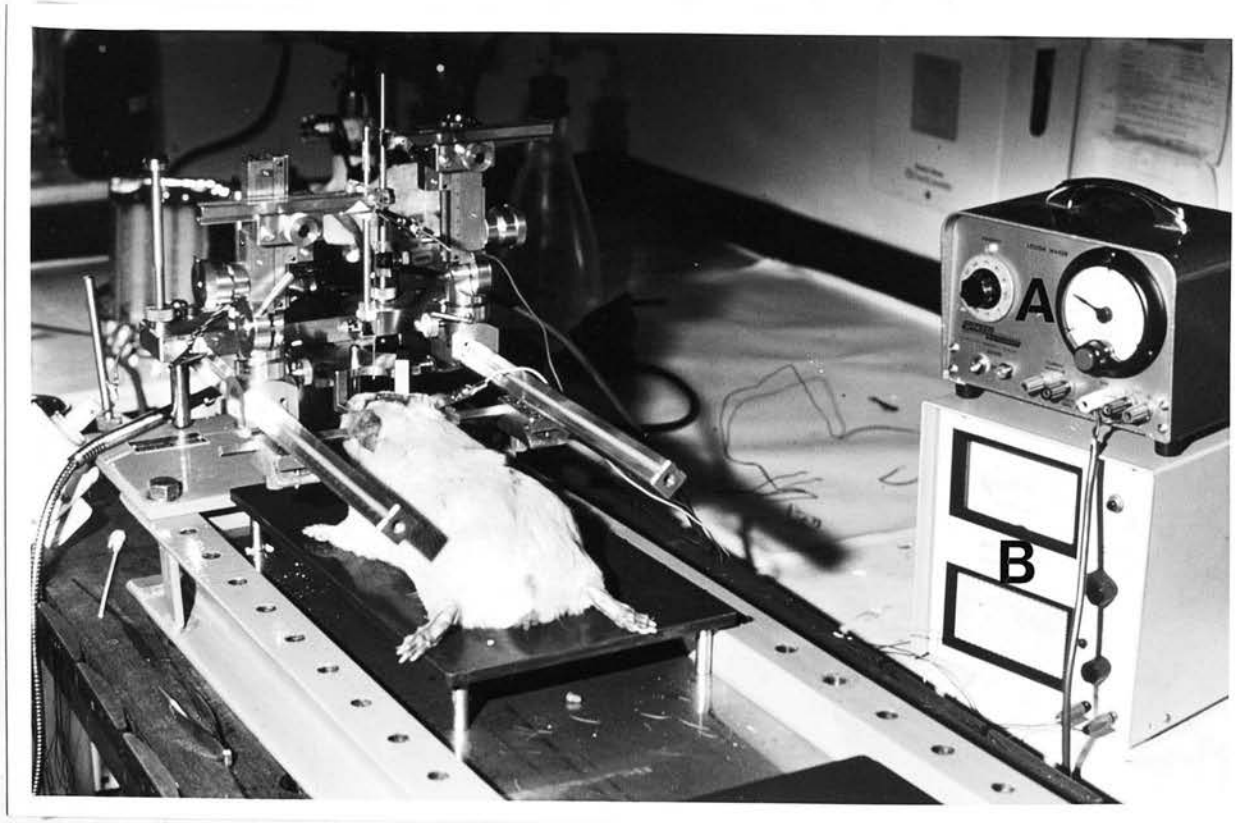


Fig. 6:1

Arrangement of guinea pig experiment (A: Lesion maker, B: Impedance meter)

The radiofrequency current was generated by a lesion maker (Grass Instruments, Model LM-3) (Fig. 6:1,B). The voltage of the current used varied from 50 - 160 volts. The duration of passage of the current ranged from 10 to 30 seconds.

Bilateral lesions were made in the basal ganglia of each of the 12 animals. The frequency employed throughout was 2 kHz, the voltage was 50, 70, 90, 110 or 160 volts and the duration of current 10, 15, 20, 25 or 30 seconds (Table 6:1).

When the lesion had been made the impedance was measured again and the animal was kept warm in order to keep it alive for 1 - 2 hours, hopefully long enough for some cellular reaction to develop and facilitate the histologic examination. At the end of this time the animal was killed by cardiovascular perfusion with 10% formaldehyde and the head was kept in formaldehyde for 2 - 3 days. The brain was then removed and fixed for a further week. Semi-serial paraffin sections, 10 μ thick at 50 μ intervals were stained with Haematoxylin-eosin for general cytology and with Solochrome Cyanin for myelin.

RESULTS

The intensity of the current, its duration and the tissue impedance before and after the lesion are presented in Table 6:1. The impedance with the electrode tip in air was several thousand ohms whereas at the target area in the brain it ranged from 550 - 1100 ohms. After completion of the lesion the impedance in two lesions was unaltered, was increased in nine and decreased in thirteen. It appeared that low voltages mostly increased and high, decreased the post-lesion impedance.

Table 6:1

Relationship between voltage, duration and impedance before and after a radiofrequency lesion in guinea pigs.

ANIMAL	LATERALISATION OF LESION	CURRENT (Volts)	DURATION (seconds)	IMPEDANCE (Ohms)	
				Before lesion	after lesion
1	L	70	10	1050	1200
	R	90	10	1100	970
2	L	110	10	850	550
	R	160	10	550	500
3	L	50	15	700	650
4	L	70	15	820	780
	R	90	15	760	1250
5	L	110	15	700	780
	R	160	15	790	750
3	R	50	20	750	700
6	L	70	20	800	980
	R	90	20	750	750
7	L	110	20	750	800
	R	160	20	750	620
8	L	50	25	650	1300
9	L	70	25	850	750
	R	90	25	950	950
10	L	110	25	1080	1100
	R	160	25	1100	800
8	R	50	30	750	700
11	L	70	30	850	900
	R	90	30	1020	1100
12	L	110	30	950	700
	R	160	30	730	500

Passage of the maximum voltage used (160V) produced a "popping" sound and when the electrode was extracted it was seen to have burned tissue sticking to its tip. This phenomenon was not seen with lower voltages.

The lesions were rather widely scattered, being found in the basal ganglia, temporal lobe or the wall of the lateral ventricle. Accurate measurement of lesion size was not, therefore, possible but it was apparent that a smaller current made a small lesion slowly while a larger current made a larger lesion more quickly. This is shown in Fig. 6:2. From the available data the maximal cross sectional diameter of the smallest (0.8mm) and largest (6.0mm) lesions in this study are presented in Figs. 6:3, 6:4, 6:5 and 6:6.

The smallest lesion is slightly elliptical, measures about 1.5 mm in its greatest diameter and is located in grey matter. It consists of a central haemorrhagic area 0.8mm in diameter which is surrounded by a pale halo of neuropil in which a little vacuolation has occurred and the cell nuclei are dense and pyknotic. No electrode track can be identified.

The largest lesion is roughly circular in outline, measures 8.0 mm in diameter and is also located in grey matter. In this, a central cavity 2.0 mm in diameter contains a little haemorrhage and is surrounded by two concentric zones of altered brain. The innermost, some 2.0 mm wide, is characterised by nuclear pyknosis and increased tissue acidophilia and is surrounded by a zone of oedematous tissue, ill-defined peripherally, in which the neuropil is pale and vacuolated. An occasional polymorph leucocyte appears to be present. Vascular thrombosis is confined to the inner, compact zone. The lesion is interpreted

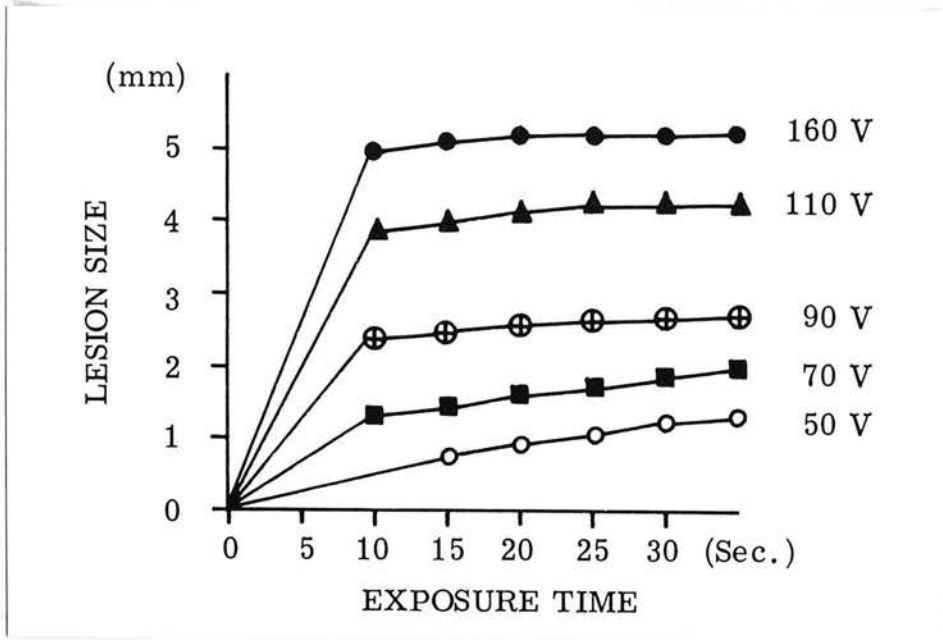

(mm)
LESION SIZE
5
4
3
2
1
0
160 V
110 V
90 V
70 V
50 V
0
5
10
15
20
25
30
(Sec.)
EXPOSURE TIME

Fig. 6:2

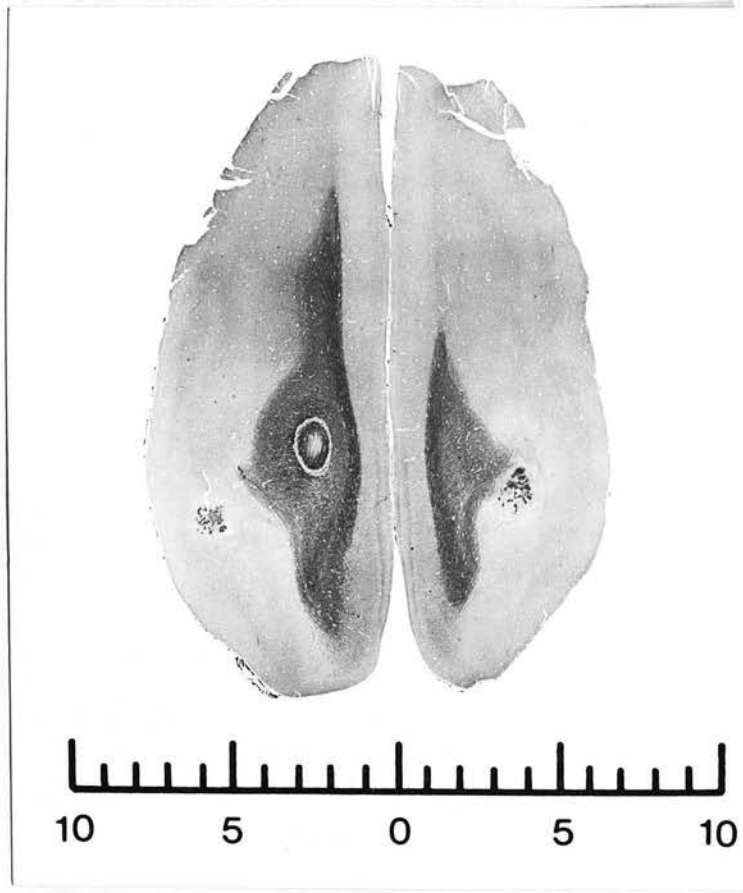


Fig. 6:3

Section through a cat brain showing two lesions; on the left the smallest lesion (50V) and on the right the next largest lesion (70V).

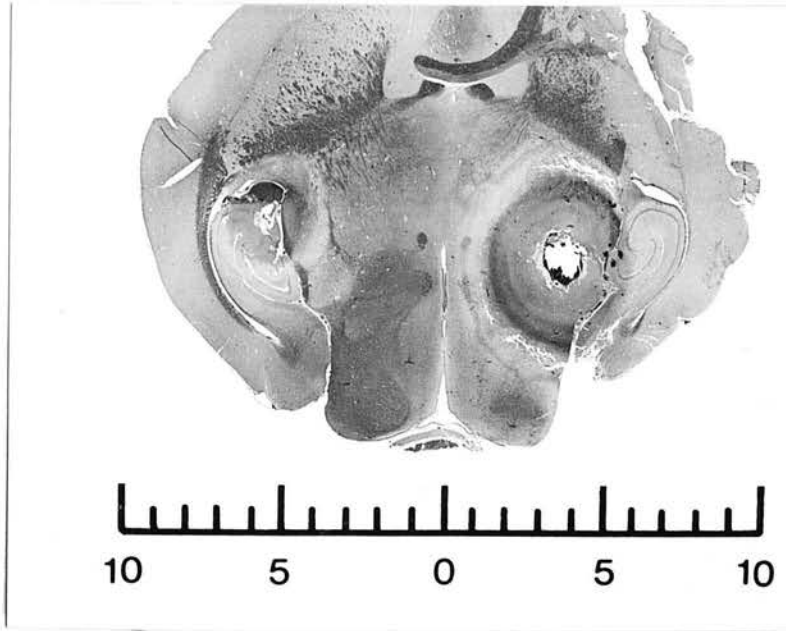


Fig. 6:4

A section of a cat brain showing the two largest lesions; on the left the second largest lesion (110V) while the right (largest) lesion was produced by 160V.

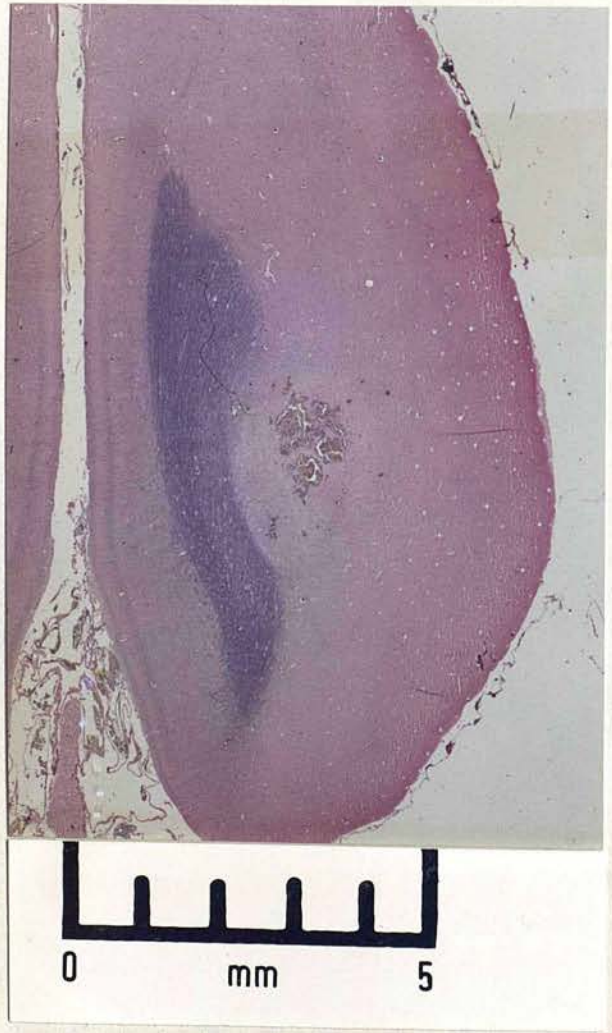


Fig. 6:5

A magnified view of the smallest lesion seen in Fig. 6:3.

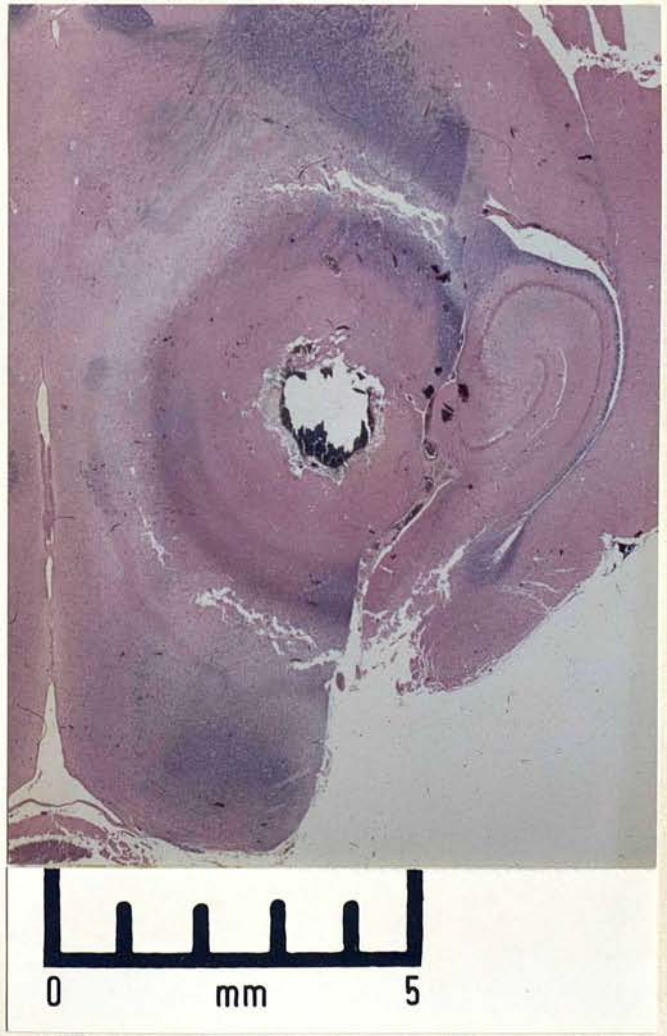


Fig. 6:6

A magnified view of the largest lesion described in Fig. 6:4.

as an electrode track, surrounded by coagulated brain which is, in turn, surrounded by a zone of reactive oedema.

DISCUSSION

When radiofrequency current is passed through tissue the energy is converted into heat within the tissue, not in the electrode. Aronow (1960) recorded temperatures as high as 435°C around the electrode tip, the tissue boiling and eventually charring. The "popping" sound heard when a high voltage current is used is probably due to the formation of a bubble of steam around the electrode tip. The maximum current density, and thus the highest temperature, is developed immediately adjacent to the tip of the electrode and both current density and temperature decrease as the square of the distance from the electrode. Brodkey et al. (1964) showed that a temperature of 42.5 - 44.0°C produced reversible inhibition of function whereas above 44.0°C the lesion was permanent.

The current required to produce a given temperature at the electrode tip and thus a lesion of predictable size varies with the physical dimensions of the tip and the thermal characteristics of the anatomical area concerned. The latter are dependent upon factors such as temperature of tissue and proximity to blood vessels, CSF, bone or other tissue which may act as a heat sink. This effect can be seen where the size of a lesion is proportional to its distance from a fluid-filled ventricle (Aronow loc.cit.).

The lowest current used resulted in a small, ill-defined area of oedema without necrosis. Well-demarcated lesions of

adequate volume resulted from the use of a current of 90-110V.

The impedance of normal tissue is considerably greater than that of fluid such as CSF. Taren et al. (1969) found that the impedance recorded in four patients after making a lesion was markedly elevated but that in one cat it was decreased. They took this to mean that damaged tissue had a greater impedance than normal and offered no explanation of the anomalous effect seen in the cat.

Our findings are essentially in agreement with these: lesions made by high intensity current mostly showed an increase in impedance while low intensity lesions showed a decrease. The reversal of the effect with low intensity current is difficult to account for but it could, conceivably, be due to greater oedema.

CHAPTER 7

THE PRODUCTION OF DECEREBRATE RIGIDITY IN CATS BY FOCAL STEREOTACTIC MESENCEPHALIC LESIONS

INTRODUCTION

By definition, the Monro-Kellie doctrine is applicable only if the brain and spinal cord are contained in a "closed box". The continuous recording of the ICP demands the anatomical integrity of this box and in the experimental investigation of decerebrate rigidity, secondary reactions of the cerebrovascular bed, disturbance of CSF circulation and cardiorespiratory complications, all of which could readily confuse the situation, must be controlled as far as possible.

Ideally, a severe degree of decerebrate rigidity should be produced by minimal, discrete and reproducible brain lesions without the complications of haemorrhage, oedema or cardio-respiratory disturbances.

Intercollicular transection: The classical technique for producing decerebrate rigidity in animals (Sherrington 1897-98) was crude in the extreme and involved tying off both carotid arteries as a preliminary to dividing the midbrain between the upper and lower colliculi through a wide craniectomy. The severity of these and similar procedures, the often uncontrollable haemorrhage and oedema and the major cardiorespiratory complications resulted in a very high mortality rate.

There was no way of entirely standardising the level of transection, which had been found to be the most important determinant of the degree and type of rigidity.

In an attempt to avoid haemorrhage, Brown and Pinsky (1970) transected the midbrain at the intercollicular level using a wide loop cautery-knife which was introduced through a small skull window. These animals, however, not only became areflexic but also showed no rigidity either, because the caudal extension

of the lesion into pons and medulla prevented its development.

Anaemic decerebration: Decerebration was produced "anaemically" (Pollock and Davis 1927) by tying both carotid and the basilar arteries; this produced an extreme degree of decerebrate rigidity but the animal rapidly died as a result of severe brain oedema and cardiovascular irregularities. Attempts to correct the latter merely accelerated the process (Borison et al. 1960).

Stereotactic methods: Localised, reproducible stereotactic lesions were made electrolytically by Ingram and Ransom (1932) in the red nuclei of cats. The lesions were cavities which varied in size and shape and in a few cases, in which severe decerebrate rigidity appeared, large haemorrhagic areas were present throughout the tegmentum. Ward (1947) in the course of an attempt to produce a lesion which would prevent the development of rigidity (in chronic experiments on cats given sodium cyanide) made an accidentally large electrolytic lesion in the pons of one animal and produced acute decerebrate rigidity.

Cryogenic techniques have been used in stereotactic surgery (Cooper 1962, Siegfried et al. 1962, Miyasaki 1962, cited by Cooper 1962) in man. Gilman and Van der Meulen (1965) produced decerebrate rigidity in cats by the use of cold; rigidity was assessed by feeling the resistance of the limbs to passive movement and by testing the deep tendon reflexes, which are known to be increased in states of rigidity and spasticity. The tip of a cannula was placed stereotactically in the midbrain and liquid refrigerant (Freon) injected; temperatures as low as -45° to -60° could be reached. Lesions at various sites in the midbrain, in particular the reticular formation, produced

good decerebrate rigidity. Although the onset of rigidity might be accompanied by halving of the respiration rate they made no reference to alterations in cardiovascular dynamics. The lesions were often so extensive that they amounted to midbrain transections.

Focused ultrasound has been used to make localised lesions in the brain. The mechanism is thought to be mechanical but the temperature is also raised locally (Nelson et al. 1959). Borison et al. (1960) produced decerebrate rigidity by this technique in cats. His best results were obtained by literally transection the midbrain, anything less being relatively ineffective.

Radiofrequency techniques, which have advantages over any other known means of producing lesions in nervous tissue (Chapter 6) have been used in this study to produce decerebrate rigidity.

MATERIALS AND METHODS

We used 20 healthy cats of a standard (2.5 - 3.5 Kg.) weight and therefore standard size so as to avoid the possibilities of errors with the stereotactic co-ordinates, as recommended by Snider and Niemar (1961), whose atlas of the cat brain we used in this study.

Cats were selected for this study because of:

a) their toughness and extreme stamina under conditions of major stress (anaesthetic, brain lesions in vital areas)

b) the fairly standard size of their brain within a relatively wide range of body weight greatly eases the problem of supply; the chances of obtaining reproducible results were therefore

much greater than if there were a wide variation in brain size.
c) most of what is known about decerebrate rigidity has derived from experiments on cats; a corpus of knowledge therefore already exists on the technicalities of the problem such as anaesthesia, ventilation and anatomical atlases.
d) cats are easy to handle and good facilities were available for their use.

The animals were anaesthetised and set up on the stereotactic frame as described in Chapter 5 where the electrodes are also described. Other parameters measured during this experiment are described in the following Chapter 8.

Unilateral lesions were made in three animals in an attempt to produce unilateral rigidity and study its effect on the ICP. Midline mesencephalic lesions were made in only one animal, whereas in the other sixteen bilateral lesions were made of the smallest possible size which would produce maximum rigidity.

RESULTS

DEPTH MICRO-ELECTRODE RECORDING

In an attempt to identify and delineate the mesencephalic reticulum the brain electrical activity was monitored by both visual and audio means as the microtip recording electrode was advanced through the cortex, subcortex, tectum and tegmentum at 2 - 0 mm anterior, 1 to 4 mm lateral and 0 to 4 mm below the interaural plane, which according to the atlas coincided with the mesencephalic reticular areas. Positions of the tip at $A_{1-1.5}$ $R/L_{3.5}$ H_{-2} were the most satisfactory sites of

monitoring for reasons given later.

When the tip of the probe was in the subarachnoid space activity was minimal (1-3 μV) but when it was in the cortex the amplitude of the tracing attained its maximum at 30-35 μV, while the firing rate as seen and heard was increased. Advancement of the tip into subcortex showed a similar pattern of activity, although its amplitude was reduced and the firing rate was apparently unaltered. At the target site the amplitude of the activity was greatly decreased but the firing rate was comparatively increased.

Representative recordings of three animals are shown in Figs. 7:1, 7:2 & 7:3.

A characteristic pattern of activity which could, of itself, label the target was not, however, obtained. This could only be identified by considering the co-ordinates of the electrode tip and the pattern of activity from neighbouring areas as well as the probe activity at target.

ELECTRICAL STIMULATION

Following stimulation of the lateral midbrain tegmentum most animals showed postural reactions similar to those described by Ingram et al. (1932) and Sprague and Chambers (1954), the so called "tegmental responses". The commonest reactions were ipsilateral (to the stimulation) flexion (inhibition of extensor and facilitation of flexor tone) and contralateral extension (facilitation of extensor and inhibition of flexor tone). This reaction was extremely violent in some animals and was more clearly developed in the fore than in the hind limbs. In most animals the head was turned towards the side of stimulation and

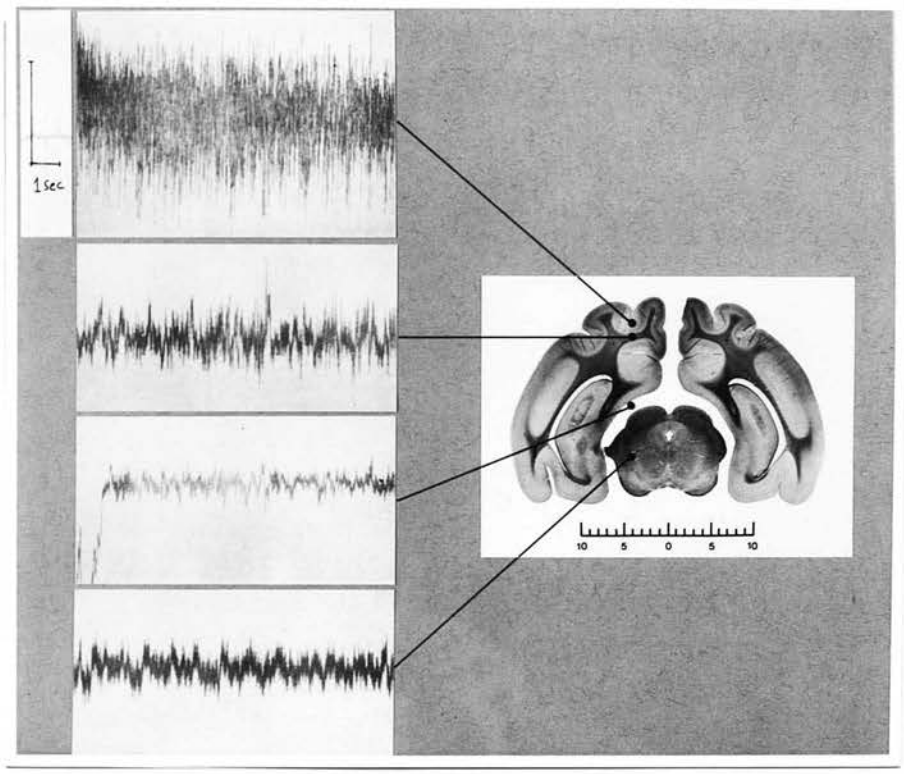


Fig. 7:1

Depth microelectrode recording from cortical, subcortical, CSF space and midbrain reticular formation of a cat.

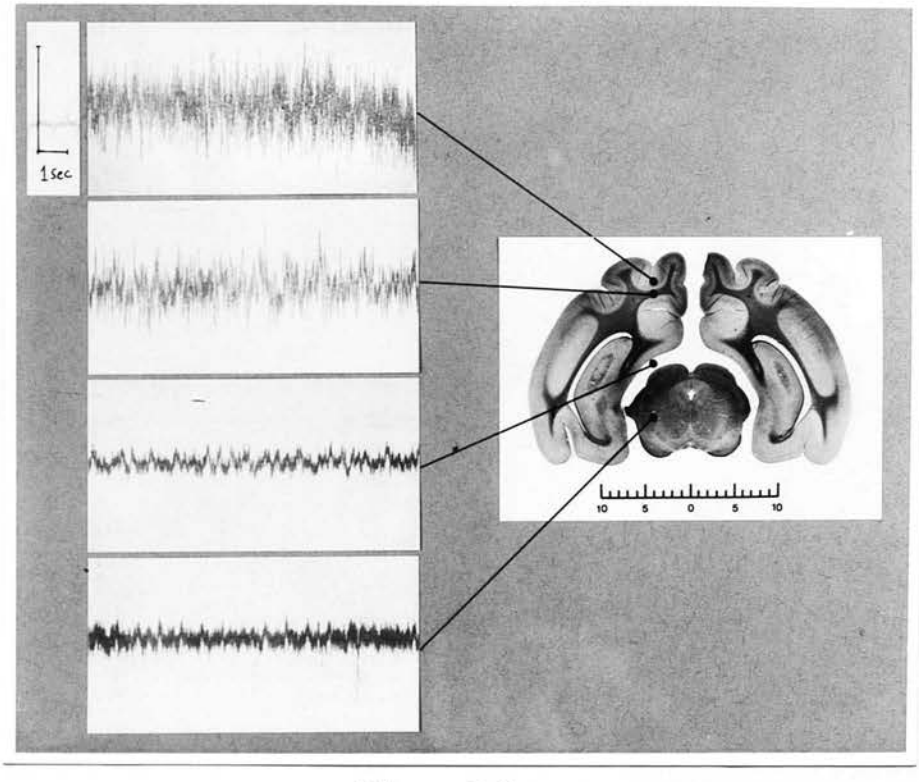


Fig. 7:2

Depth microelectrode recording from cortical, subcortical, CSF space and midbrain reticular formation of a cat.

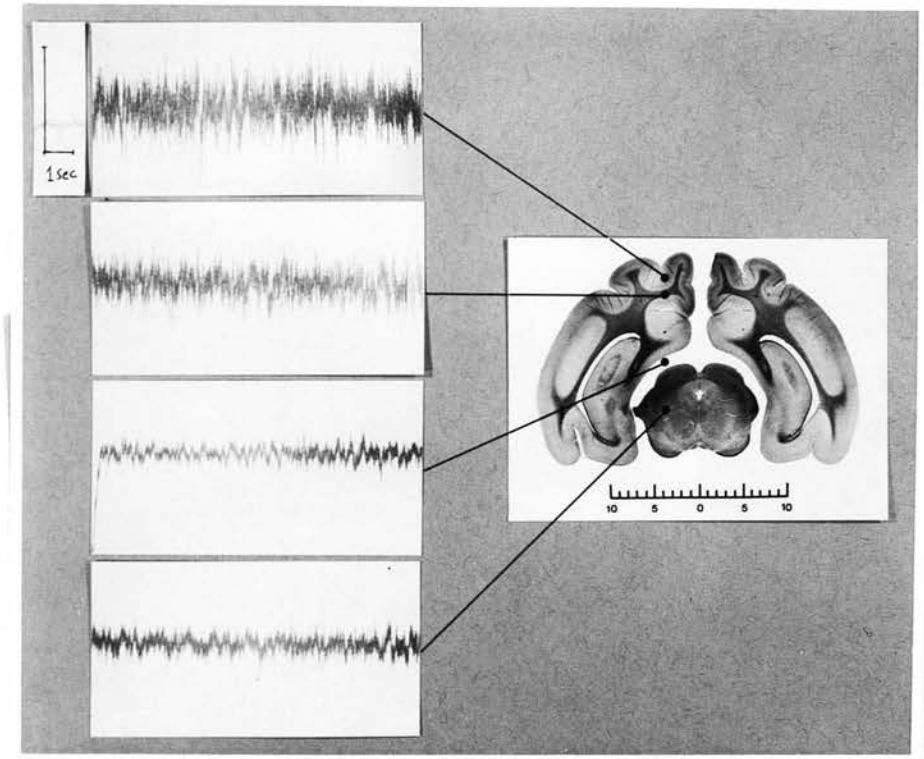


Fig. 7:3

Depth microelectrode recording from cortical, subcortical, CSF space and midbrain reticular formation of a cat.

in many, especially those which developed a violent reaction, the trunk became concave towards the same side. In two animals the only reaction was ipsilateral forelimb flexion with rotation of the head, or rotation of the head alone without changes in the limb posture.

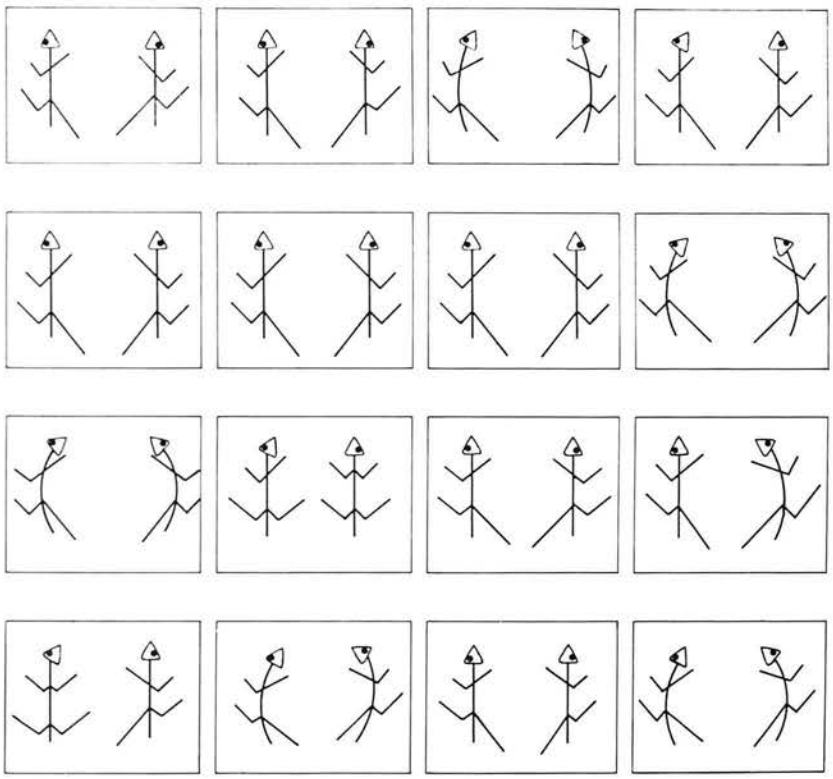
All tegmental reactions are shown in Fig. 7:4.

Once a positive reaction had been obtained the stimulus was discontinued. Reactions could be obtained at the co-ordinates shown in Table 7:1.

RADIOFREQUENCY LESIONS

In cats, lesions within the reticular formation of the mid-brain and involving the oral part of the pontine reticular formation are known to cause decerebrate rigidity (Denny-Brown 1962, Gilman and Van der Meulen 1965). When such a lesion involves the caudal reticular formation of pons and medulla, decerebrate rigidity does not appear because of damage to the facilitatory centres for postural tone and to the efferent pathways through which rigidity is mediated; the rostral end of the pontine reticular formation lies 2 mm caudal to the intercollicular level (Snider and Niemer 1961, Reinoso-Suarez 1961).

In our first two animals, with the tip of the electrode at A_0 R/L_{3-4} H_{-2} and using 160 volts no rigidity developed. This was found to be due to the fact that the lesions were so large that the whole pontine reticular formation had been damaged (Fig. 7:5). Subsequently, a lower voltage (90-110) was used and the electrode tip placed further rostrally.



Postural responses of the head, body and legs of sixteen cats during stimulation of the mesencephalic tegmentum.

Fig. 7:4

$A_{0.5}\ R/L_{3}\quad H_{-1}$	$A_{1}\ R/L_{3.5}\ H_{-1}$	$A_{1.5}\ R/L_{3}\quad H_{-1}$
$A_{0.5}\ R/L_{3.5}\ H_{-1}$	$A_{1}\ R/L_{3.5}\ H_{-2}$	$A_{1.5}\ R/L_{3}\quad H_{-2}$
		$A_{1.5}\ R/L_{3}\quad H_{-3}$
		$A_{1.5}\ R/L_{3.5}\ H_{-1}$
		$A_{1.5}\ R/L_{3.5}\ H_{-2}$
		$A_{1.5}\ R/L_{3.5}\ H_{-3}$
$A_{0.5}$	$A_{1.0}$	$A_{1.5}$

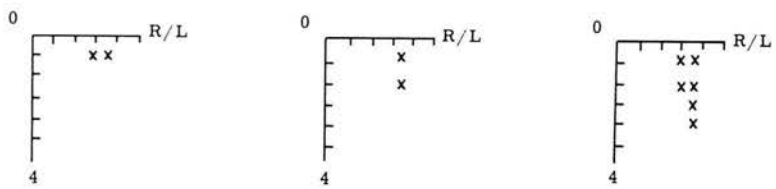


Table 7:1

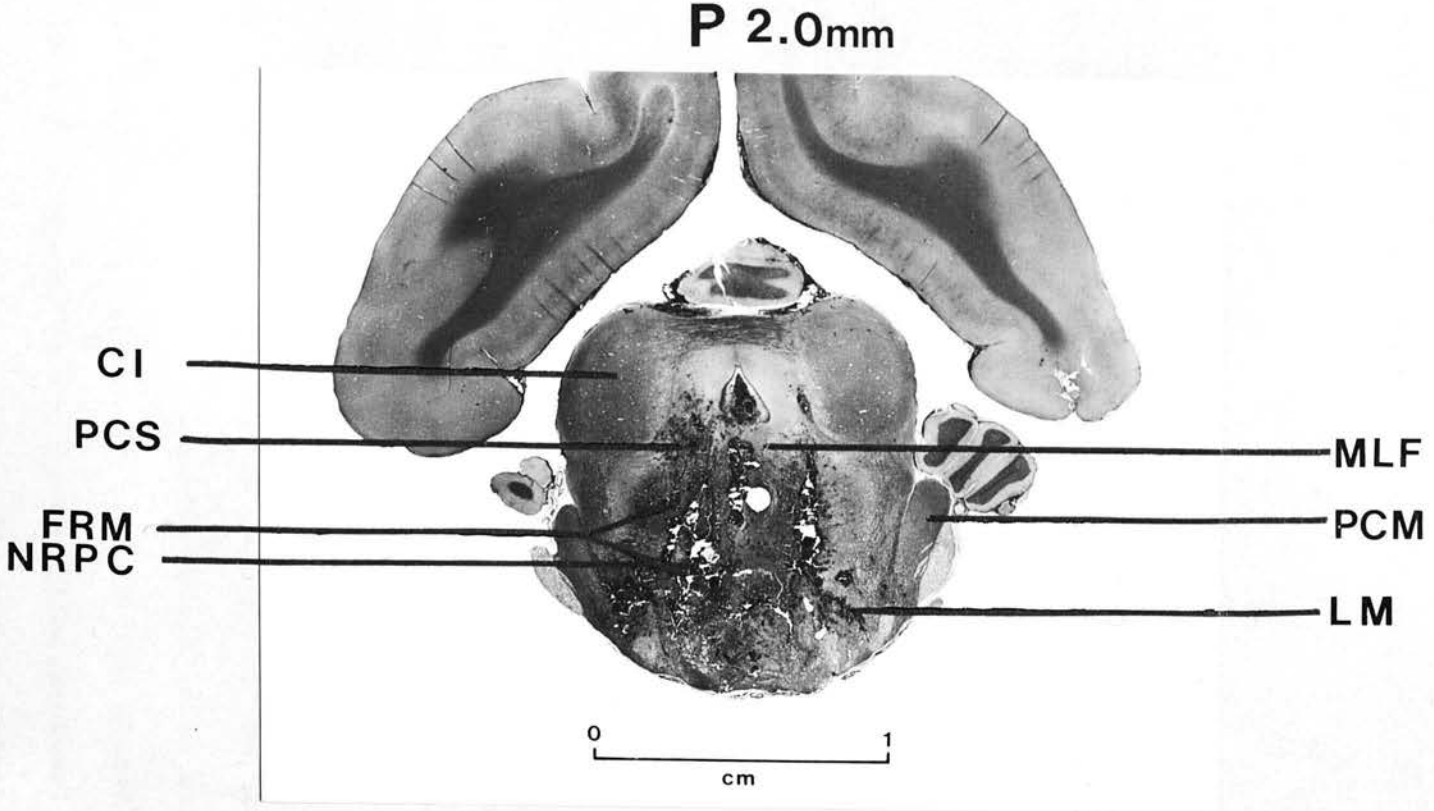


Fig. 7:5

Section of cat brain. The caudal end of the pontine reticular formation is destroyed. This animal never developed decerebrate rigidity.

Unilateral lesions

A solitary lesion at $A_{1.5}\ L_{3.5}\ H_{-2}$ using 70 volts for 15 seconds resulted in predominantly unilateral decerebrate rigidity within 1 - 2 minutes after its completion. The extensor muscles of the forelimb were mainly affected, those of the hindlimb being less affected, as judged from the EMG (Fig. 7:6). The contralateral limbs showed slight rigidity. The rigidity was enhanced by manipulation of the animals' joints. The rigidity was discontinuous, periods of rigidity alternating with periods of spontaneous relaxation. The animal was active at times, making progression and struggling movements, switching its tail and vocalising.

In two animals a similarly placed lesion did not result in rigidity even after some time. Additional lesions were made at:

$A_{1.5}\ L_{3}\ H_{-2.5}$, $A_{1.5}\ L_{4}\ H_{-3}$, $A_{1.5}\ L_{4.5}\ H_{-3}$ and

$A_{1.5}\ R_{3}\ H_{-3}$, $A_{1.5}\ R_{4}\ H_{-3}$, $A_{1.5}\ R_{3.5}\ H_{-2.5}$ in each cat respectively. Within half an hour homolateral rigidity appeared which was reinforced by touching the paws of the animal. Contralateral rigidity developed only after handling and was minimal.

Midline lesions

Fig. 7:7 illustrates a coronal section of the brain stem 4.0 - 4.5 mm anterior to the intercollicular level stained with Solochrome Cyanin; the electrode tip had been placed in the midline, 3.5 mm anterior to the intercollicular level and 2.0 mm below the interaural plane. The slight bilateral rigidity which resulted was greatly increased by cutaneous

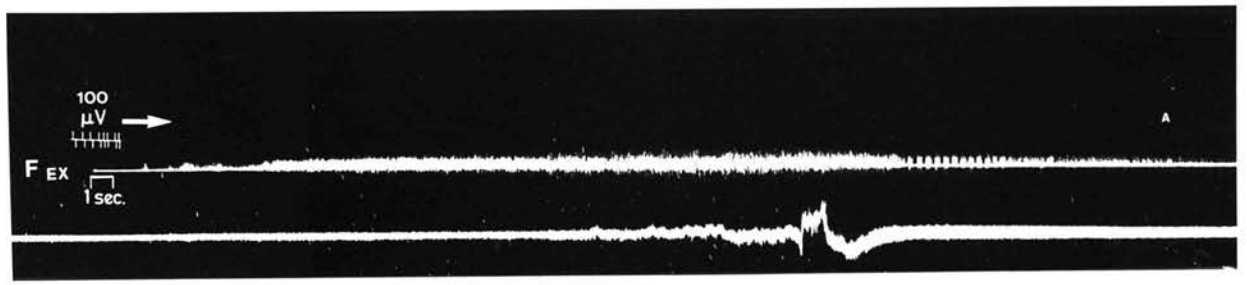


Fig. 7:6

Unilateral decerebrate rigidity. EMG from extensor (top trace) and flexor (bottom trace) of the fore limb of a cat. Unilateral rigidity with predominantly extensor features was produced by one laterally placed small (2 x 2 mm) mesencephalic lesion. The tonic contraction of high amplitude and frequency was turned into a periodic, short-lasting tremor, which tailed off into a continuous tonic and small amplitude muscle discharge.

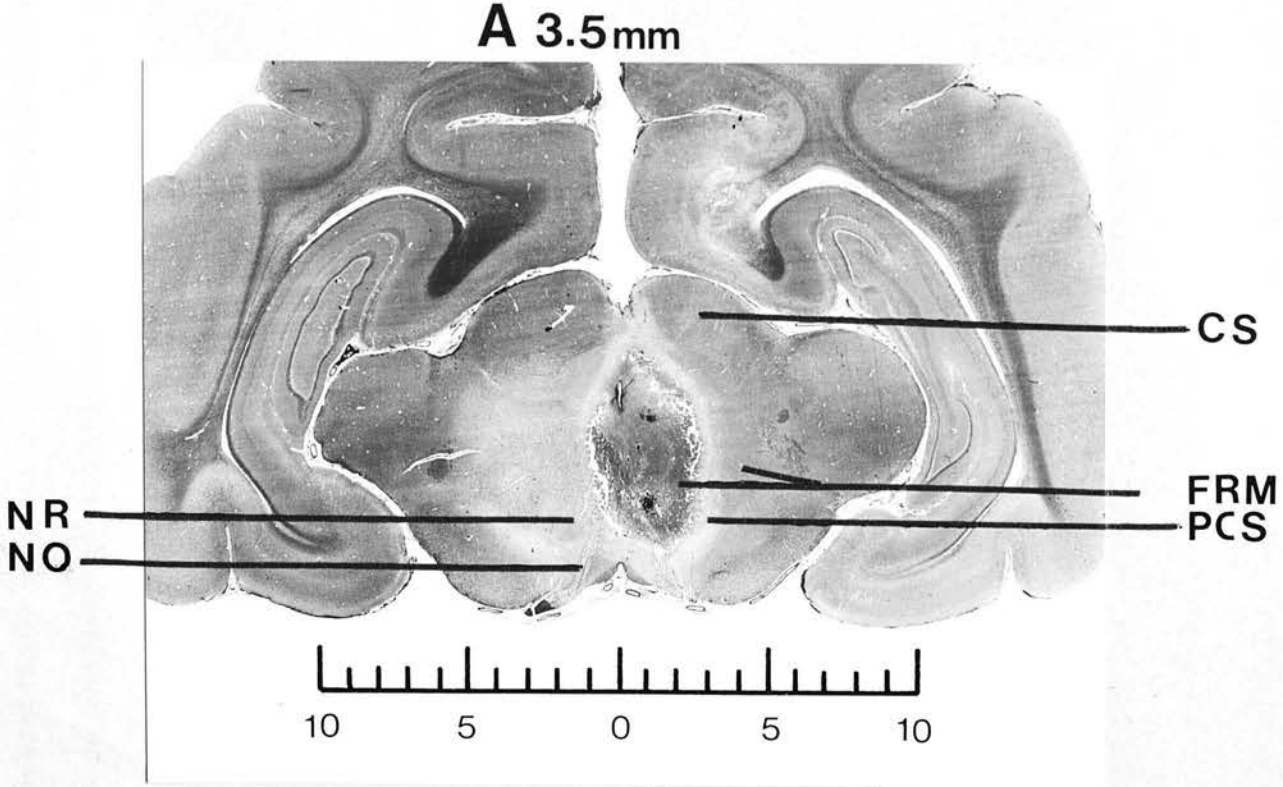


Fig. 7:7

A central lesion of the midbrain at $A_{3.5}$ to produce decerebrate rigidity.

stimulation; this produced marked overactivity and progression movements. A similar result was obtained with one other animal.

In one of these two animals bilateral lesions of the lateral reticular formation of the mesencephalic tegmentum were then made with the electrode tip at A_2 $R/L_{3.5}$ H_{-2}. This resulted in conspicuous enhancement of the spontaneous rigidity.

Combined bilateral and midline lesions

These findings suggested that combined lesions of the lateral and midline reticular areas of the mesencephalic tegmentum might produce more intense rigidity than either bilateral or midline lesions alone. Presumably this would operate by the more complete exclusion of higher inhibition and thus permit increased contralateral facilitatory activity, i.e. enhanced rigidity.

We therefore placed the lesion electrode tip at those co-ordinates which had given a positive reaction to stimulation: these were usually $A_{1.5}$ $R/L_{3.5}$ H_{-2} for lateral and $A_{1.5}$ L_0 $H_{-2.5}$ for midline lesions.

In six animals, one lesion at each of these three locations produced typical decerebrate rigidity: extensor muscle hypertonicity in all four limbs and erection of the tail and dorsal hair (Fig. 7:8). No cardiovascular or respiratory changes were observed.

A representative series of brain stem sections of one animal with severe decerebrate rigidity and without cardio-respiratory complications is shown in Fig. 7:9.

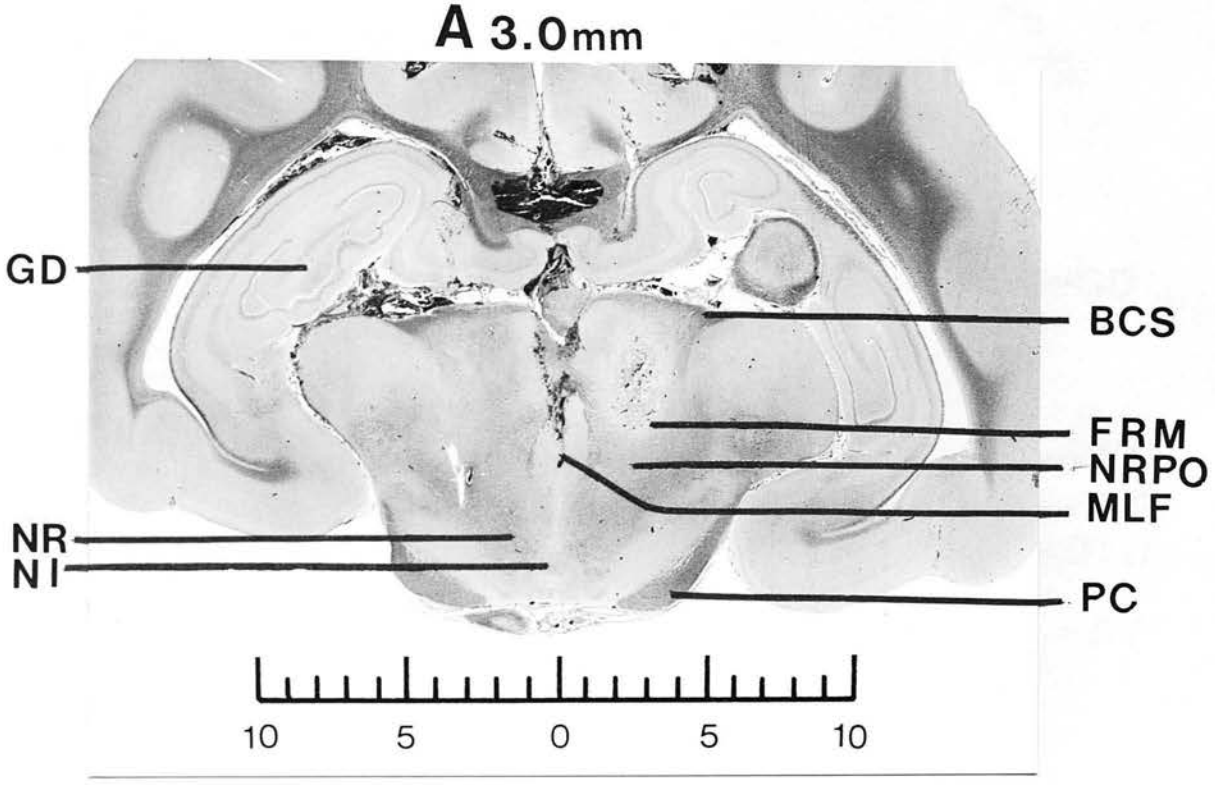
This was not an invariable result, however, and two or even four coagulations at each position were necessary in a few animals (Fig. 7:10). Even this was not always successful

Fig. 7:8

One of the animals with a typical decerebrate posture. The fore limbs are abducted, fully extended and pronated, this being obviously seen in the paws. The hind limbs are outstretched and piloerection of the dorsum hair and erection of the tail is seen.

Fig. 7:9

The following four pages show serial sections of cat brain stem showing the extent of the lesions which produced severe rigidity without being associated with any cardiovascular and respiratory complications.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NR
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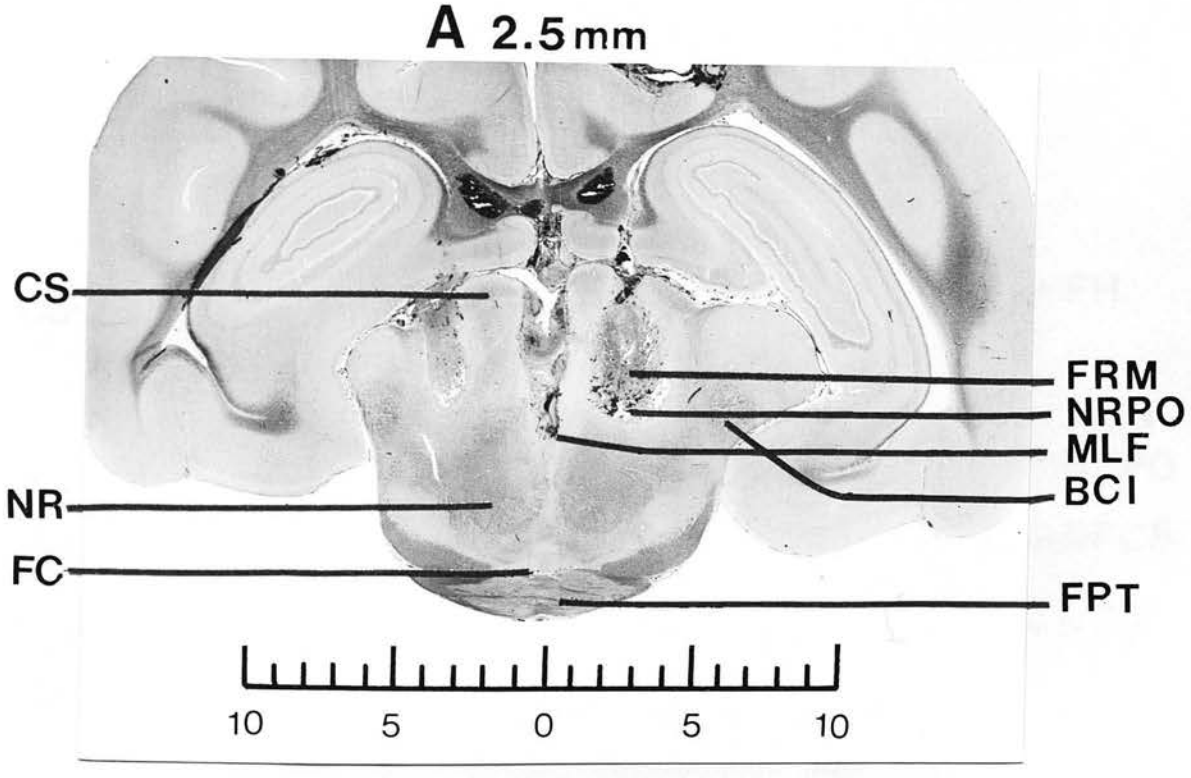
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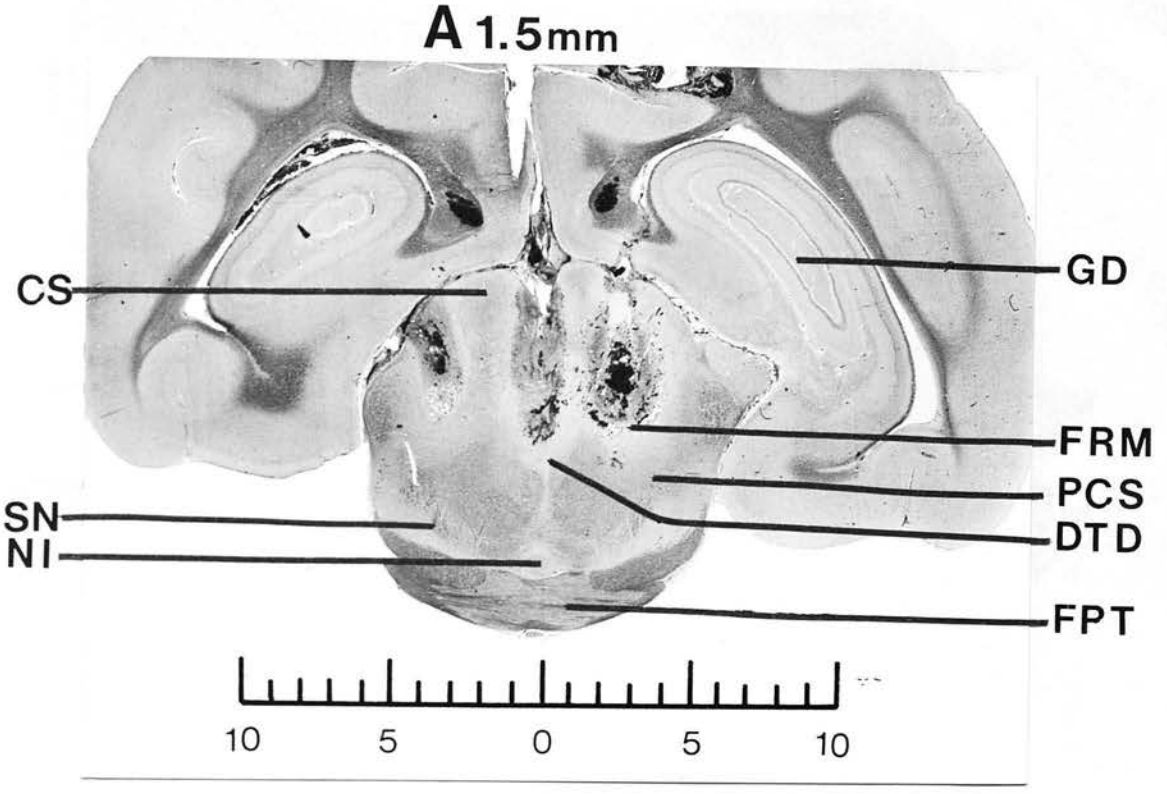
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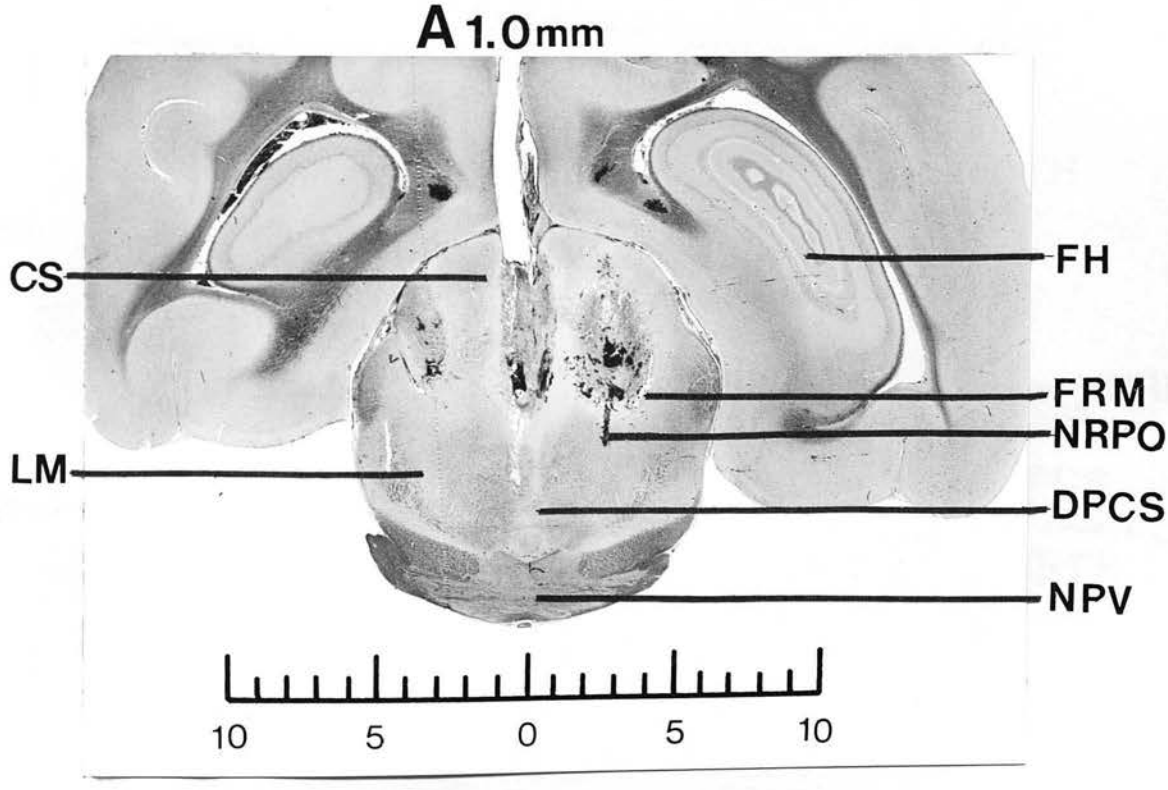
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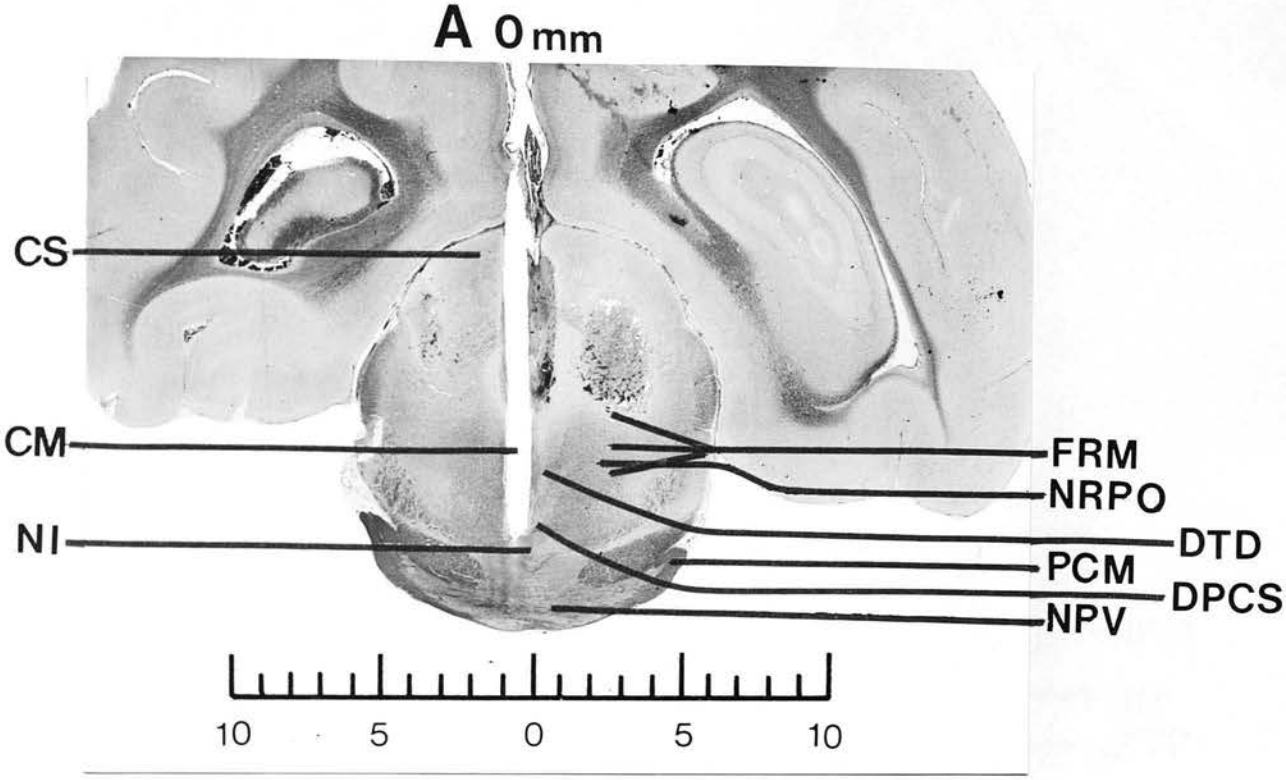
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DPCS
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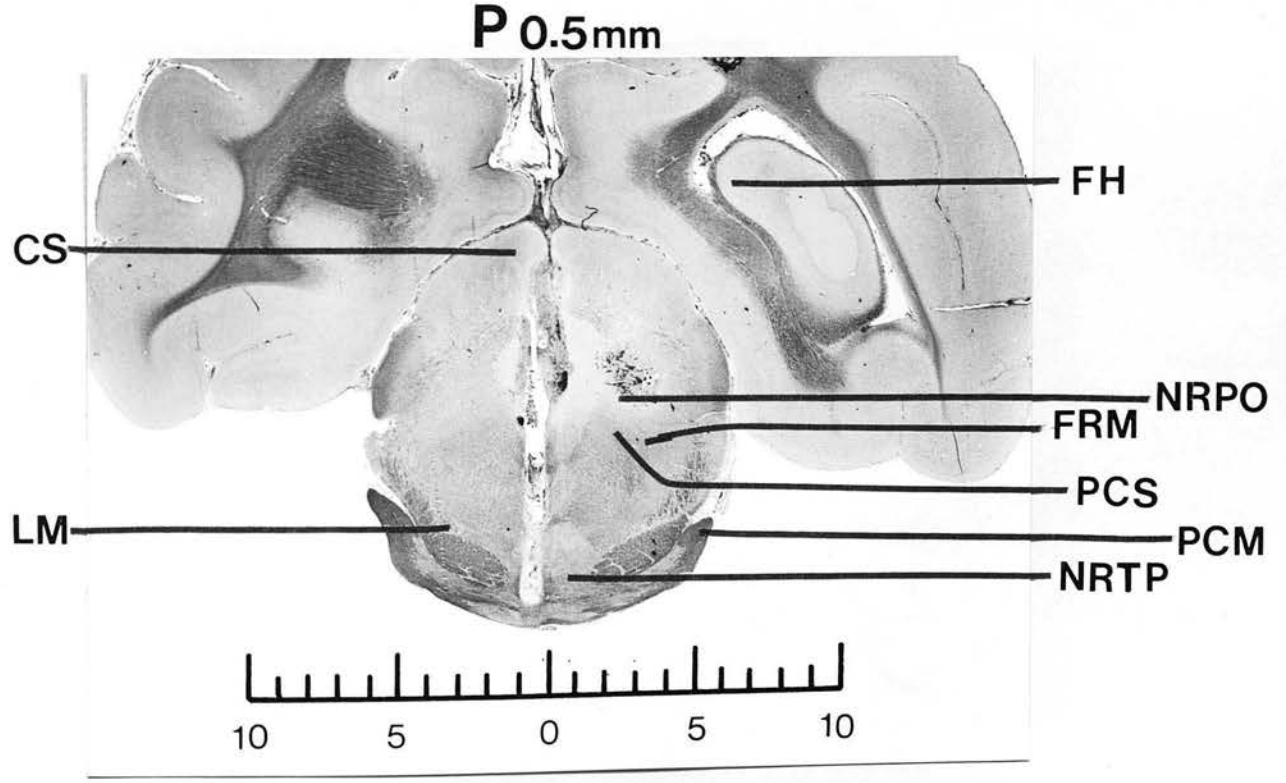
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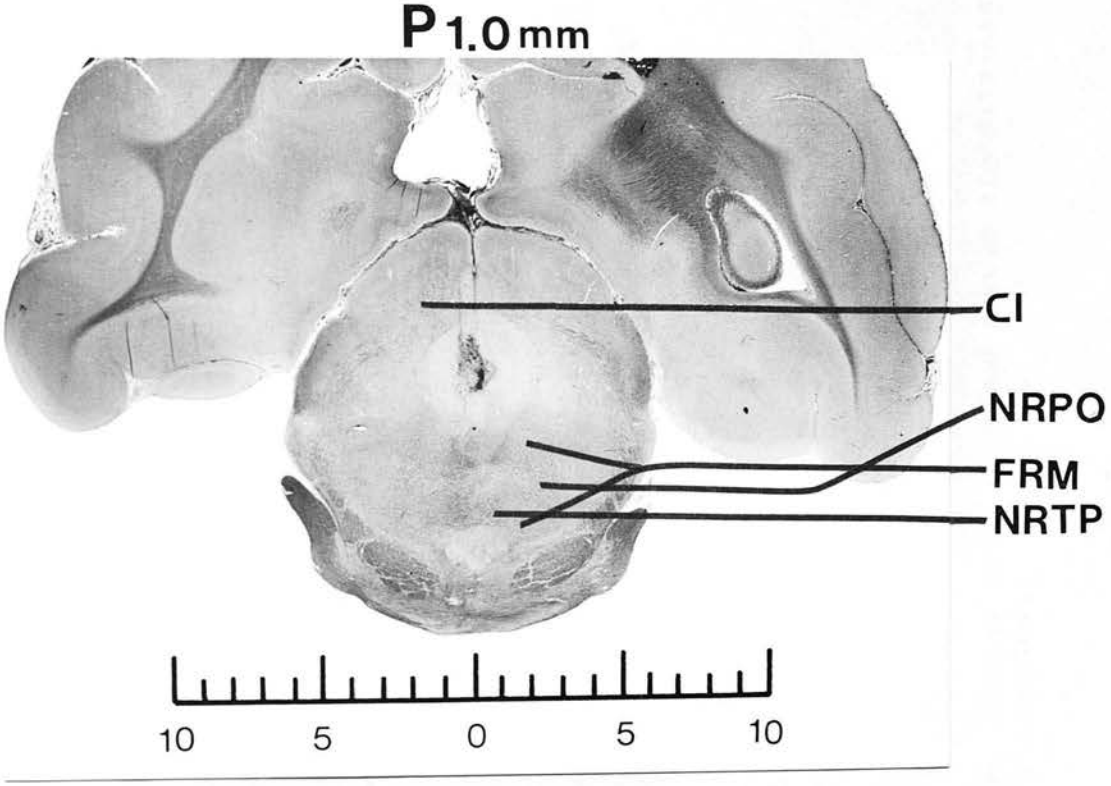
P 1.0 mm
CI
NRPO
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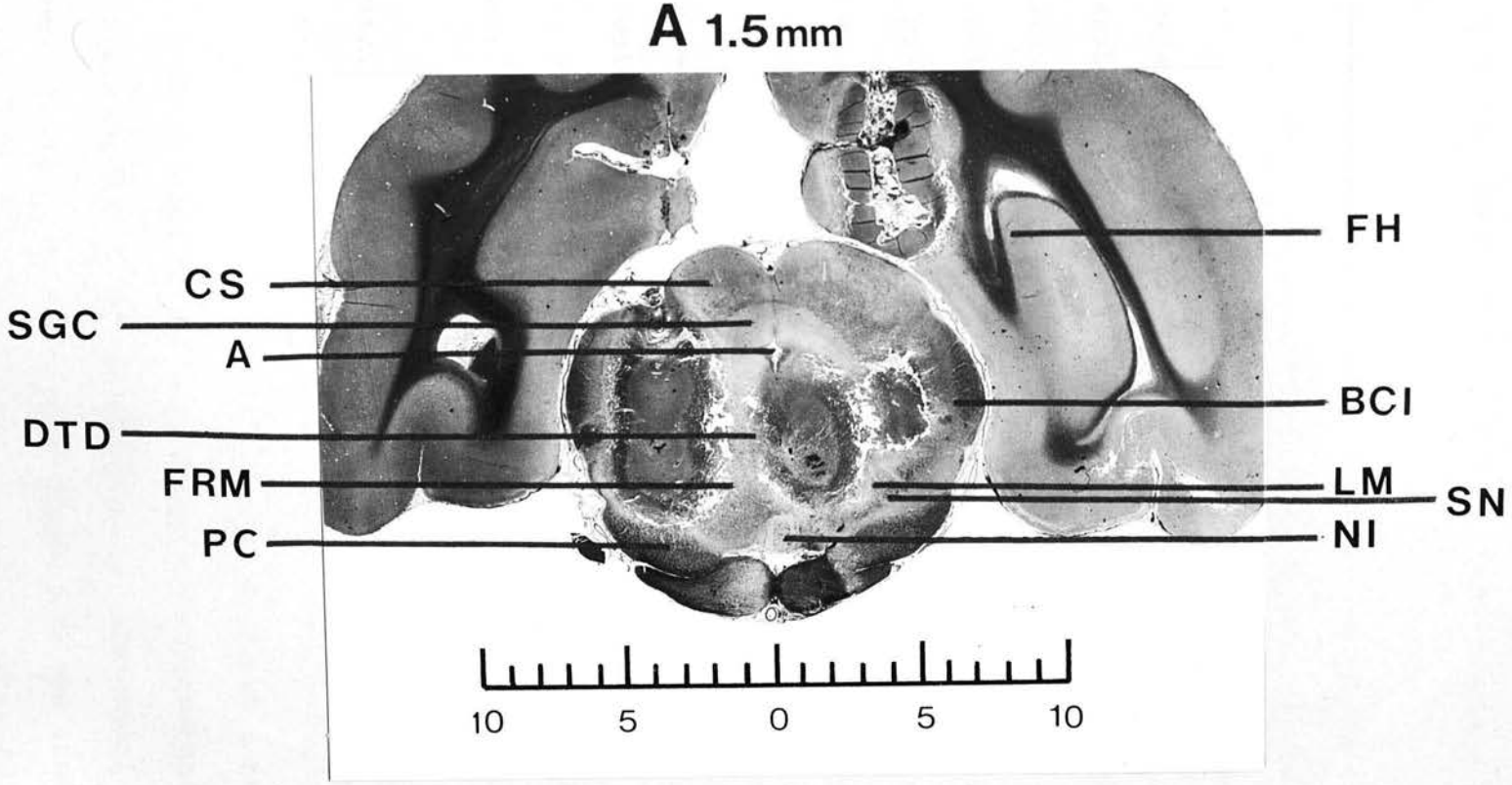


Fig. 7:10

A section through brain stem showing lesions which produced severe rigidity associated with cardiovascular and respiratory complications.

and while extension of the lesions might not increase the rigidity it certainly created cardiovascular and respiratory problems. A 40% reduction in respiratory rate was seen which, however, lasted for only 10-15 minutes; after this time the rate returned to normal during relaxation and was increased during the spasms.

An enormous increase in the systemic arterial pressure was seen in four animals during spasms, the pressure returning to normal with the end of the spasm. In all other animals little or no arterial hypertension developed.

Two animals with severe rigidity had their midbrain mechanically transected by moving the electrode laterally at the intercollicular level. The rigidity, as judged by the EMG activity, was unaltered in one and in the other rigidity was abolished so completely that even handling of its joints failed to bring it on.

PATHOLOGICAL STUDY OF THE LESIONS

The lesions are essentially the same as those seen in the guinea pigs but vary considerably in appearance, depending on the exact relationship of the section to the axis of the lesion.

A central cavity is surrounded by a zone of tissue in which all staining tends to be exaggerated and the nuclei are dense and compact; this, in turn, is surrounded by a halo of tissue in which similar nuclear changes are accompanied by pallor of staining and a variable degree of parenchymal vacuolation. Vascular thrombosis is limited to the inner zone of coagulation and a polymorph inflammatory reaction is well-developed in only one case.

DISCUSSION

There is no doubt that lesions of the mesencephalic reticular areas result in decerebrate rigidity (Denny-Brown 1962) but the minimum lesion which will elicit this effect remains to be defined. Denny-Brown (1966) believed that the lesion essential for the development of rigidity was one in the interstitial nucleus of Cajal whose inhibitory influence on the caudal reticular formation would thus be diminished. Rigidity would then be due to enhancement of the facilitatory effect of this structure on spinal motorneurons, via the uncrossed medial reticulospinal tract.

Mettler (1968), whilst agreeing with this account of the pathophysiology of rigidity, argued that precise details of the pathways involved were still lacking. In his experience, not only could lesions of the tegmental reticular complex occur without rigidity but rigidity could also result from lesions which did not directly involve it at all. He considered that Denny-Brown's definition of the interstitial nucleus was not one generally agreed, including as it did, elements beyond the fibres of the medial longitudinal fasciculus. All investigators (Brown 1914, Ranson and Hinsey 1929, Ward 1947, Denny-Brown 1966) are in general agreement that the pontine reticular substance is primarily involved in the facilitation of muscle tone and that, if its activity is released from inhibition, rigidity ensues; and that this inhibitory centre is located somewhere about the level of the inferior colliculus.

In the two cats in which large lesions were made at the intercollicular level with the highest voltage not only was the mesencephalic but also the pontine reticulum destroyed; this

probably prevented any manifestation of decerebrate rigidity even after handling stimulation of the animal.

In all other animals the mesencephalic and in some the oral but never the caudal pontine reticular areas were affected.

The six animals in which minimal lesions produced maximum rigidity without either respiratory or cardiovascular irregularities were considered to be ideal preparations because the absence of such complications allowed their study to be prolonged for as long as necessary.

While most would agree that the mesencephalic reticulum was indeed damaged as shown in Fig. 7:9, it can always be argued that there might have been physiological lesions in areas important for the development of rigidity. Radiofrequency lesions do involve production of heat and damage to blood vessels at a distance may result in oedema. It is very difficult to get round this objection in acute experimental decerebrate rigidity because the animal cannot be kept long enough to obtain clear-cut evidence of what is functional and what is not. Chronic experiments might have been more informative but these were beyond the purpose of the present study. There is no doubt that this is a fascinating problem which requires a great deal of technical ingenuity and skill as well as much help from devoted animal personnel for its proper investigation.

Relevant clinical cases are those who have survived unconscious for one or two years following an interpeduncular haemorrhage. Such patients may show no decerebrate rigidity, either flexor or extensor, despite the presence of very extensive tegmental lesions. Such human material is regrettably rare.

The degree of rigidity ranged from mild to severe and did not necessarily correlate with the size of the lesion. Two small bilateral lesions were enough to produce severe rigidity whereas in an animal with slight to moderate rigidity extension of the lesion did not always increase the rigidity. The wide variation in rigidity which has been seen by all investigators after even the most complete transections (Ranson and Hinsey 1929, Creed et al. 1932) has been attributed to details in local trauma. The variability of the rigidity in this study could be due either to incomplete destruction of the inhibitory circuit or to extension of the lesion to the facilitatory pathways.

Pathways for the cortical recognition of respiratory activity are known to pass up through the rostral tegmentum as also do the cortical connections of the cardiac medullary centres. Sparing of these pathways by lesions located as in Fig. 7:9 would explain why the animals showed none of the respiratory and cardiovascular complications of larger lesions.

Spontaneous progression movements, vocalisation and occasional switching of the tail were observed in animals in which a midline lesion only was made or when bilateral lesions were made 2.0 mm or more anterior to the intercollicular level. Similar motor reactions have been described by Woodworth and Sherrington (1904), Bazet and Penfield (1922) and Ranson and Hinsey (1929) in acutely decerebrate animals with pre-collicular lesions. These movements were attributed to incomplete inhibition of the mesencephalic reticulum in which the integration centres for such primitive reflex motor phenomena are known to be located.

When a lesion was made 1.5 to 1.0 mm anterior to the intercollicular level the animal became quiet and immobile. Sprague et al. (1961) observed similar akinetism in cats following lateral tegmental lesions of the midbrain and attributed it to sensory deprivation from damage of the medial lemnisci. Denny-Brown (1962), however, was able to show that such an effect was produced even when both lemnisci were intact. The absence of reaction is a motor phenomenon analogous to the "akinetic mutism" seen clinically.

The mesencephalic reticular formation is known to be driven by the perceptual facilitatory apparatus of the tectum, stimulation of which leads to a variety of movements, including these of the eyes and limbs (Lance 1970). A lesion of the tectum would partially inactivate the mesencephalic reticulum. Tectal lesions in the brain stem of the cat impaired wakefulness as judged from the EEG trace (Lindsley et al. 1949). Sparing of the tectum, therefore, in some of our preparations evidently preserved a degree of reactivity which could be abolished by relocating the tip of the electrode to the intercollicular level at a depth near the vertical zero position. The fact that cessation of progression movements is associated with well-developed decerebrate rigidity suggests that complete inactivation of the mesencephalic reticulum occurs. Progression movements were seen in cases in which much of the rigidity had been induced by handling the animal, whereas in spontaneous rigidity such movements were not seen. This observation would suggest that severe rigidity in an akinetic animal is compatible with complete inactivation of the mesencephalic reticulum.

CHAPTER 8

THE EFFECT OF DECEREBRATE RIGIDITY ON INTRACRANIAL PRESSURE IN THE CAT

INTRODUCTION

Elucidation of the effect of pure decerebrate rigidity on the ICP demanded that, as far as possible, other factors which might affect intracranial dynamics, such as haemorrhage, swelling, acute hydrocephalus and hypoxia (all of which frequently complicate brain stem injuries) should be eliminated. An experimental study of the effects of decerebrate rigidity produced in cats by focal mesencephalic lesions was undertaken in parallel with a clinical study of this problem.

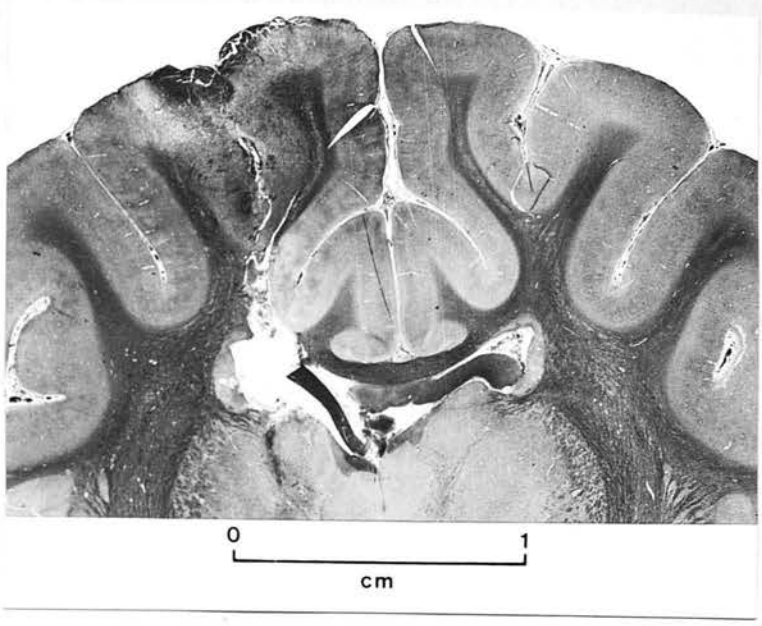
MATERIAL AND METHODS

Twenty-six healthy cats weighing between 2.5 and 3.5 Kg were used.

Anaesthesia was induced with Halothane (Halothane - May and Baker Ltd.), nitrous oxide and oxygen. An endotracheal tube (Y - Portex) was inserted and light anaesthesia maintained with Halothane 0.5 - 1%. nitrous oxide 70% and oxygen 30%.

The intracranial pressure was measured by means of a micro-tip catheter pressure transducer (Millar 7F, PC-470) in the right lateral ventricle (described earlier) (Fig. 8:1). Accurate recording did not depend on precise ventricular implantation, the transducer giving a perfectly adequate reading when implanted in the brain parenchyma of the cat (Clark et al. 1975) and human (Jeffreys and Wood 1977).

Central Venous Pressure (CVP), systemic arterial pressure (SAP): The venae cavae were cannulated through either the external jugular or left femoral vein in order to measure the CVP, and the SAP was measured through a cannula introduced into the thoracic



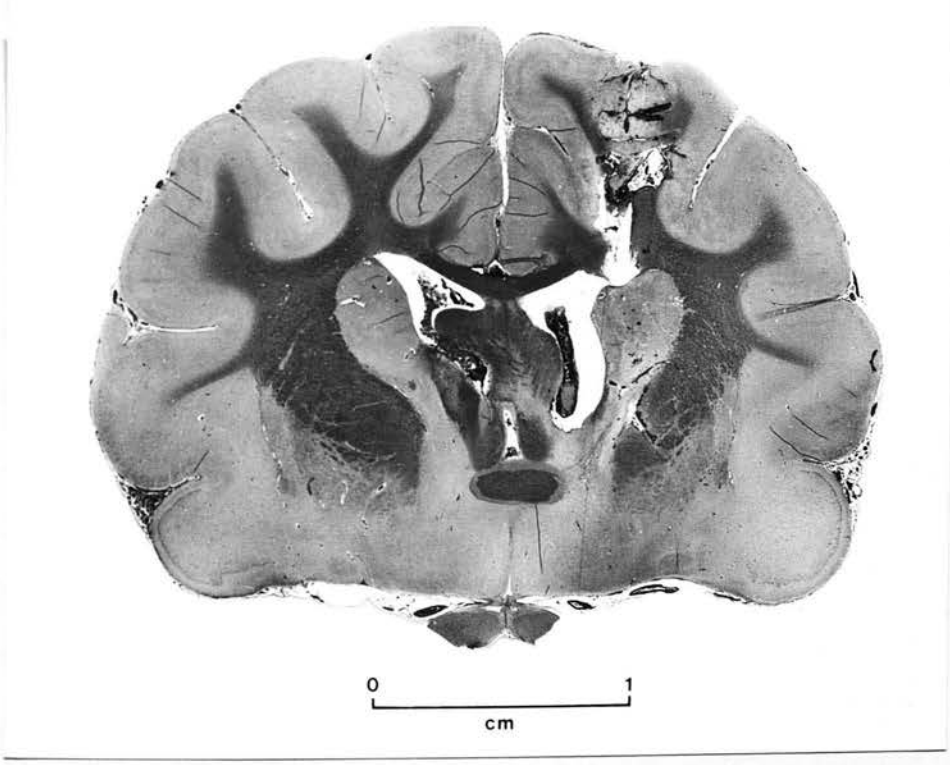


Fig. 8:1 a & b.

Sections of two cat brains through the ventricular system; track of insertion of the Millar transducer into the lateral ventricle. (Loyez stained. Magnification x 4).

aorta via the left femoral artery; in each case a 60 cm, OD 1.65 mm (12G) cannula (Portex) was used.

Intrathoracic (ITP) and intra-abdominal pressure (IAP): These were measured by small oesophageal catheters (Morgan Ltd) introduced into the lower end of the oesophagus and the stomach (see Chapter 5).

Respiration: In the majority of the animals respiratory events were assessed from the ITP tracing but in a few the chest was encircled by a mercury-filled rubber tube so that the respiratory excurions could be displayed on a calibrated chart (stethogram).

The vascular cannulae and the oesophageal catheter(s) were connected, via physiological pressure transducers (Bell and Howell, type 4-422-0001/2 - described in detail in Chapter 3), along with the Millar micro-tip transducer, to a heat-pen recorder (Devices - M-19) for the continuous recording of the ICP,CVP, SAP, ITP and IAP.

Muscle tone was assessed from the electrical activity recorded with bipolar needles from the upper and lower limb muscles (Fig. 7:8) on a multichannel EEG recorder (Officine Galileo, Mod. E8a).

Electrocardiogram (ECG) was continuously recorded (lead II, intramuscular needles) on a heat-pen recorder (Devices - M-4).

Temperature: The animal's rectal temperature was kept constant at 38.0 - 38.5^{o}C by means of a thermostatically controlled electric blanket.

Arterial blood gases and acid-base balance: Systemic arterial pCO_2, pO_2, hydrogen ion activity (H^+) and standard bicarbonate were determined at approximately 20 minute intervals throughout the investigation. An intravenous infusion of Ringer lactate

solution was continued throughout and 2.3 ml of sodium bicarbonate solution were given intra-muscularly every hour. The arrangement of the animal set up is shown in Figs. 8:2, 8:3 and 8:4.

RESULTS: PRELIMINARY STUDY IN NORMAL NON-DECEREBRATE ANIMALS

In view of the probable complexity of the interplay of factors involved in alteration in ICP during decerebrate rigidity we undertook a pilot study of some of these on six non-decerebrate animals (Table 8:1).

These were set up as described and differed from the decerebrate animals only in so far as no stereotactic procedures were performed.

In two animals the external and internal jugular veins were temporarily occulded by ligatures. The internal jugular vein of the cat receives blood from the venous sinuses of the brain (inferior cerebral), from an occipital vein, from muscular branches and from pharynx and palate (Crouch and Lackey 1969).

The SAP was increased by the use of intravenous angiotensin (Vasopressin - Ciba), 0.01 µg/Kg and 0.1 µg/Kg.

The CVP was raised by the quick injection of a bolus of 30 ml of physiological saline into the venae cavae, repeated if necessary.

Paediatric sphygmomanometer cuffs were used to increase the intrathoracic and intra-abdominal pressures.

During induction, the mean normal ICP in the six cats was found to be 6.5 $\pm$ 1.9 mmHg (range 3.0 - 11.0 mmHg).

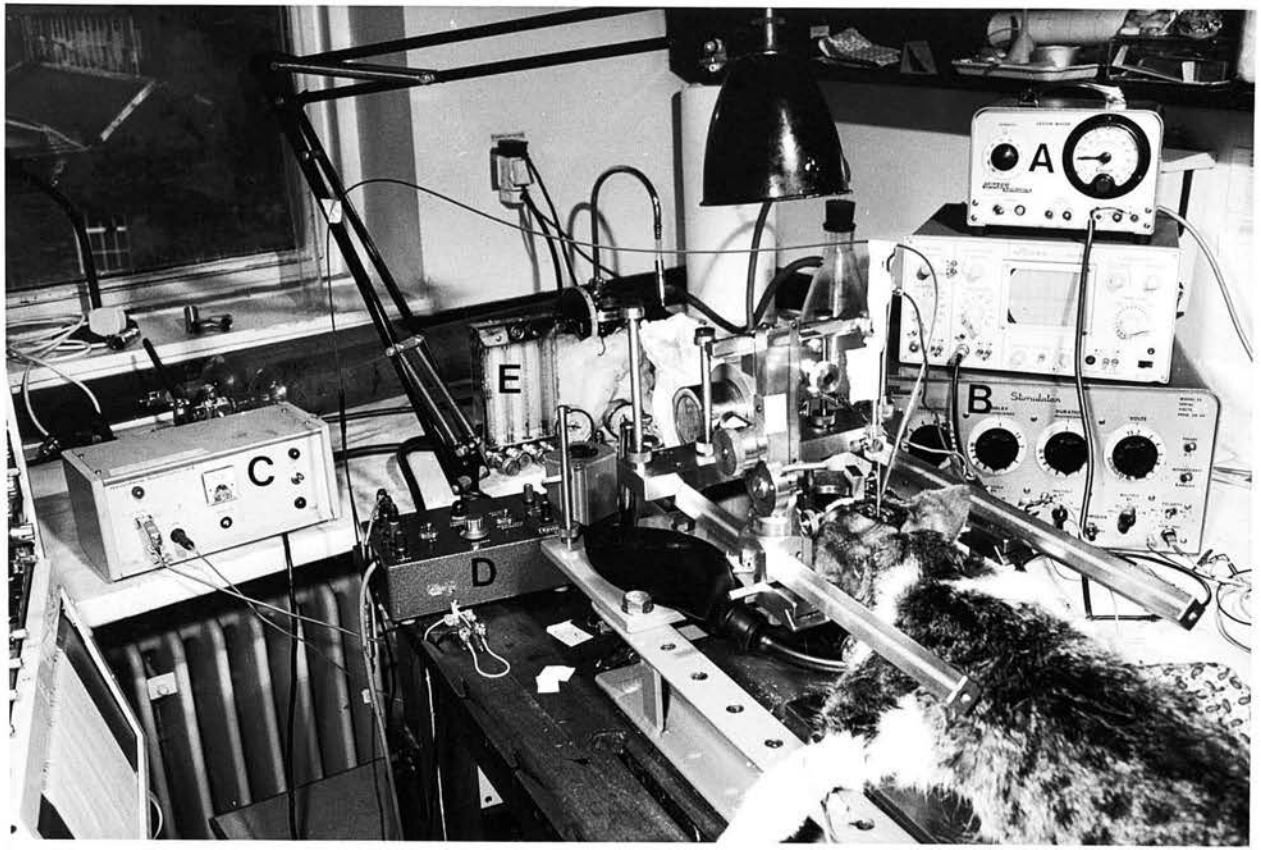


Fig. 8:2

Arrangement of experiment: A: Lesion maker, B: Stimulator, C: Homeothermic blanket control, D: Impedance control, E: Anaesthetic gas flow meter.

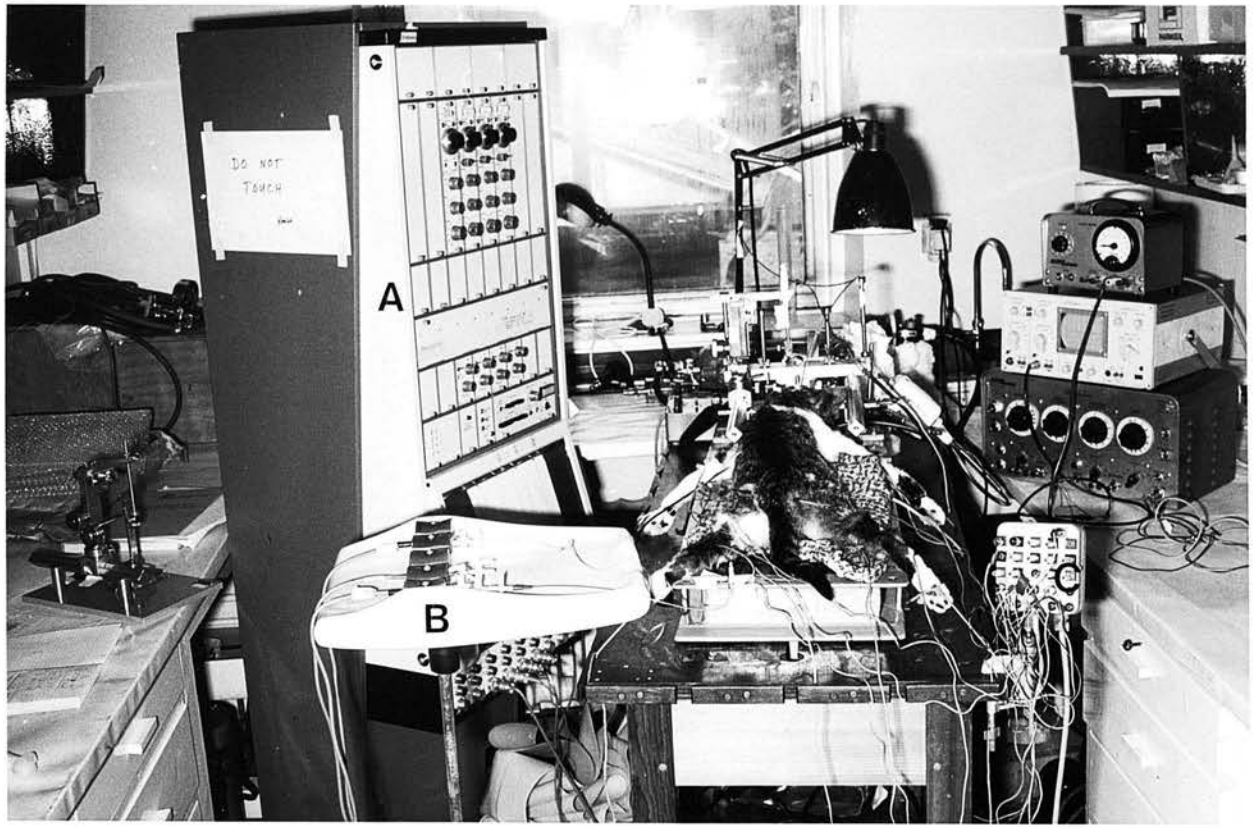


Fig. 8:3
Arrangement of experiment: A: Recorder, B: Table for fixing the transducers, C: EMG electrode panel.

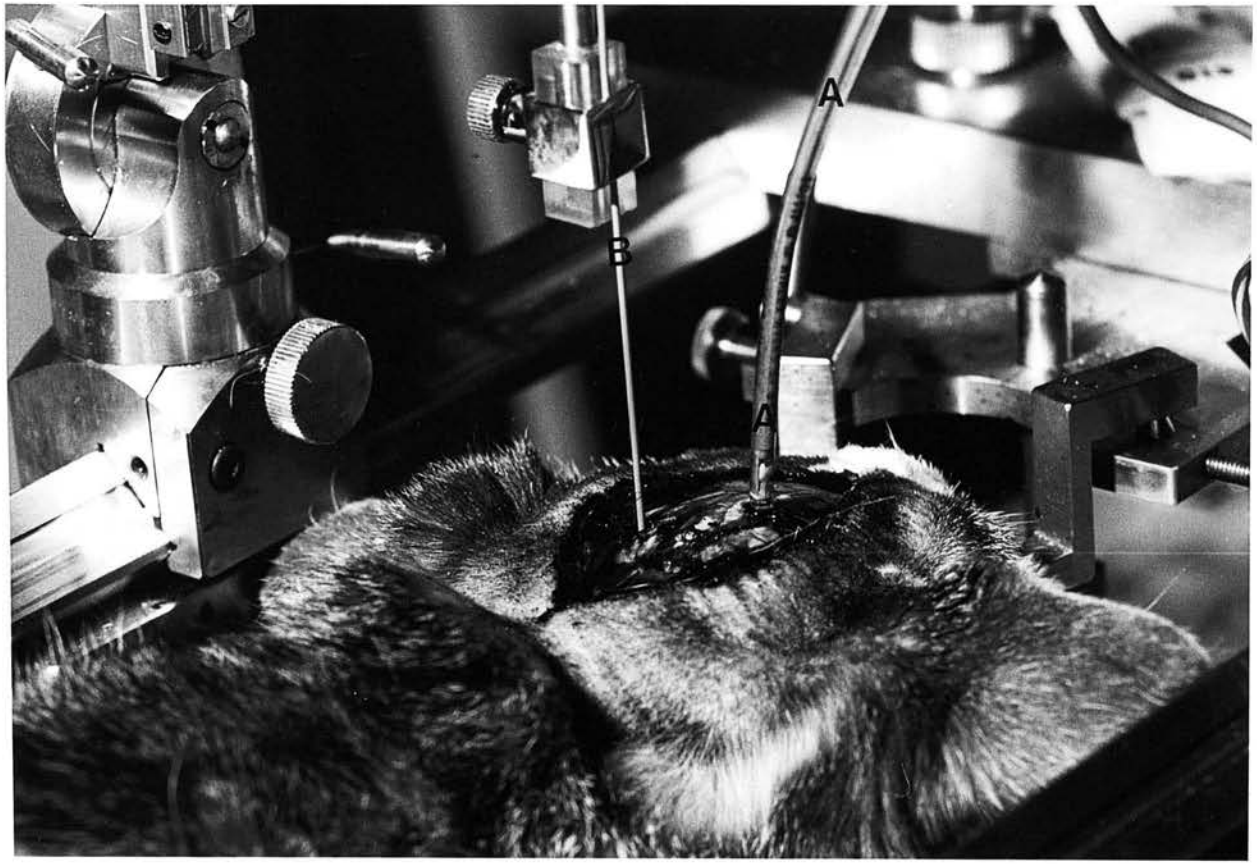


Fig. 8:4
Arrangement of Millar transducer (A) and stimulation electrode (B)

ANIMALS WITHOUT DECEREBRATE RIGIDITY

1) LIGATION OF BOTH JUGULAR VEINS BILATERALLY

2) ELEVATION OF THE CENTRAL VENOUS PRESSURE (CVP)

3) ELEVATION OF THE SYSTEMIC ARTERIAL PRESSURE (SAP)

4) ELEVATION OF THE INTRATHORACIC PRESSURE (ITP)

5) ELEVATION OF THE INTRABDOMINAL PRESSURE (IAP)

6) SIMULTANEOUS ELEVATION OF THE ITP AND IAP.

7) SIMULTANEOUS ELEVATION OF THE ITP, IAP AND SAP.

Table 8:1

Obliteration of the internal & external jugular veins

Obliteration of the internal jugular veins alone or in conjunction with the external jugular veins produced a sudden but minor and transient (lasting a few seconds) rise in the mean ICP of 4.7 $\pm$ 1.9 mmHg (range 3.0 - 8.0 mmHg) above the normal level (Fig. 8:5).

Increase in the central venous pressure

The rapid injection of a bolus of 30 ml of saline into the venae cavae produced an immediate small (6.3 $\pm$ 1.5 mmHg) and very transient increase in ICP which had, in fact, returned to normal by the end of the injection.

Increase in the intrathoracic pressure

A pressure of 60 mmHg applied to the thorax via a sphygmomanometer cuff raised the mean ICP to 12.4 $\pm$ 3.1 mmHg (range 8.5 - 16.0 mmHg) above its normal value and this increase was maintained as long as the ITP was kept elevated. Further elevation of the external pressure, up to 100 mmHg, resulted in a profound drop in the mean systemic arterial pressure (MSAP) and a great reduction in both the amplitude and frequency of the arterial pulse (Fig. 8:5). These changes were severe enough to endanger the animal, and the cuff was deflated immediately (Table 8:2).

Increase in the intra-abdominal pressure

The external application of 60 - 100 mmHg pressure to the abdomen increased the mean ICP to 20.5 $\pm$ 4.5 mmHg (range 16.0 - 25.0 mmHg) above normal level; the amplitude of its fluctuations was also increased. In contrast to the effect of elevating the ITP, the MSAP was slightly increased, while the amplitude of

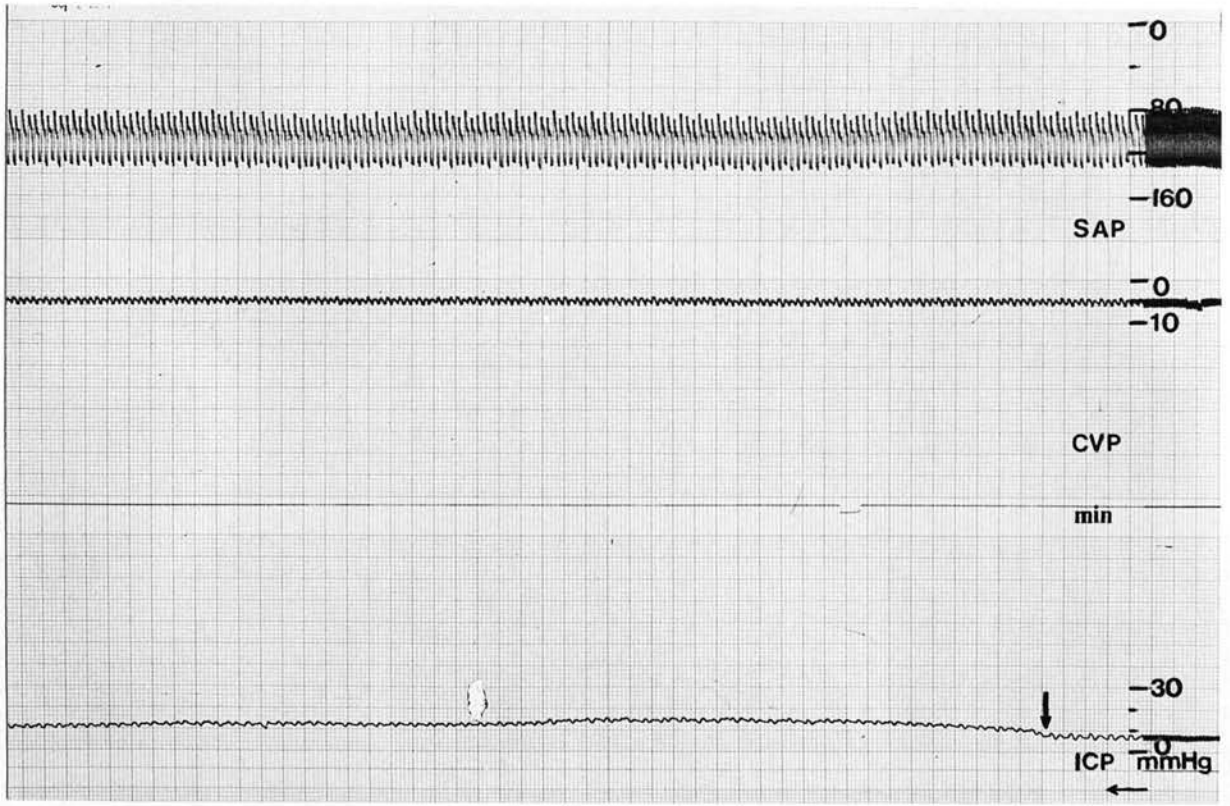


Fig. 8:5

Effect of occlusion of the internal and external jugular veins bilaterally (arrow) on the ICP, SAP and CVP.

the arterial pulse was increased and the rate marginally decreased. The CVP remained unaltered (Fig. 8:6).

Simultaneous increase in the ITP and IAP

Simultaneously increasing the ITP and IAP resulted in a very marked increase in the average ICP to 57.8 $\pm$ 3.4 mmHg (range 53.0-62.0 mmHg) which is much more significant ($t=13.2$, $P < 0.001$) than the increase in ICP produced by raising the ITP and IAP separately. This intracranial hypertension was accompanied by a very significant ($t=4.91$, $P < 0.005$) elevation in CVP; the MSAP was largely unaffected and the amplitude of the arterial pulse was reduced. The intracranial hypertension was maintained for as long as the ITP and IAP were kept elevated (fig. 8:7).

Simultaneous increase of the ITP, IAP and SAP

The SAP was raised by the intravenous injection of Vasopressin. This produced a very small and insignificant increase in ICP. When the systolic pressure had risen to 220 mmHg or more and the diastolic to 160 mmHg (the MSAP being 150.4 $\pm$ 15.3 mmHg, range 137-176 mmHg) the thoracic and abdominal cuffs were rapidly inflated to a pressure of 60 mmHg. This resulted in a marked increase in the average ICP of 64.0 $\pm$ 4.4 mmHg (range 58-70 mmHg) above the normal level; this rise, however, was not significantly different ($t=2.20$, $P > 0.05$) from that which resulted from the simultaneous increase in ITP and IAP. Release of the thoracic and abdominal compression instantly reduced the ICP to a level just slightly above normal (Fig. 8:8).

The CVP was greatly increased at the same time as the ICP; the mean CVP reached levels of 25.8 $\pm$ 2.3 mmHg (range 22.0-28.0 mmHg) above the normal level.
Although this is highly significant

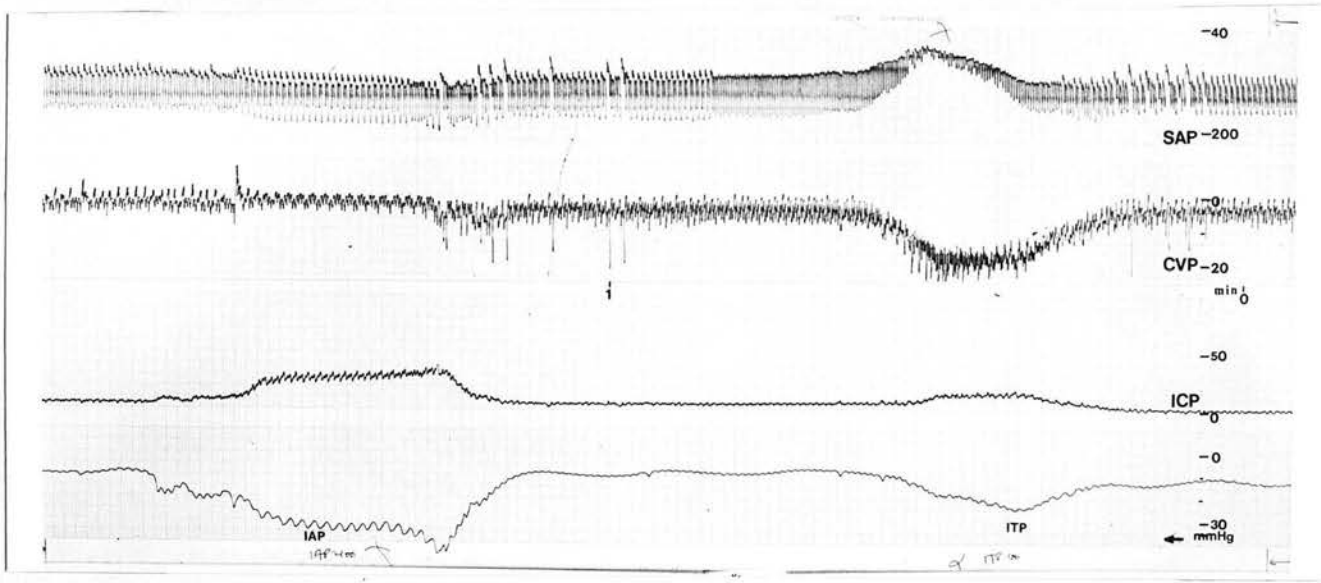


Fig. 8:6

Effect of the directly raised ITP and IAP separately upon the ICP, CVP and SAP. The lower trace is that of the IAP.

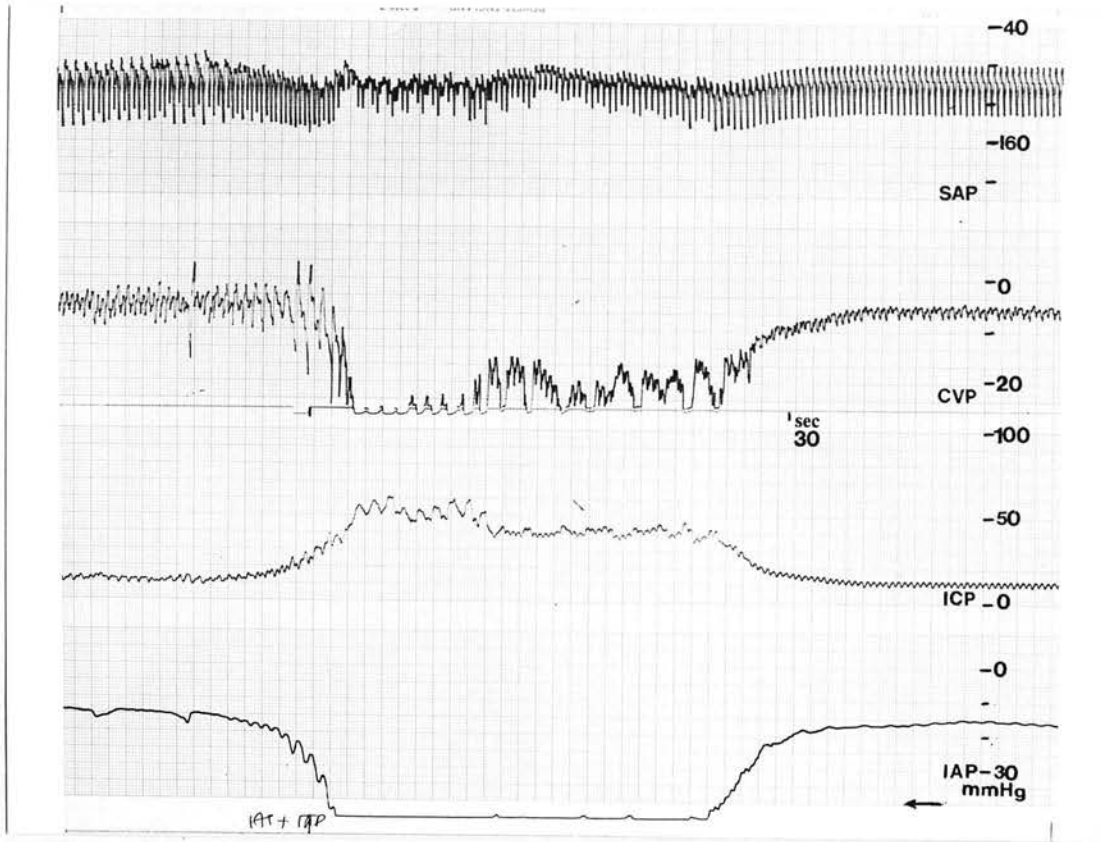


Fig. 8:7

Effect of the simultaneous increase in ITP and IAP upon the ICP, CVP and SAP.

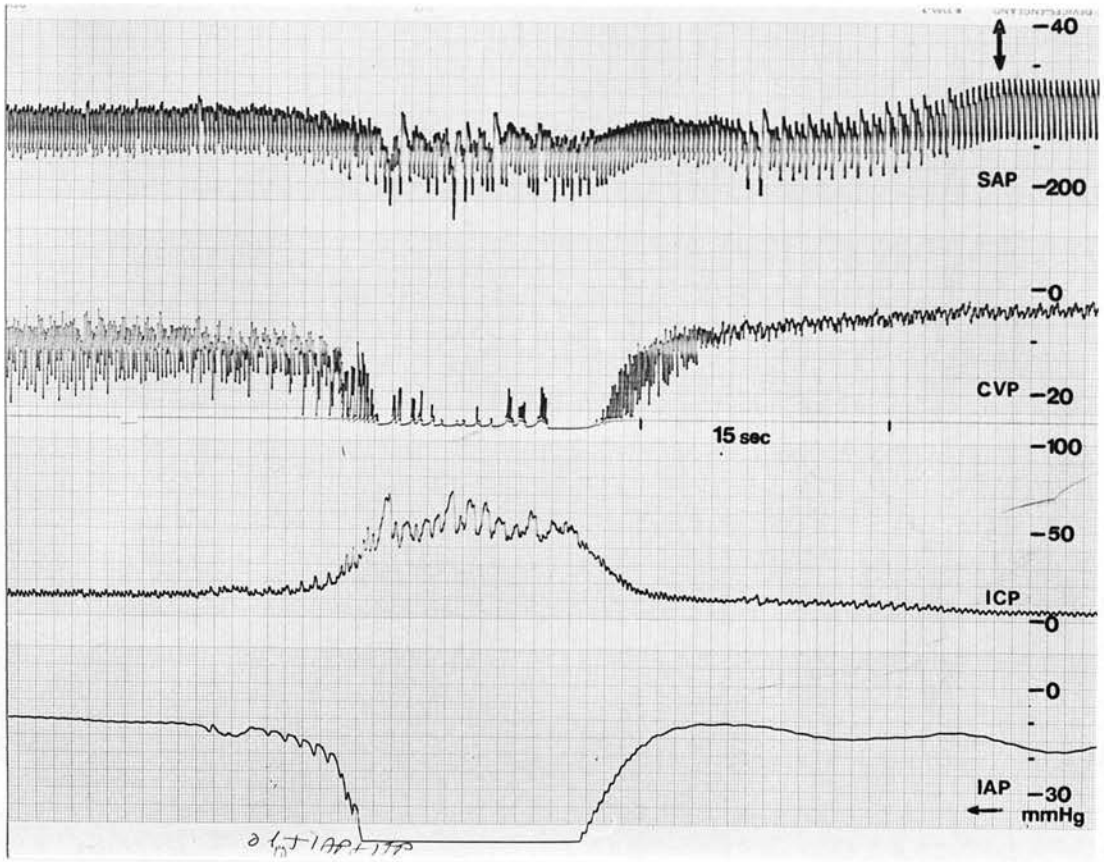


Fig. 8:8

Effect of the simultaneous increase in SAP (arrow shows time of injection of Vasopressin) ITP and IAP upon the ICP.

($t = 8.2$, $P < 0.001$) it is not significantly different from the mean CVP rise due to elevation in ITP ($t = 1.89$, $P > 0.05$).

These changes are summarised diagrammatically in Figs. 8:9a and 8:9b.

RESULTS: MAIN STUDY IN ANIMALS WITH DECEREBRATE RIGIDITY

Each of the twenty animals used in this study was attached to a Narishige stereotactic frame (Model SN-2: Chapter 5). A dental burr (Werk-Bürmoos) was used to make the skull holes, which were sealed with dental cement (Directon Sealant) after completion of the lesions. The method of producing decerebrate rigidity has been described earlier (Chapter 7).

The anaesthetic was discontinued just before the lesions were made and the animal maintained on 40% oxygen. The observations were terminated as soon as decerebrate rigidity had developed and its effects recorded.

Muscle relaxants were not used as

a) we preferred to take advantage of the full time during which the animal was fully rigid and had its gas tensions normal and

b) they were not necessary because the spasms spontaneously waxed and waned and the administration of relaxants would abolish rigidity.

Decerebrate rigidity was produced in twenty cats (Table 8:3).

UNILATERAL LESIONS (3 animals)

All three developed decerebrate rigidity which was predominantly unilateral.

In two of them a continuous tonic muscle contraction (50 μV) had no effect on either the ICP, ITP, CVP or SAP.

In one animal an extreme extensor and flexor spasm (150 μV)

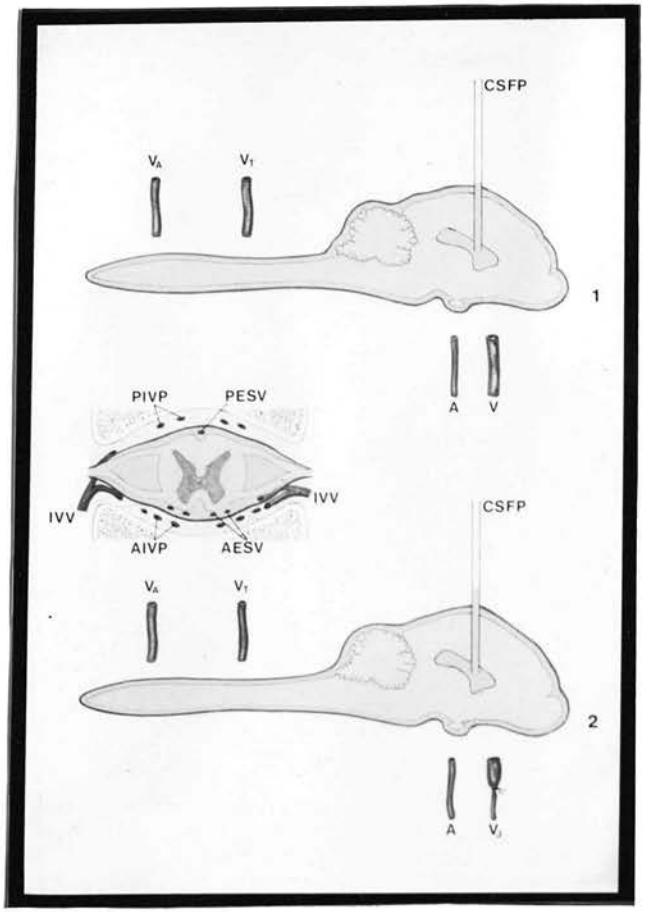


Fig. 8:9a

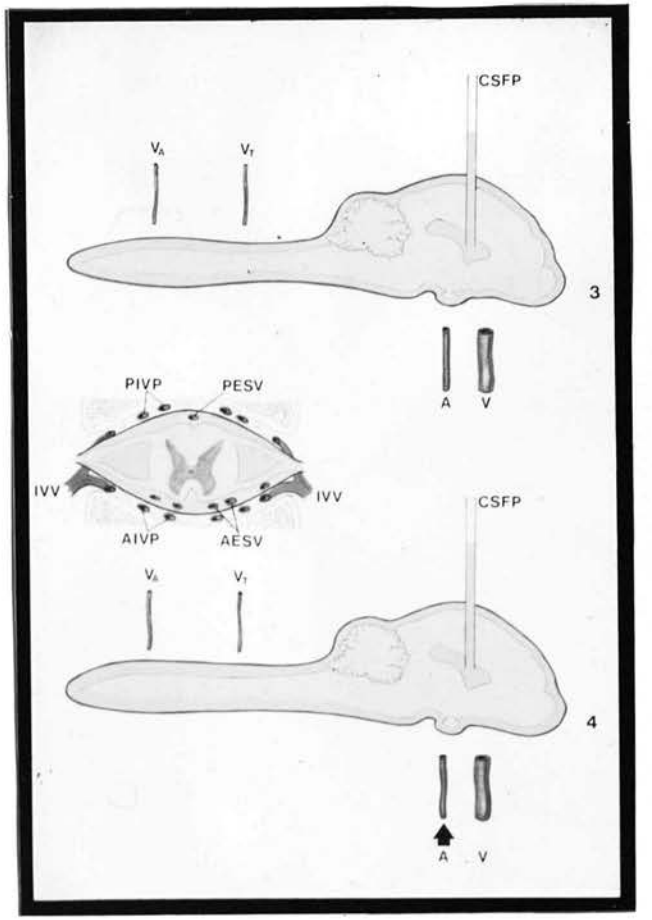


Fig. 8:9b

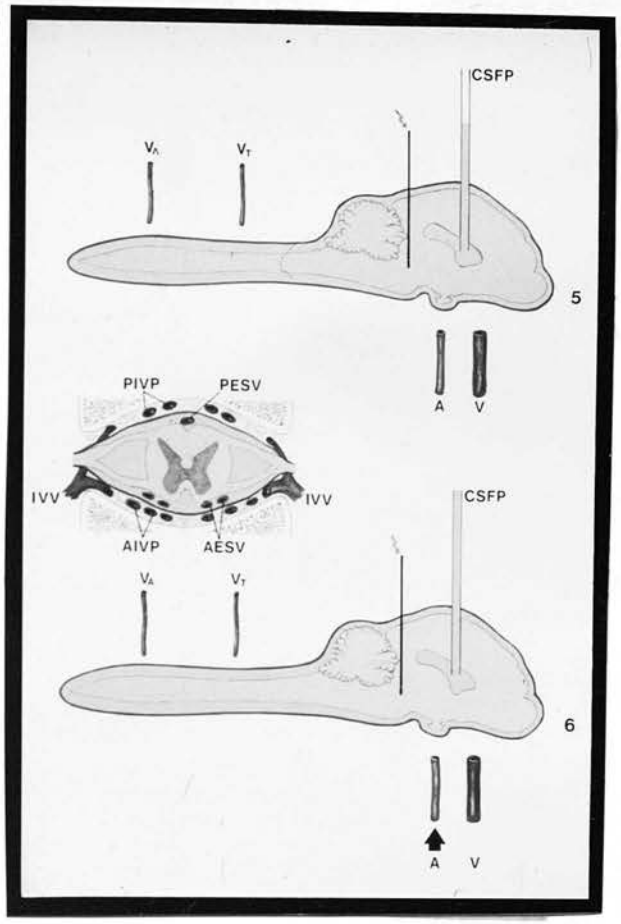


Fig. 8:9c

Schematic representation of the alterations in ICP and its mechanisms in both decerebrate and non-decerebrate animals. 1 normal, 2 ligation of both jugular veins bilaterally, 3 simultaneous elevation in ITP and IAP, 4 simultaneous elevation in SAP (↑), ITP and IAP, 5 changes in ICP during decerebrate rigidity without increase in SAP and 6 changes in ICP during decerebrate rigidity and raised SAP (↑) under conditions of a defective cerebral homeostasis.
A = systemic arterial pressure, V= central venous pressure, V_J = jugular veins, V_T= intrathoracic veins, V_A= intra-abdominal veins, CSFP = cerebrospinal fluid pressure, IVV = intervertebral veins, AIVP = anterior internal vertebral plexus, AESV = anterior external spinal plexus, PIVP = posterior internal vertebral plexus, PESV = posterior external spinal veins.

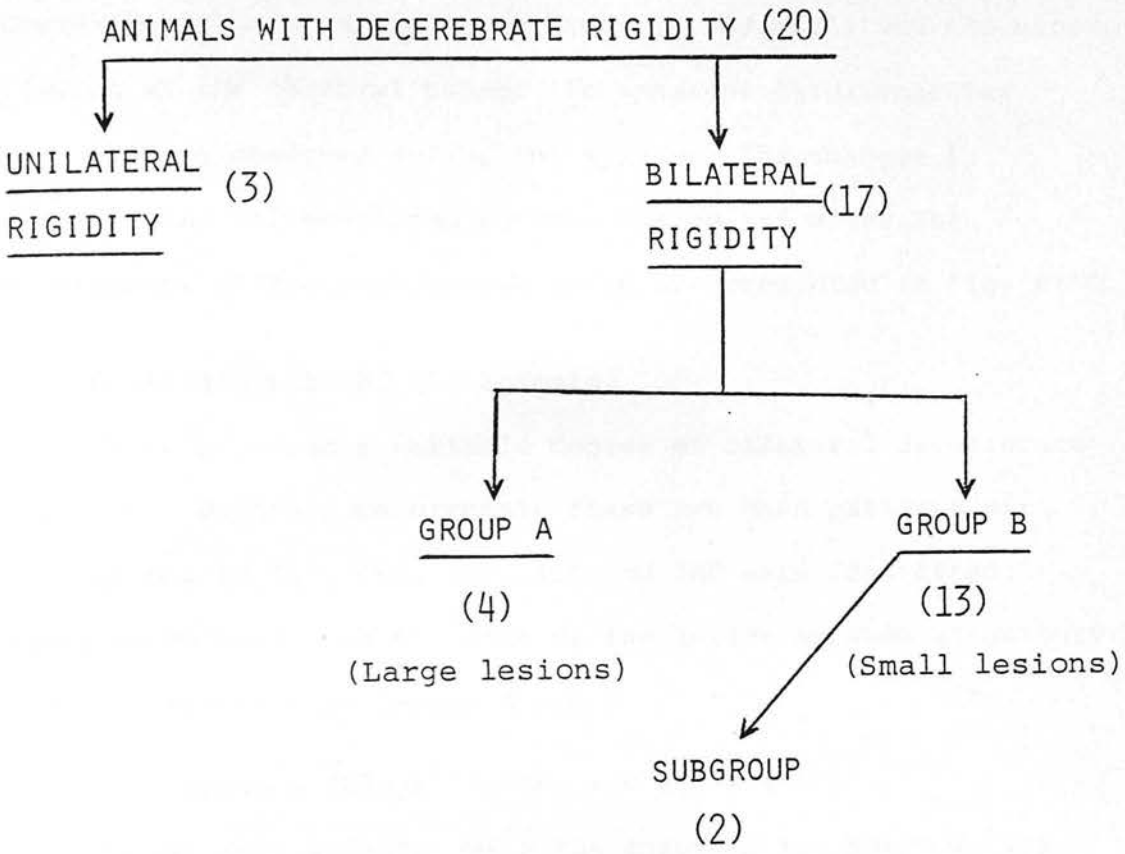

ANIMALS WITH DECEREBRATE RIGIDITY (20)
UNILATERAL RIGIDITY (3)
BILATERAL RIGIDITY (17)
GROUP A
(4)
(Large lesions)
GROUP B
(13)
(Small lesions)
SUBGROUP
(2)

Table 8:3

produced small, transient, phasic changes in the ICP only; these consisted of minimal increases in the amplitude and minor slowing of the cerebral pulse. No apparent cardiovascular changes were observed during the spasms. The changes in ICP, ITP and SAP monitored before, during and after the development of the decerebrate spasm are presented in Fig. 8:10.

BILATERAL LESIONS (17 animals)

These produced a variable degree of bilateral decerebrate rigidity. During a decerebrate spasm two main patterns of alterations in ICP, CVP, SAP, ITP and IAP were identified; these correlated with the size of the lesion as seen at autopsy and are presented as Groups A and B.

Group A (Large lesions - 4 animals)

In all four animals, with the onset of the spasm a very large increase was seen in both the ICP and SAP, while the CVP was relatively less affected (Figs. 8:11 and 8:12); data are presented in Table 8:4.

Intracranial pressure

Introduction of the coagulation electrode into the target area had no effect on either the ICP, SAP or CVP. During coagulation a marked increase in ICP alone was observed. This returned to its previous normal level when the current was switched off (Figs. 8:11 and 8:12).

In the first two animals studied, the peak of the pressure wave was well above the calibration scales of 50 and 100 mmHg; because the increase in ICP during decerebrate rigidity had not been expected to reach such levels, the calibration scale on the recorder had been limited to 0-50 and 0-100 mmHg. Subsequently

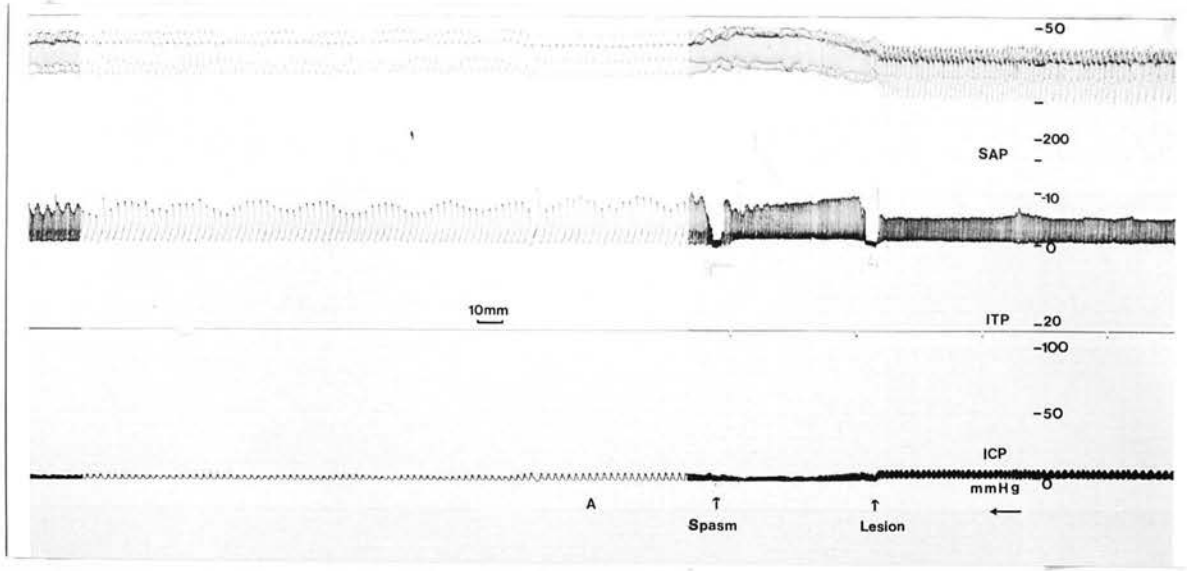


Fig. 8: 10

Changes in ICP, ITP and SAP in a cat before, during and after the development of unilateral severe decerebrate rigidity. The ICP was raised, but only by 2-3 mmHg, above the normal level. Small phasic changes are seen which comprise an increase in the amplitude and slowing of the frequency of the cerebral pulse. The animal virtually stopped breathing in expiration and there was also a small rise in the mean ITP. Despite the initial small fall in SAP following the lesion, which was followed by a reduction of the amplitude of the cerebral pulse, the SAP remained within normal limits and did not alter during the spasm. The ITP regained its previous level when the spasm passed off. Similarly the ICP returned to normal level only when rigidity was decreased (A). The remaining rigidity did not affect the ICP, ITP thereafter (time in minutes: m).

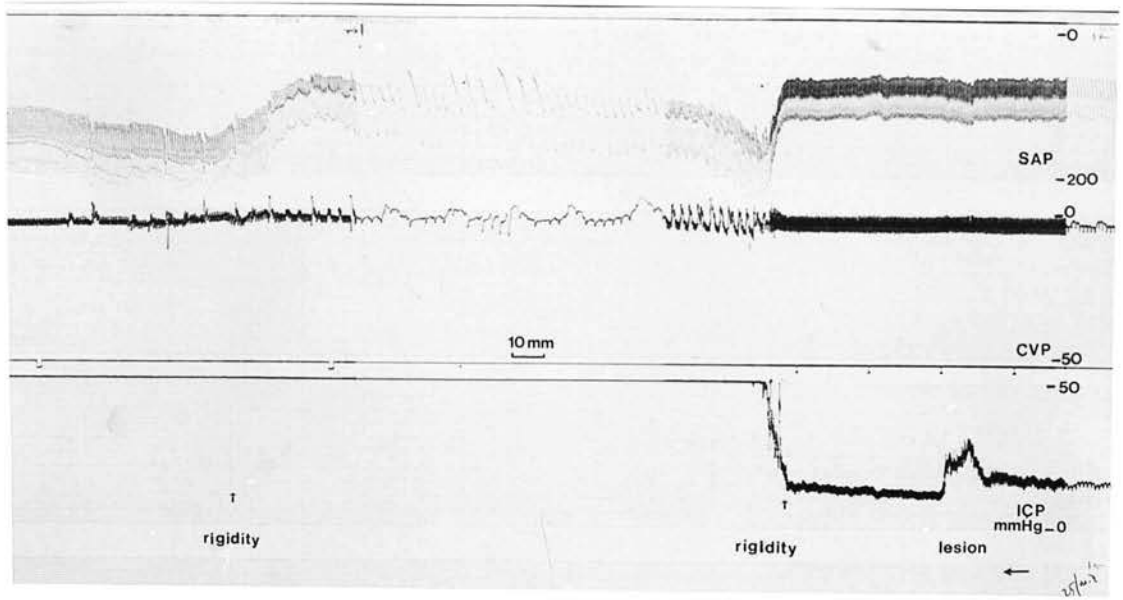


Fig. 8:11

Fluctuations in ICP, CVP and SAP before, during and after the development of bilateral severe decerebrate rigidity in cats. A substantial increase in ICP during coagulation is observed without concomitant alterations in SAP and CVP. Within two minutes of completion of the lesions bilaterally an intense and prolonged decerebrate spasm occurred which produced an abrupt and marked rise in ICP (plateau waves). This increase, the peak of which well exceeded the top calibration scale (50 mmHg), lasted throughout the decerebrate spasm. A concomitant marked increase in SAP (systolic as well as diastolic) occurred. Bradycardia and extrasystoles also appeared. By comparison with the rise in ICP and SAP there was only a small increase in CVP.

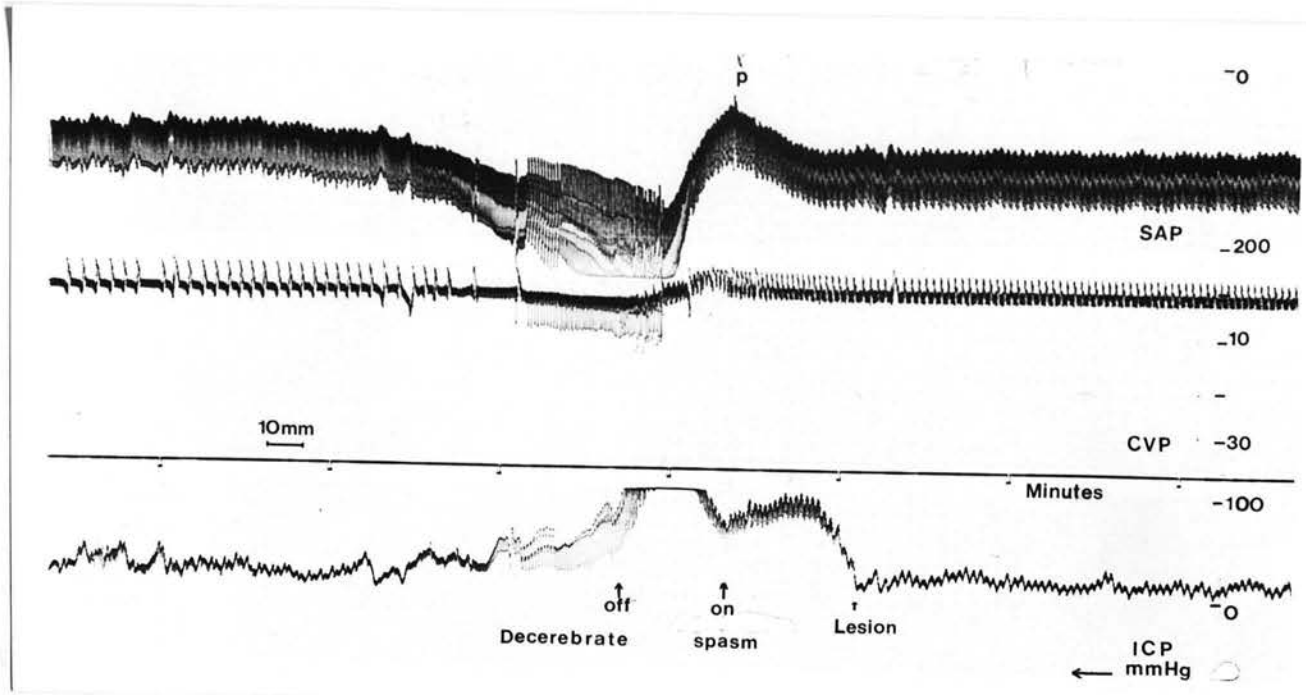


Fig. 8:12

Fluctuations in ICP, CVP and SAP before, during and after the development of decerebrate rigidity. A substantial increase in ICP without alteration in SAP and CVP occurred during coagulation and under normal blood gases. Approximately 30 seconds elapsed between the completion of the bilateral lesions and the development of bilateral severe decerebrate rigidity which produced a marked increase in ICP to well above the cal. scale (0-100 mmHg). The amplitude and frequency of the cerebral pulse was increased, as it is seen at the declining part of the ICP tracing. A striking increase in SAP was recorded during the spasm, affecting both the systolic and the diastolic pressure. The CVP was slightly elevated during the spasm. During the spasm tachypnoea occurred and on its termination was replaced by a reduction of approximately 40% in the respiratory rate which lasted for about 10 minutes. All changes returned to their previous appearances and characteristics by the end of the spasm.

Cat No.	I.C.P.		S.A.P.		C.V.P.		I.T.P.		E.M.G.	
	Rest	Spasm	Rest	Spasm	Rest	Spasm	Rest	Spasm	During spasm Extensors	Flexors
1	$11.0^{+}_{-}0.4$	50*	$64.0^{+}_{-}4.4$	$150.8^{+}_{-}19.0$*	$4.0^{+}_{-}0.2$	-	-	-	$120.5^{+}_{-}4.6$	$106.4^{+}_{-}5.15$
2	$4.5^{+}_{-}1.0$	100*	$99.0^{+}_{-}2.6$	$172.7^{+}_{-}15.3$*	$1.3^{+}_{-}0.2$	$7.8^{+}_{-}0.8$**	-	-	$165.0^{+}_{-}8.5$	$89.7^{+}_{-}6.0$
3	$10.1^{+}_{-}1.5$	$134.0^{+}_{-}12.4$*	95.0^{+}_{-}	$169.0^{+}_{-}20.1$*	$7.1^{+}_{-}0.7$	$18.6^{+}_{-}1.6$*	$3.9^{+}_{-}0.2$	$30.8^{+}_{-}5.8$*	$172.0^{+}_{-}11.3$	$56.9^{+}_{-}8.5$
4	$6.1^{+}_{-}0.9$	$128.3^{+}_{-}8.7$*	$76.5^{+}_{-}1.9$	$156.5^{+}_{-}13.6$*	$3.3^{+}_{-}0.7$	$14.7^{+}_{-}0.8$*	-	-	$104.0^{+}_{-}7.2$	$73.8^{+}_{-}4.3$

Table 8:4

The mean values of ICP, SAP, CVP, ITP and EMG activity in animals of group A during rest and spasm.

ICP, SAP, CVP and ITP (mm Hg); EMG activity (μV).

* = highly significant ($P < 0.001$): ** = very significant ($P < 0.01$)

Mean ICP, SAP, ITP and CVP were all calculated by the formula: $\frac{\text{Max. Pressure} + (\text{Min. Pressure} \times 2)}{3}$

(Yang et al. 1972)

the widest range of the scale available was used. In the other two animals of this group the average ICP reached a level of 134.0 $\pm$ 12.4 mmHg and 128.3 $\pm$ 8.7 mmHg respectively. These increases affected not only the mean value, but also the amplitude and frequency response of the cerebral pulse. The onset and duration of the intracranial hypertension exactly matched those of the rigidity. Spontaneous decrease or cessation of the spasms for short periods brought both the mean value and the variations in amplitude and frequency of brain pulsations to normal levels (Fig. 8:12).

Systemic arterial pressure

The SAP was markedly elevated during decerebrate spasms. Both systolic and diastolic pressures were affected, the former slightly more so. The mean SAP was very significantly raised from its resting value (data in Table 8:4). The elevation in SAP correlated with the onset, duration and severity of the decerebrate spasms.

Bradycardia occurred in all animals, and arrythmias were recorded in two of them.

Central venous pressure

The CVP remained unaltered in one animal during the period of rigidity, whereas in all other animals it was significantly elevated (data in Table 8:4).

Intrathoracic pressure

In the one animal in which the ITP was measured it was found to be significantly elevated, mean ITP 31.7 $\pm$ 8.2 mmHg.

Respiration

During decerebrate rigidity all animals showed an increase

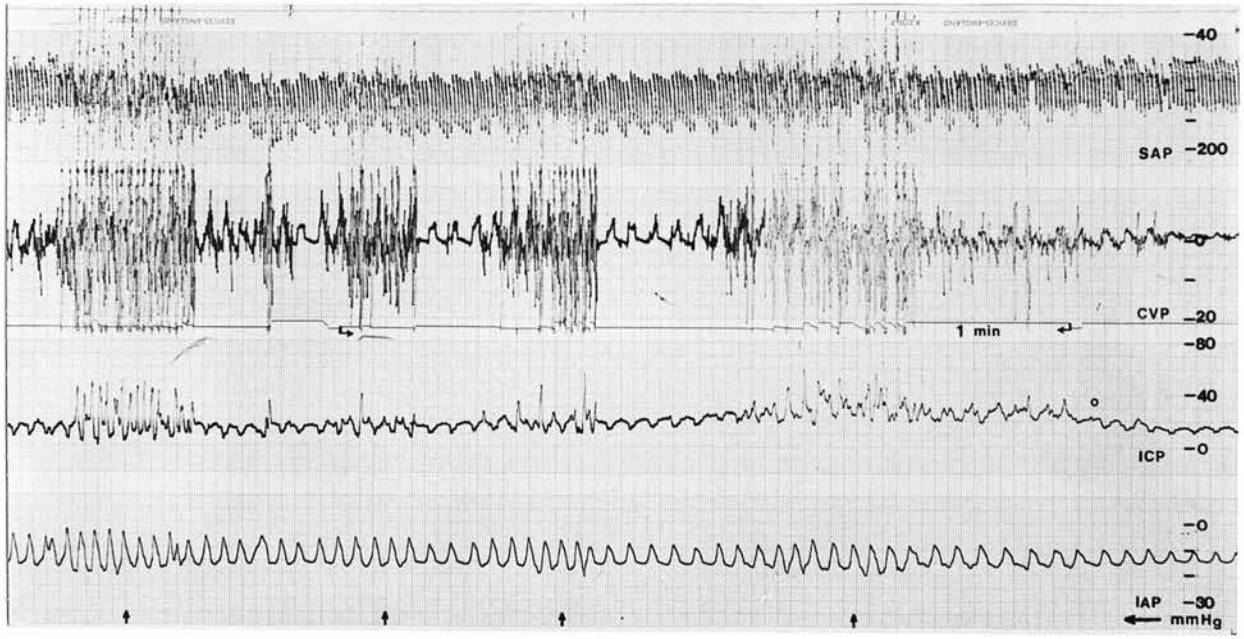


Fig. 8:13

Recording of ICP, CVP, SAP and IAP of a cat during decerebrate rigidity. Spontaneous increase in rigidity (arrows) produced a marked increase in CVP and ICP and small increase in IAP, while the SAP remained virtually unchanged.

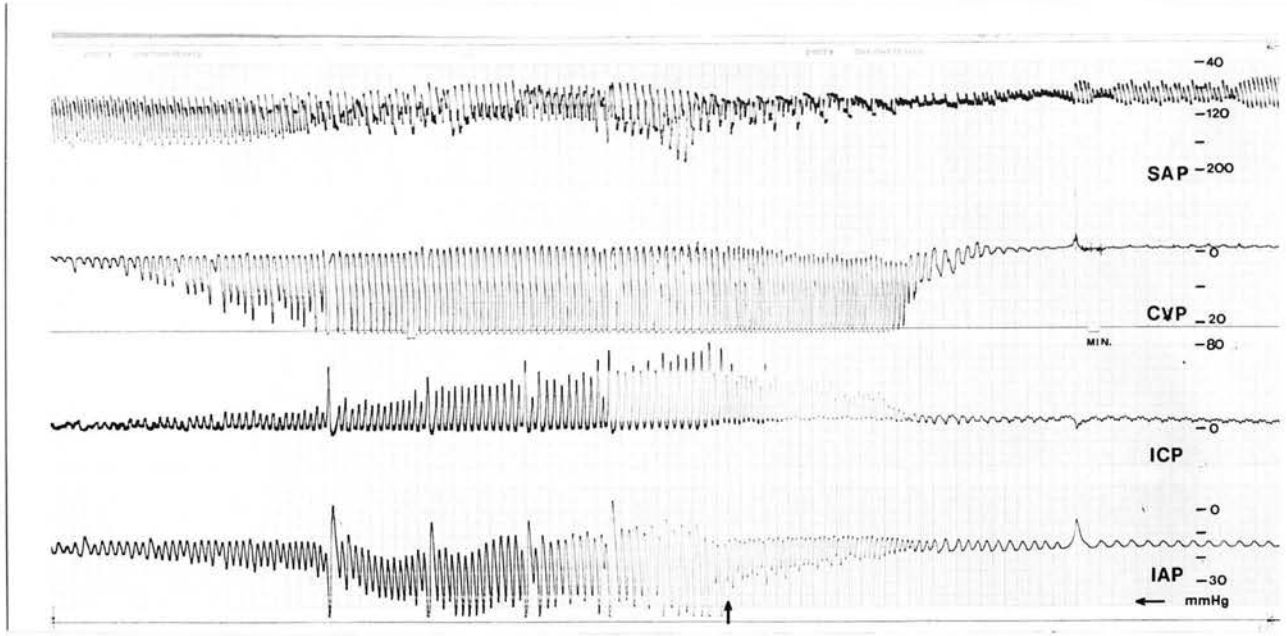


Fig. 8:14

Continuous recording of SAP, CVP, ICP and IAP during decerebrate rigidity in a cat. An extreme decerebrate spasm increased in ICP, IAP and most substantially the CVP, while the arterial pulse was greatly reduced. An indication of raised ITP alone, as it is discussed in the text. A spontaneous further intersification of the rigidity (arrow) produced a further increase in IAP and ICP, and increased the SAP in its absolute level and amplitude of the arterial pulse when compared with the previous recording or after the reduction of the rigidity. Reduction of the intensity of rigidity reduced the rise in IAP, ICP, CVP and SAPto the previous level immediately.

in both amplitude and rate of respiration. The respiratory rate was reduced by approximately 30% for 10 - 15 minutes immediately after the lesion had been made and decerebrate rigidity had developed.

The arterial blood values of pCO_2, pO_2H^+ and HCO_3 before, during and after the period of decerebrate rigidity remained within relatively normal limits; they are presented in Table 8:5.

Decerebrate rigidity

These animals developed extreme and violent spasms almost immediately (within 1 - 2 minutes) after completion of the lesions. In the EMG high frequency spike potentials of up to 200 μV were recorded during maximal contraction. The decerebrate rigidity was intermittent, periods of maximal spasm alternating with those of relaxation.

Group B (Small lesions - 13 animals)

These animals showed either no change in ICP or a range of increases from small, through medium to large (Figs. 8:13 and 8:14). When an increase occurred, simultaneous, directly proportional increases in the ITP, IAP and CVP were recorded. The SAP was usually unaltered.

Intracranial pressure

During decerebrate spasms, short-lasting oscillations of the cerebral pulse, of variable amplitude and increased frequency were recorded. The level attained and the appearance of the tracing during the spasms closely resembled those seen in the preliminary study (Fig. 8:14) when both the ITP and IAP had been directly increased.

Arterial blood values(Mean) for Hydrogen Ion activity(H^+), carbon dioxide tension(pCO_2), oxygen tension(pO_2), and standard bicarbonate(Stand. -HCO_3) in decerebrate cats. Group(A):animals with larger lesions than those in Group(B) which manifested decerebrate rigidity with the smallest lesions.

GROUP		H^+ (nmol/l)				pCO_2 (KPa)				pO_2 (KPa)				HCO_3 (mM/l)			
Animals		I	II	III	IV	I	II	III	IV	I	II	III	IV	I	II	III	IV
A		37.65	37.70	38.05	39.55	3.88	3.88	3.86	3.82	12.50	12.70	12.17	11.72	21.12	21.12	20.42	19.25
(4)	SD±	0.88	0.82	0.75	0.80	0.20	0.17	0.15	0.12	0.86	0.77	0.77	0.53	0.92	0.98	1.05	0.63
B		37.28	37.33	37.67	38.64	3.96	3.94	4.01	3.87	12.46	12.50	12.13	11.86	20.99	20.85	20.45	19.50
(11)	SD±	0.90	0.94	0.83	0.93	0.20	0.17	0.14	0.12	0.66	0.70	0.72	0.57	1.00	0.91	1.06	0.92
A+B	t	0.71	0.68	0.80	1.71	0.81	0.60	1.83	0.61	0.09	0.17	0.09	0.42	0.22	0.49	0.45	0.49

I : Before making lesions, II : Before the development of decerebrate rigidity, III : Approximately 20-30 min. after the development of decerebrate rigidity, and IV : 60-80 min. after the development of decerebrate rigidity.

t : Students t-test

Table 8:5

Intrathoracic, intra-abdominal & central venous pressure

All three parameters showed similar phasic changes. The cerebral, venous and respiratory pulses were all of the same configuration and because the alterations in their values were synchronous it was impossible to determine which pressures changed first.

Systemic arterial pressure

The SAP in general did not alter. On a few sporadic occasions, however, short-lived widening of the pulse pressure was recorded; these phasic changes were immediately preceded by equally brief but much more prominent increases of the venous pulse. Elevation of the SAP was recorded only during extreme decerebrate rigidity and especially when the IAP was markedly raised as a result of the spasm (Fig. 8:14).

Respiration

Pulmonary hyperventilation occurred during the decerebrate spasms and the amplitude and rate of respiration returned to normal on termination of the spasm.

The arterial pCO_2, pO_2, H^+ and standard HCO_3 remained within normal limits throughout the period of study; their values are presented in Table 8:5.

Decerebrate rigidity

By making the smallest lesions which would produce maximal rigidity, it was hoped not only to identify structures which might be involved in the production of rigidity but also - and most important - to avoid the cardiovascular and respiratory complications which appeared in the animals of Group A. We could thus study the isolated effect of the muscular contractions

only on the ICP.

These small and discrete lesions produced a variable amount of rigidity, which we graded as mild, moderate or severe. The anatomical distribution of the rigidity also varied. Both extensor and flexor rigidity, but predominantly the former, developed in the majority of animals (Fig. 8:15). In a few pure extensor rigidity of fore and hind limbs occurred (Fig. 8:16). Sometimes the rigidity would be predominantly flexor and would then affect mainly the hind limbs (Fig. 8:17). The first pattern of rigidity was the more effective in raising the ICP; the third had no effect on the ICP.

Subgroup (2 animals)

In two animals of Group B no change in either ICP, ITP, CVP or SAP was recorded during rigidity and there were no cardiovascular or respiratory complications. Clinically the animals were "quiet" but showed continuous, severe decerebrate rigidity and the typical extensor decerebrate posture. In the EMG continuous high frequency action potentials of 25 - 170 μV were recorded in all four limbs particularly in the flexors of the hind limbs.

Hexamethonium bromide (10mg/Kg IV) was administered to one animal of Group B which during spasm had shown moderate increases in ICP, CVP and ITP and a slight increase in SAP. The SAP fell rapidly to 70/40 mmHg, a level capable of maintaining adequate cerebral perfusion (Harper 1966). Decerebrate rigidity of the same order of severity as before the administration of the drug now produced almost as much of a rise in ICP, CVP and ITP as before but the SAP remained unchanged. The amplitude

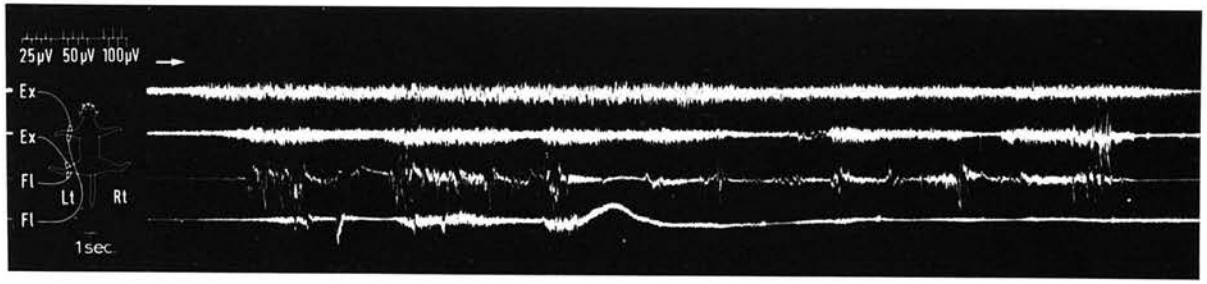


Fig. 8:15

Decerebrate rigidity in cat. EMG of the extensors (Ex) and flexors (Fl) of the fore and hind limbs of a cat. Decerebrate rigidity of extensor type. The extensors of both limbs are most affected. Spontaneous progression movements seen in both flexors enhanced the extensor discharge which took a fusiform appearance (stretch reflex). Clinically the animal showed a vigorous onset of spasms, with rigidity of all four limbs especially of the proximal joints, pilo-erection and erection of the tail.

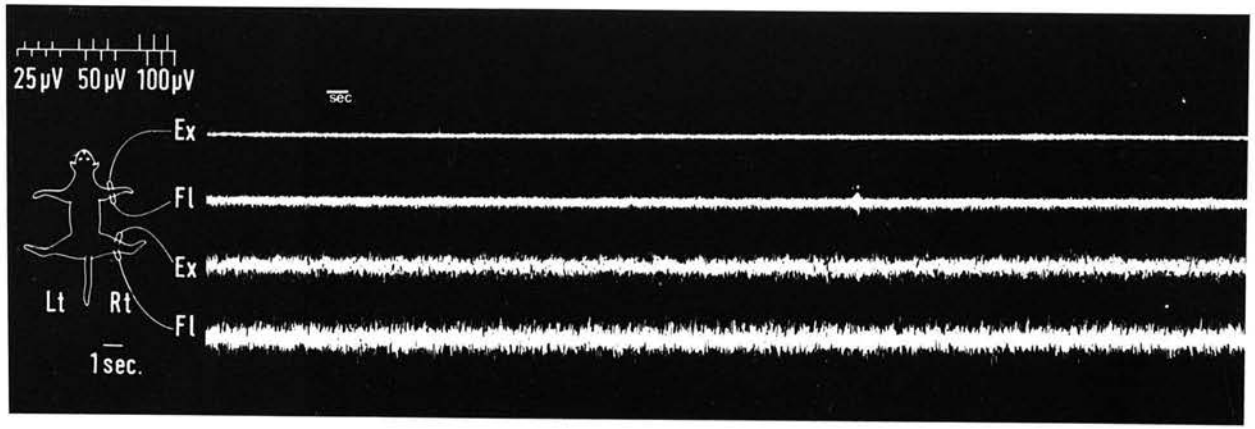


Fig. 8:16

Decerebrate rigidity in a cat. EMG of extensors (Ex) and flexors (Fl) of the fore and hind limbs. Continuous tonic contraction of all four limbs has developed following bilateral mesencephalic lesions. Rigidity was mainly of the hind limbs and it was of the flexor more than the extensor muscles. Clinically the animal was "quiet", and showed the typical posture of decerebrate rigidity.

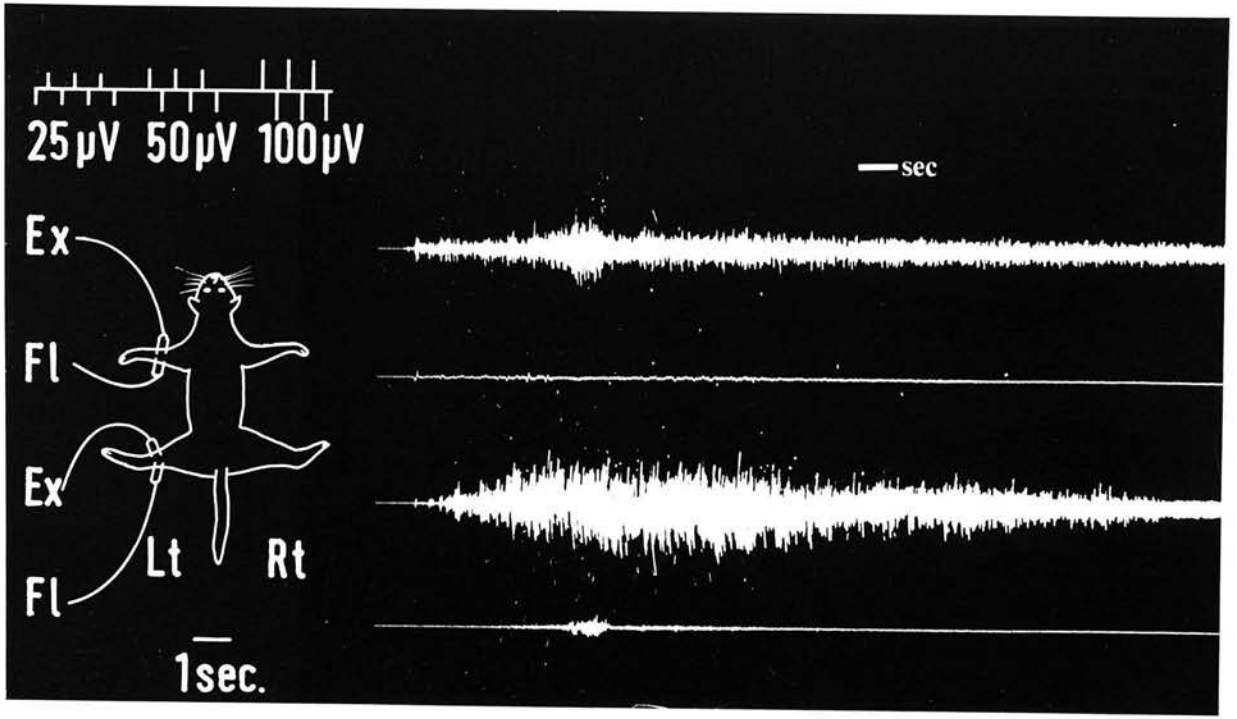


Fig. 8:17

Decerebrate rigidity in a cat. EMG of the extensors (Ex) and flexors (Fl) of the fore and hind limbs. Extensor decerebrate rigidity with "silent" or little activation of the flexor muscles following bilateral mesencephalic lesions.

of the cerebral pulsations, however, was moderately reduced.

Towards the end of the recordings the brain was exposed but it did not bulge into the bony defect; as the effect of the hexamethonium wore off, the SAP started to rise and the cerebral cortex soon herniated through the skull window.

We attempted to reproduce the conditions in which decerebrate rigidity is associated with or is due to an intracranial space occupying lesion (haemorrhage, swelling or acute hydrocephalus). In one animal with established decerebrate rigidity the ICP was raised by slowly inflating an intracranial epidural latex balloon with air; an increase of even 38-40 mmHg in the ICP had no effect on the SAP or CVP. As anticipated, even short-lasting spasms now produced a 100% increase in the already high ICP whereas under conditions of normal intracranial elastance similar spasms had no effect on the ICP (Fig. 8:18).

The variations in ICP during decerebrate spasms in both Groups A and B are presented diagrammatically in Fig. 8:9c.

AUTOPSY

No gross intracranial haemorrhage was seen at necropsy in any of the animals.

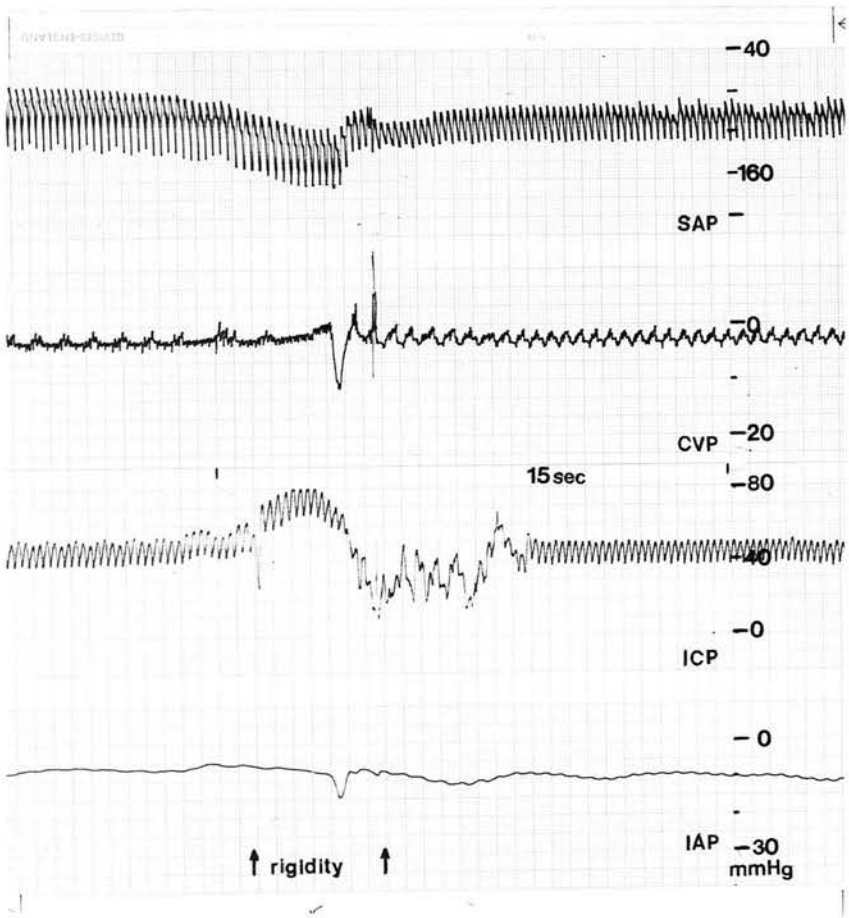


Fig. 8:18

Continuous recording of IAP, ICP, CVP and SAP during decerebrate rigidity. Increase in brain elastance and ICP by inflating slowly an air-filled balloon epidurally without increase in SAP, CVP or IAP. A mild, short-lasting spasm produced a very substantial increase in ICP while similar spasms produced no change in ICP under conditions of normal brain elastance and ICP. The SAP, CVP and IAP were also increased.

DISCUSSION

These experiments showed that only bilateral and severe decerebrate rigidity substantially increased the ICP and that there were two distinct patterns to the increase.

In animals with large lesions large "plateau" waves appeared in the ICP tracing, like those described by Lundberg (1960), as sudden increases in pressure ranging from 50 to 100 mmHg, lasting 5 to 20 minutes and followed by a rapid fall to or below the previous resting pressure. The only concomitant event of significance was an elevation of SAP; the CVP was essentially unchanged.

Animals with small lesions, however, never developed such "plateau" waves and the elevation of the ICP varied directly with the increase in ITP, IAP and CVP and with the degree of rigidity. A close parallelism between the cerebral, venous and respiratory pulses in time and magnitude was evident. The rise in SAP was insignificant.

The explanation of two such different patterns of behaviour must be sought in differences in the intensity and distribution of the decerebrate rigidity and in the cardiovascular events.

In the classical mesencephalic transections of Sherrington (1897-98), Thiele (1905), Bazet and Penfield (1925) and Ranson and Hinsey (1927) great variations were seen in the intensity and distribution of rigidity between extensor and flexor muscles as well as between fore and hind limbs, despite the use of an apparently standard technique. The degree of rigidity was also influenced not only by variations in the physiological state of the animal but also by physical factors, such as the temperature at which the experiments were performed and the

precise details of the technique employed. Creed et al. (1932) admitted that the degree of rigidity varied from experiment to experiment, probably because of small unavoidable differences in the level or detail of the section.

In this study the situation was further complicated by the fact that the small and discrete lesions employed may have incompletely damaged some target areas. Fulton (1943) has stressed the importance of the completeness of the lesion for the full development of rigidity. Clinically, muscle tone has usually been assessed by monitoring of the EMG activity (Hoefer and Putman 1940, Leavitt and Beasley 1964, Levine et al. 1969, Jones et al. 1970) and in the experimental animal (Lindsley et al. 1949, Schreiner et al. 1949, Feldman 1971) this method has been employed almost exclusively. Under physiological conditions this is based on measurement of the amplitude of action potentials and frequency analysis of the spikes and correlates well with clinical estimates of muscle tone (Watts 1924, Seyffarth 1941, Loofbourrow 1948). When their one decerebrate patient was "at rest", Hoefer and Putman (1940) recorded a continuous, low voltage discharge (20-40 μV) from all muscles tested; passive movements increased this activity. Lindsley et al. (1949), in their study of the spasticity which resulted from a lesion of the supressor area in the brain stem of the cat, reported a stretch-evoked discharge which had an amplitude of almost 200 μV. Similar observations were reported by Sprague et al. (1948) in the most severe grade of animal decerebrate rigidity.

The findings in the present work are in general agreement with these. The constant tonic discharge which was recorded

had an amplitude of 25-50 μV, and was of low frequency. During spontaneous, paroxysmal intensification of the rigidity, action potentials of much greater amplitude, 170 - 200 μV, were recorded.

Two cases were selected as having a similar degree of rigidity and almost identical EMG activity (underlining the good correlation of mechanical and electrical events); in only one of these, however, was the ICP raised. This animal showed severe contraction of its thoracic and abdominal musculature and the ITP,IAP and CVP were all increases, all of which features were absent in the other animal. This event was repeatedly observed in these two animals.

It thus appears that:

a) decerebrate rigidity does not always affect the ITP and IAP (and consequently the CVP and SAP) even if the limb rigidity is extreme and

b) the ICP is raised only if ITP and IAP are increased by the rigidity. Decerebrate rigidity, therefore, will increase the ICP only if it increases the truncal cavity pressures (i.e. ITP and IAP).

These observations may explain the finding of a normal ICP in the presence of severe extensor decerebrate rigidity by Jennett and Plum (1972) and by Jennett and Johnston (1972).

Before discussing the factors responsible for the production and maintenance of the intracranial hypertension seen during acute decerebrate rigidity it is necessary to consider the mechanism whereby the ICP is raised.

Theoretically an increase in the volume of CSF, brain tissue or cranio-spinal blood could be responsible.

The hypothesis that widespread compression of the intramuscular veins of the limbs by spasm, the displacement of blood into the central veins and a subsequent rise in CVP would produce a rise in the ICP is not supported by our observations. If indeed there is an increased venous return from the limbs during decerebrate rigidity, it appears to play no direct role in the elevation of ICP. It may be, however, that in cases with simultaneously raised ITP and IAP it exacerbates the effect of these on the ICP by increasing the volume of the central venous pool; this blood, it is argued later, is displaced into the veins of the spinal canal and cranial cavity. Conceivably the greater the volume within the capacitance veins the more is available for displacement into the cranio-spinal system and, therefore, the more the ICP is raised.

The mean rate of CSF production is 0.3 ml/min (Lorenzo et al. 1970). Lundberg (1960) reported that in a patient with aqueduct obstruction the ICP took nearly three hours to increase from 10 mmHg to 20-30 mmHg. In the present study while the increased production and reduced absorption of the CSF may have played small addiitive roles, the rapid dynamic changes in the ICP which were observed cannot reasonably be explained as due to such alterations.

An increase in the brain tissue volume due to oedema is unlikely to play a major role in such a sudden increase in ICP; it it were indeed due to oedema, one might expect a progressive elevation in ICP uninfluenced by cessation of the decerebrate spasms.

Phasic changes in the amplitude and frequency response of the cerebral pulsations during decerebrate rigidity were

associated in detail with changes in the systemic arterial and venous pressures; this observation strongly suggests that the changes in ICP characteristics were due to increases in the cranio-spinal blood volume. Such an increase can be produced by:

a) an increase in the systemic arterial pressure

b) a decrease in cerebrovascular resistance (CVR)

c) an increase in the cranio-spinal venous blood volume

Roy and Sherrington (1890) first stressed the importance of the SAP and factors such as carbon dioxide and oxygen tensions in the control of cerebral vascular tone and consequently of the ICP. Pure systemic hypertension, whether induced by vasopressin (Sokoloff 1959) or by L-noradrenaline (Moyer and Morris 1954), has no effect on the cerebral blood flow or volume in man. The CBF and volume are unaltered in normal subjects whose SAP and cardiac output have been increased by exercise (Kleinerman and Sancetta 1955, Hedlund et al. 1962). In the present "non-decerebrate" experiments a significant rise in the SAP and, therefore, of the perfusion pressure had virtually no effect on the resting ICP. The cerebral blood volume and its rate of flow, therefore, are not passive functions of the SAP as was postulated at the end of last century (Hill 1896); they are maintained within normal limits even though the SAP and perfusion pressure are increased well beyond their physiological range. This is believed to be accomplished, at least under physiological conditions, by adjustments of the cerebrovascular resistance but the mechanism of these is far from clear.

Cerebrovascular resistance (the ratio of perfusion pressure to blood flow) is the resultant of blood viscosity, extravascular tissue pressure and vascular calibre as modulated by vasoactive agents and neural reflex arcs. A decrease in the viscosity, as in anaemia (Robin and Gardener 1953), increases and an increase, as in polycythaemia (Nelson and Fazekas 1956), decreases the CBF. The extravascular pressure - the ICP - may be increased to 450-500 mmH_2O without significant effect on the CBF (Wolff 1948, Zwetnow 1970); if it is raised to the level of the MSAP, however, the cerebral circulation stops (Pribram 1960, Langfitt et al. 1969).

It has been repeatedly demonstrated in both man and animals that cerebral vasomotor tone is profoundly influenced by arterial carbon dioxide (Harper and Glass 1965, James et al. 1969) and oxygen tensions (Schmidt et al. 1945, McDowall 1966) and the extracellular, including CSF, hydrogen ion concentration (Siesjo et al. 1971). Carbon dioxide is, in fact, the most potent vasodilator substance known and because it is also the end product of brain metabolism some investigators have concluded that it is the main regulator of cerebral vascular tone (Harper 1966, Michenfelder et al. 1969); they conceded no significant vasomotor function to the extensive perivascular autonomic nerve net on the meningeal and cerebral vasculature. Support for this view came from the experimental work of Dumke and Schmidt (1943), Harmel et al. (1949) and Shendkin et al.(1951). Dumke and Schmidt showed that section of the cervical sympathetic nerves had no effect on the CBF but their observation that low oxygen or high carbon dioxide concentrations separately had no significant effect on either respiration or CBF suggests

that their operation had injured the sinus nerve and thus altered the response of vessels to both neural and chemical factors. Harmel et al. (1949) and Shenkin et al. (1951) observed no changes in CBF after bilateral blockage of the stellate ganglion. Removal of the superior cervical ganglion abolished the catecholamine fluorescence of the intracranial perivascular adrenergic nerves but excision of the stellate ganglion only reduced and did not abolish it.

Chrobski and Penfield (1932) and McNaughton (1938) ascribed both constrictor and dilator functions to the cerebrovascular sympathetic nerves. More recent evidence also favours the existence of an autonomic control mechanism of the cerebral vascular tree. Bridges et al. (1958) showed that stimulation of the superior cervical ganglion decreased the cerebral blood volume whereas procaine blockade increased it, an effect also obtained by the administration of high pCO_2 or low pO_2. Stimulation or blockade of the stellate ganglion produced similar but weaker reactions. James et al. (1969) and Purves and James (1969) showed that section of the cerevical sympathetic nerves significantly increased the CBF. The blood gases and SAP were rigidly controlled and when the operation was performed under conditions of high pCO_2 or low pO_2 the increase in CBF was found to be much greater than at normal partial pressures of these gases and it was no longer independent of the SAP. This suggests that, as might be anticipated, neural vasomotor activity interacts with other regulatory factors; the details of this interaction await elucidation.

During coagulation in all four animals of Group A, a substantial increase in ICP was observed but there was no

alteration in either the arterial pressure (elevation of which could account for the rise) or in respiration, the arterial blood gases were normal and the EMG showed the electrical activity of relaxation. The increase could plausibly be explained as the result of transient, local (i.e. cerebral) vasodilatation but the mechanism of such vasodilatation is unknown.

In the same four animals the onset of decerebrate rigidity coincided with an elevation of both ICP and SAP. The latter may be a central effect of the midbrain lesions, mediated by sympathetic overactivity. The major vasomotor centres are located within the medulla but there is also a separate cortico-spinal pathway by which vasomotor tone is regulated; vasomotor neurons have been demonstrated within the mesencephalic tectum and tegmentum, activation of which can elicit both pressor and depressor responses (Eliason et al. 1954, Lindgren 1955, Lindgren et al. 1956). The rise in SAP, however, occurred immediately after completion of the lesion in only one animal; usually its appearance was synchronous with the development of decerebrate rigidity. This would suggest that the systemic hypertension is not a central phenomenon but is secondary to muscular hyperactivity, a hypothesis which is supported by the fact that the SAP returned to a normal level at the end of a spasm.

We have previously discussed why a rise in the SAP alone does not raise the CBF and ICP. It could be argued that simultaneous increases in SAP, ITP, IAP and CVP might be responsible; that this is not the case was demonstrated in the control animals, in whom artificial elevation of all these

parameters to levels even more extreme than those seen during rigidity not only had comparatively little effect on the ICP but also resulted in an ICP waveform which differed from that of decerebrate rigidity.

Primary cerebral vasodilatation was considered to be responsible for the rapid and generalised increase in brain blood volume (swelling) which resulted from lesions in the midbrain (Le Beau and Bonvallet 1938) and in the floor of the fourth ventricle (Obrador and Pi-Sunër 1943). While acute swelling could certainly explain the rapid and large augmentation in the ICP of these animals this should have been maintained independently of the muscle spasms. The increase seen in both ICP and SAP was limited to the duration of the spasms.

Located within the mesencephalic tegmentum are not only pathways controlling the vasomotor tone but also the reticular formation, lesions of which produce decerebrate rigidity (Denny-Brown 1962). In the present experiments, lesions located in this region produced both decerebrate rigidity and imbalance of the cerebral vasomotor tone. It can be argued that vasoconstrictor paresis allowed the substantial increase in SAP to drive arterial blood freely through the cerebral vessels, thus increasing the cerebrovascular volume and consequently the intracranial pressure.

The finding that intracranial hypertension occurred regardless of the CVP level and that in only one case was it related to an elevation of ITP strongly suggests that neither of these factors significantly influences the ICP. They may, of course, have exerted some minor contributory effect.

In the animals of Group B who showed a much smaller increase

in ICP the craniospinal venous blood volume (which results from the rise in central venous pressure) were the major determinants of intracranial events, systemic hypertension and vasomotor activity being minor additive factors. None of the animals in this group ever developed anything like the degree of intracranial hypertension seen in those of Group A and "plateau" waves never appeared on their ICP traces, as they did in Group A. More impressive than the absolute level attained was the occurrence of very substantial phasic changes.

Cerebrospinal fluid pulsations are considered to reflect events in the cardiovascular system and most investigators believe that they originate from the arterial pulsation and are modified by respiration (Antoni 1946, Bering 1955, Dunbar et al. 1966). There is some evidence, however, that they follow the contour of venous rather than arterial pulsation and it has been argued that this applies also to brain pulsation (Hamit et al. 1965). These workers further postulated that although the static CSF pressure is maintained by the arterial pressure, its phasic changes are largely of venous origin.

The prominent phasic changes seen in the cerebral pulse tracing in Group B were synchronous with those in the tracings of the respiratory and venous pulses. The CVP, ITP and IAP were greatly elevated simultaneously while the SAP remained virtually unaltered. The height of the cerebral pulse varied in parallel with that of the venous pulse and respiratory excursions, an observation which strongly suggests that cerebral pulsations and ICP reflect venous rather than arterial events.

It is well established that CSFP is modified to some extent by changes in the venous pressure (Becht 1920, Weed and Flexner 1933, Bedford 1935, Ryder et al. 1952). The cranial venous blood can be "backed up" by raising the pressure in the superior vana cava, and this increases the ICP. That this elevation is, however, only temporary has been shown in experiments involving occlusion of the jugular veins; Meyrson and Loman (1932) and Bedford (1935) produced a transient increase in ICP by ligation of both internal jugular veins, the normal level being speedily restored. This restoration was attributed to an "escape mechanism", namely the collateral drainage of the cerebral venous sinuses into the spinal epi- and subdural veins.

Brescht (1829) and Batson (1940, 1942, 1944) have illustrated the communication of the internal spinal veins with the venae cavae through the azygos and hemiazygos veins and petrosal sinuses; they pointed out that blood can flow freely in either direction in this valveless system. An increase, therefore, in ITP and IAP (as occurs during severe decerebrate rigidity) by preventing drainage of cerebral venous blood into the capacitance veins via Batson's plexus, increases the cranio-spinal volume and results in a significant rise in the ICP. (We found that a maximal increase occurs only if <u>both</u> the ITP and IAP are elevated).

Various investigators have stressed the importance of either an increase in ITP (coughing) or in IAP (abdominal compression) in the genesis of intracranial hypertension; few, however, have measured either the ITP or the IAP and compared these figures with simultaneous recordings of the CSFP. Hamilton et al. (1936) studied the effect of increased

ITP on the SAP and on the CSFP in normal and tuberculous subjects with an artificial pneumothorax. During straining or coughing the ITP rose by about 50 mmHg and a similar increase occurred in CSFP and the SAP. They speculated that the systemic hypertension was due to an increase in CVP.

The findings in this study are at variance with these.
a) A great increase in ITP has relatively little effect on ICP, and elevation of the IAP is only slightly more effective. When, however, these two factors are combined the effect is not linear but exponential and in these circumstances rises in ICP are seen comparable with those reported by the above workers.
b) An isolated increase of any magnitude in either the ITP or IAP cannot be produced because the mobility and elasticity of the diaphragm freely transmits applied pressures from one cavity to the other. A so-called "isolated" increase in ITP produced very profound systemic <u>hypotension</u> which persisted for as long as the ITP was kept elevated. Increase of the IAP alone or in combination with the ITP produced a small increase in SAP; of the two only the increased IAP has this effect, despite the fact that the CVP was increased by both procedures.

The fact that straining and coughing increases not only the ITP but also the IAP is the probable explanation of the finding of a great increase in the CSF and the systemic arterial pressures by the above workers.

From the experiment in which the ICP was artificially raised it appeared that the magnitude of the rise in ICP in clinical decerebrate rigidity might depend not only on the degree of rigidity, the amount of the increase in ITP and IAP and systemic arterial hypertension (in the presence of impaired homeostasis) but also on the cerebral elastance. This was investigated clinically (Chapter 10).

PART FOUR

HUMAN WORK

CHAPTER 9

TWO METHODS OF MEASURING MUSCLE TONE IN PATIENTS WITH DECEREBRATE RIGIDITY

INTRODUCTION

Muscle tone is normally estimated by subjective assessment of the resistance encountered when a limb is passively moved. This, however, is liable to human error because of the common, normal physiological variations in muscle tone which occur. Instrumentation which would reproduce the manoeuvres adopted in the clinical assessment of muscle tone is highly desirable.

There are two traditional techniques for the measurement of muscle tone:

a) monitoring of electromyographic activity (EMG), based on the principle that, under physiological conditions, increased muscle contraction is associated with increased electrical activity (Hoefer and Putman 1940, Levine et al. 1964) and

b) measurement of the resistance of a passively moved limb, with or without EMG recording (Brumlic and Boshes 1961, Webster 1964, Nashold 1966).

The advantages and limitations of both methods were discussed in the symposia on Skeletal Muscle Hypertonia (1964) and on Parkinson's Disease (1966).

Whereas evaluation of the force changes which result from the imposition of position changes on a limb has commonly been used for the measurement of muscle tone, Roberts (1963) first appreciated the importance of selecting force rather than position change as the independent variable. In experiments on decerebrate cats he showed that the imposition of changes in length on muscles produced irregular and unpredictable fluctuations in tension: the responses to changes in the applied force were, however, much more consistent.

Wilkie (1950) has shown that the velocity of the movement and the EMG response are both dependent on the frequency and amplitude of the applied force. Granit et al. (1959) and Jansen and Rudjord (1964) have shown that the muscle receptors of a cat respond to changes in force rather than in position. This has also been shown to be the case for at least some of the corticospinal neurons in man by Evarts (1967).

Sinusoidal forces have been used successfully for evaluation of the dynamic properties of the muscle receptors and of the stretch reflex (Jansen and Rack 1966, Terzuolo and Poppele 1968). Bertholz and Metral (1970) applied sinusoidal forces to the forearm under visual control of limb position in order to make a frequency analysis of the neuromuscular control mechanisms of the elbow joint. Joyce et al. (1974) used a fly-wheel device to apply sinusoidal displacement rather than force to the elbow, but displacement and force are not equivalent in nonlinear systems, such as the skeletomuscular (Machin and Pringle 1960, Roberts 1963). Similarly, displacement rather than force was measured by Duggan and McLellan (1973) in their study of the resonant frequency of the elbow and evaluation of its muscle tone. Agarwal and Gottlieb (1975) examined the effects of forced low-frequency sinusoidal oscillations on the ankle joints of normal subjects but this method presented problems due to the action of gravity on the limb under examination.

In the present study we quantified decerebrate rigidity by measuring in the wrist the changes in the displacement and its angular velocity which resulted from variations in an applied torque, either sinusoidal or square in waveform.

The method was developed in the Department of Clinical Neurophysiology, University of Edinburgh and has been used successfully for the study of the servocontrol of the posture of the normal human wrist (Walsh 1973) and jaw (Walsh 1970). It has also been used in the study of tremor (Walsh 1969) and clonus (Walsh 1971). It is much more versatile than previous devices and is applicable to virtually any distal joint. Whereas contemporary methods measure length changes in response to imposed tension changes this was designed to allow the muscle to "choose" whether to keep length constant and allow tension to vary, or to keep tension constant and allow length to vary.

PATIENTS AND METHODS

Thirteen head injured patients with decerebrate rigidity were selected for study as having well-developed rigidity on clinical assessment. Ten of the cases were investigated in the acute stage of decerebrate rigidity; i.e. as soon as possible after surgery and a short interval on mechanical ventilation in order to stabilise the arterial gas tensions. When instrumentation had been set up and several measurements of muscle tone had been obtained, the relaxant drugs were allowed to wear off. Decerebrate rigidity soon developed and measurements were repeated over a period, at the end of which the patient was returned to mechanical ventilation.

The other three cases, who suffered from post-traumatic hydrocephalus, still exhibited severe decerebrate rigidity 3 - 4 weeks after injury. They were examined repeatedly and

also provided the opportunity to study the effects on rigidity of diazepam (10 mg intramuscularly or continuously by intravenous infusion of 5 - 10 mg/Kg body weight/24 hours) and chlorpromazine hydrochloride (repeated doses of 25-50 mg intramuscularly).

Twenty four volunteers were used as control subjects. They were divided into two groups in order to determine whether forces of square (10 subjects) or sinusoidal (14 subjects) waveform would give the more reliable and consistent results. The period of study was limited to 20-30 minutes on each subject because measurements of muscle tone are highly susceptible to fatigue.

The measurement of rigidity has been described in Chapter 4.

RESULTS

LOW FREQUENCY ABRUPTLY REVERSING TORQUES OF SQUARE WAVEFORM

Normal control subjects

1) Torque-position changes

By means of slow square waves of displacements of constant amplitude, and reversing abruptly from extension to flexion and vice versa every few seconds, torques were delivered to the hand. As seen in the position tracing, the hand moved in the same direction until a steady level was reached after an initial overshoot followed by a few decrementing oscillations. In a fully relaxed subject the amplitude of these oscillations was greater in flexion than in extension and their frequency varied from 1.5-2.0 Hz in flexion and 1.0-1.5 Hz in extension.

When the subject stiffened voluntarily the displacement of the hand was reduced and it was virtually fixed in the middle position. The frequency of the oscillations was increased proportionately to the degree of effort (ranging from 3.0-8.9 Hz) while their amplitude was greatly reduced. The first oscillation was the largest and brought the hand back to its starting point almost immediately.

2) Electromyography

When reciprocating forces were applied to the wrist of a relaxed subject myotatic activity, i.e. a burst of electrical activity of a stretched muscle, was observed mainly in the extensor muscles. Moderate voluntary contraction against a background of tonic activity enhanced the myotatic activity, mainly in the extensor muscles during flexion and less so in the flexors during extension (Fig. 9:1). Out of ten subjects, seven showed definite myotatic activity of the extensors and only four of the flexor muscles. Myotatic activity was most prominent as the torque was reversed and it was directly affected by the torque; as assessed on the EMG, greater forces produced greater activity. Myotatic activity disappeared when the subject was maximally stiff.

Instead of showing the usual myotatic activity, two relaxed subjects to whom square reciprocating forces were applied developed shortening reactions (Sherrington 1909). Removal of tension sometimes caused reappearance of muscular activity after a short interval and without obvious change in the mechanical parameters (torque, position and velocity) to account for this phenomenon.

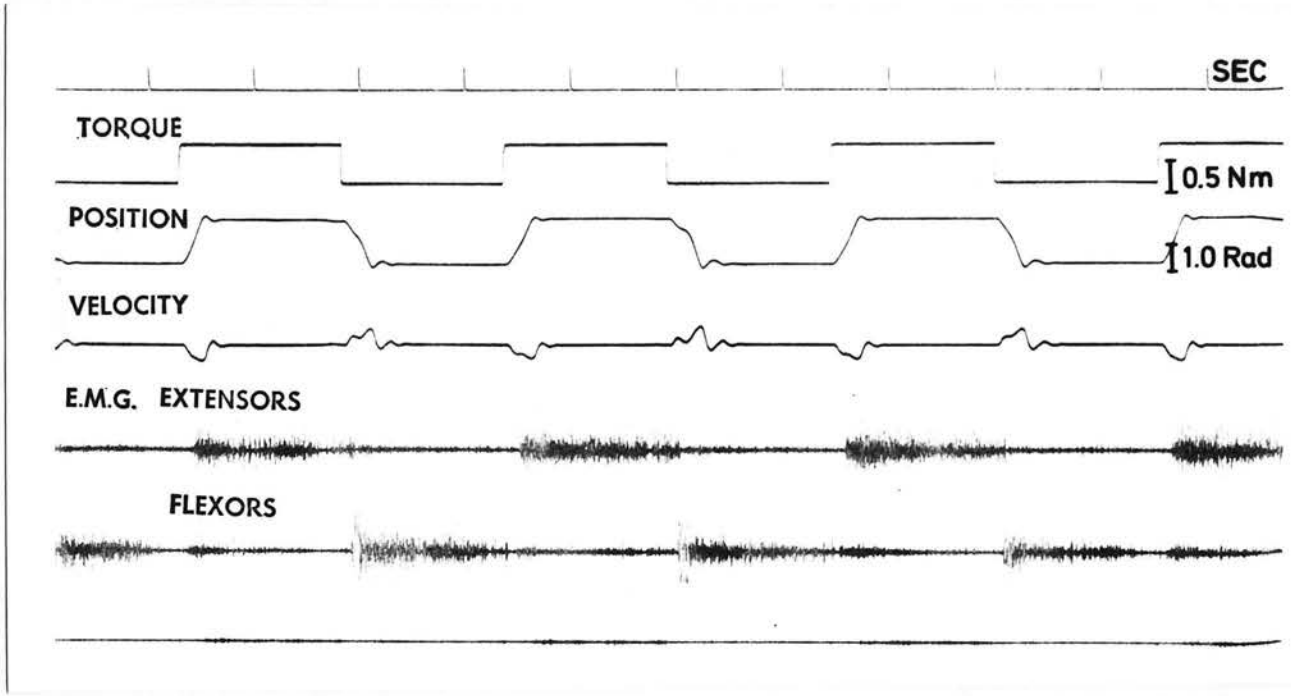


Fig. 9:1

Myotatic activity seen in both extensor and flexor muscles of the forearm produced by the application of an abruptly reversing torque of square waveform in a normal relaxed wrist.

The average amplitude of electrical activity of the extensor muscle was 9 μV and 11 μV for the flexors on voluntary relaxation. Maximal stiffening increased this activity to 144 uV in the extensors and 95 uV in the flexors, a significant shift of balance towards the extensors (Table 9:1).

3) Measurement of muscle tone

Joint compliance, defined as the ratio of displacement to applied force, reflects changes in muscle tone. A normally relaxed joint moves easily and has high compliance, whereas the compliance of a tense or rigid limb is low.

The angular displacement of the wrist (measured in radians, rads) per unit of applied torque (newton meters, N.m), was calculated. This is the compliance of the system and is used as an index of muscle tone (in this case, 1.0 rad displacement per 0.35 N.m on the recorder represents a compliance of 2.86 rad/N.m).

The EMG was also monitored and its amplitude (in microvolts, μV) was correlated with compliance values (Table 9:1).

Summarised results from ten normal volunteers are presented in Table 9:1. The average compliance of all subjects during voluntary full relaxation was 2.06 rad/N.m. During maximal stiffening this was reduced to 0.43 rad/N.m. The scatter, however, among individuals was great: the Standard Deviation was $\pm$ 0.84 rad/N.m during relaxation and $\pm$ 0.20 rad/N.m during stiffening. This means that there is a considerable individual variation in the resistance to passive movement. Neither occupation, age nor sex affected these results. This variability in the base line compliance during relaxation is reflected in

Wrist compliance and EMG activity of the forearm muscles of ten normal volunteers during voluntary full relaxation and maximal stiffening.

SUBJECT	AGE	SEX	WRIST	TORQUE APPLIED (N.m)	COMPLIANCE (rad/N.m)		EMG (μV)	
					RELAXED	STIFF	RELAXED (Extensors/Flexors)	STIFF (Extensors/Flexors)
S.T	32	M	R	0.7	1.34	0.18	30 / 0	128 / 86
P.B	24	M	R	0.6	0.61	0.08	18 / 8	84 / 113
J.W	23	F	R	0.6	2.39	0.54	0 / 5	164 / 47
P.H	21	M	R	0.6	1.67	0.38	0 / 13	138 / 72
			L	0.5	1.87	0.50	14 / 16	179 / 43
G.F	24	M	L	0.6	3.30	0.71	11 / 13	115 / 75
G.W	18	F	L	0.6	2.87	0.64	5 / 18	152 / 53
			R	0.6	2.88	0.53	6 / 14	170 / 91
G.W	45	M	R	0.7	3.14	0.72	0 / 21	175 / 109
			L	0.5	3.09	0.65	0 / 21	137 / 109
S.P	26	F	L	0.6	2.00	0.36	15 / 2	185 / 100
			R	0.4	2.22	0.36	0 / 0	148 / 177
M.McC	19	F	F	0.5	0.88	0.10	0 / 4	112 / 114
M.L	25	M	R	0.7	1.20	0.29	17 / 11	152 / 109
			L	0.6	1.11	0.41	14 / 11	125 / 122
				MEAN	2.06	0.43	8.7 / 10.5	144.4 / 94.7
				SD±	0.84	0.20	9.0 / 7.0	28.4 / 34.4

t: 0.6 , $P < 0.5$ (d.f. 28), t:4.3, $P < 0.001$ (d.f.28)

Table 9.1

the wide range of changes in compliance when the subject went maximally stiff. When compliance values during relaxation were plotted against similar values at maximal stiffening an overlap was found.

Decerebrate rigidity

1) Torque-position changes

The wrist, initially at rest in the mid position, moved in the same direction as the applied torque, i.e. from extension to flexion and vice versa. This displacement reached a steady level after an overshoot and decrementing oscillations, as with the control subjects. When the patient relaxed spontaneously the EMG activity was minimal and the oscillations were of the same amplitude and frequency as in the control subjects. During a severe decerebrate spasm, however, oscillations of greater frequency (up to 12 Hz) were recorded than in the control subjects while their amplitude was similar (Fig. 9:2). When inertia was added to the hand of one patient by adding iron weights to the crank, the oscillatory frequency was decreased in inverse proportion to the inertia, i.e. the greater the inertia the more the reduction in oscillatory frequency and vice versa. With the subject rigid the oscillation frequency was 7.78 Hz; the mean frequency was 6.81 Hz when 0.0025 $Kg.m^2$ was added to the system: with 0.005 $Kg.m^2$ it was 5.93 Hz and with 0.01 $Kg.m^2$ the mean frequency was reduced to 3.83 Hz (Table 9:2). Throughout the period of recording the EMG of flexor and extensor muscles of the forearm remained unchanged.

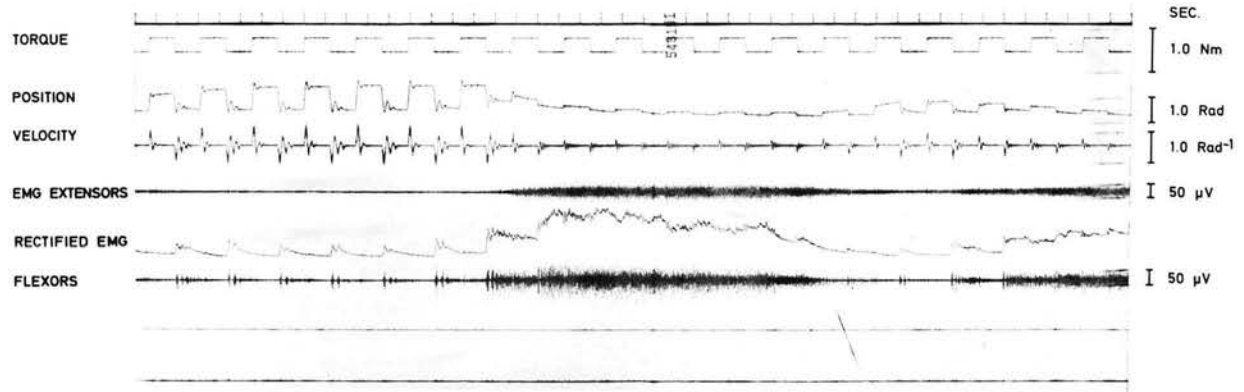


Fig. 9:2

Oscillatory transients at 3.0 - 3.5 Hz during spontaneous relaxation increasing up to 11.0 - 12.0 Hz during decerebrate rigidity. Wrist compliance (displacement/ torque/ is reduced in proportion to the degree of rigidity.

MEASUREMENT	TORQUE APPLIED		INERTIA ADDED $Kg.m^2$ 0.0025	0.005	0.01
	Nm	Hz	Hz	Hz	Hz
1	1.0	8.14	7.05	6.74	3.84
2	"	8.14	7.05	5.51	3.84
3	"	8.14	7.22	5.95	3.84
4	"	7.35	6.45	5.51	3.86
5	"	7.58	6.32	5.95	4.01
6	"	7.58			3.74
7	"	7.58			3.74
		MEAN 7.78	6.81	5.93	3.83
		SD $\pm$ 0.34	0.40	0.50	0.09
			t = 4.50 (P <0.001) d.f. 10	t = 7.67 (P< 0.001) d.f. 10	t = 29.63 (P< 0.001) d.f. 10

Table 9:2

Oscillatory transients of the wrist (Hz) produced by low frequency abruptly alternating forces (Nm) during maximal voluntary stiffening in one normal subject and the effect of added inertia.

Wrist compliance and EMG activity of forearm muscles of patients with decerebrate rigidity during spontaneous relaxation, relaxation achieved by pharmacological agents and decerebrate rigidity.

CASE	AGE	SEX	TORQUE	JOINT COMPLIANCE (rad/N.m) and EMG ACTIVITY OF FOREARM MUSCLES (μV ; Extensors/Flexors)									
				SPONTANEOUS RELAXATION		RELAXATION PRODUCED BY						DECEREBRATE RIGIDITY	
						Pancuronium bromide		Diazepam		Chlorpromazine hydrocloride			
			(N.m)	(rad/N.m)	(μV)	(rad/N.m)	(μV)	(rad/N.m)	(μV)	(rad/N.m)	(μV)	(rad/N.m)	(μV)
B.S	25	M	0.6	2.88	22 / 28	4.78	4 / 7					1.51	128 / 96
A.B	10	M	0.9	0.96	10 / 10	1.25	3 / 2					0.09	151 / 111
I.L	19	M	0.9	1.23	17 / 17	1.64	0 / 6					0.16	158 / 119
J.W	8	F	0.9	1.93	14 / 15	2.85	4 / 3					0.28	150 / 160
G.McD	58	M	0.5	2.68	34 / 31	4.27	4 / 4					0.60	213 / 170
D.C	27	M	0.5	2.67	32 / 17			2.90	8 / 10	2.84	9 / 23	0.46	240 / 58
M.J	9	M	0.9	0.89	5 / 12			0.75	5 / 9			0.10	50 / 168
S.C	14	M	0.9	1.21	27 / 9	1.35	3 / 0					0.10	120 / 79
A.M	8	M	0.9	2.95	21 / 7	3.29	7 / 2					0.46	125 / 109
G.B	53	M	0.9	1.17	7 / 5	1.32	0 / 0					0.10	133 / 79
A.N	26	M	0.5	3.00	18 / 0	3.36	7 / 0					0.47	126 / 110
D.T	20	F	0.9	3.09	18 / 10	4.23	4 / 1	3.53	12 / 6	2.61	10 / 0	0.25	119 / 58
			MEAN	2.11	19.0/13.0	2.83	4.0/3.0	2.39	8.0/8.0	2.73	10.0/12.0	0.38	148.0/ 107.0
			SD±	0.88	8.9/ 8.8	1.36	2.3/2.5	1.45	3.5/2.0	0.16	0.7/16.2	0.38	49.5/ 39.2
		Student's	t:		1.77	1.53+	1.00	0.45+		0.95+			2.43(*)
					P < 0.1	P<0.1	P<0.2	P<0.5		P<0.2			P<0.025

(*) : Significant , (+) : As compared with values at spontaneous relaxation.

Table 9:3

2) Electromyography

Simultaneous study of the EMG at rest showed myotatic activity which was more pronounced in the extensor than in the flexor muscles in all patients but one who showed the converse. Myotatic activity was observed only when rigidity was minimal against a background of tonic muscle discharge. During decerebrate spasms no myotatic activity was present, although not infrequently myotatic activity preceeded the tonic discharge (Granit 1975). Forces too small to elicit stretch responses in the normal subjects produced detectable stretch responses in decerebrate subjects.

Shortening reactions were observed in only four patients; they were brief and intermittent and the electrical activity of both muscle groups was small.

3) Measurement of rigidity

Wrist compliance was calculated in all patients with decerebrate rigidity; summarised results are presented in Table 9:3. Mean compliance during spontaneous relaxation was 2.11 $\pm$ 0.88 rad/N.m whereas during maximal rigidity this was reduced to 0.38 $\pm$ 0.38 rad/N.m. The scatter among individuals, as with the normal subjects, was great in both conditions and there was an overlap in the values.

During muscular paralysis with pancuronium bromide the compliance was insignificantly (t: 1.53, $P < 0.1$) increased (2.83 $\pm$ 1.36 rad/N.m) from its value during spontaneous relaxation. Diazepam and chlorpromazine were less effective than the pancuronium but which of them is more effective in reducing rigidity cannot be definitely decided because of the small number examined.

SINUSOIDAL TORQUES OF LOGARITHMICALLY VARYING FREQUENCY

Preliminary study

When a sinusoidal torque of varying frequency is applied to a joint the amplitude of the resulting movement is greatest at a particular frequency due to a "resonance" phenomenon at a frequency correlated with the compliance (Walsh 1972).

As the velocity of a joint's movement is determined by the frequency and amplitude of the applied sinusoidal force, it is necessary to investigate the relationships between:

a) torque and resonance in the joint

b) torque frequency and resonance

c) sweep length (an interval during which a suitable range of torque frequencies is applied) and resonance.

The wrist joint was selected for the study as being most accessible and presenting fewer mechanical problems than other peripheral joints.

Patients and methods

Fourteen normal subjects, six males and eight females, of different handedness and widely differing body build and occupation were studied.

Sinusoidal torques were delivered to the hand which, therefore, oscillated with approximately the same phase. The peak force could be set at any level from 0.1-0.9 N.m which is enough to agitate a human wrist vigorously, and the frequency was automatically swept from 1.5-21.5 Hz in a known time interval. Two sweep rates were used:

a) 1/3 octave per second, i.e. the frequency doubling every 3 seconds over a range from 1.5 to 16.0 Hz (a scan of this range thus taking about 8 seconds) and

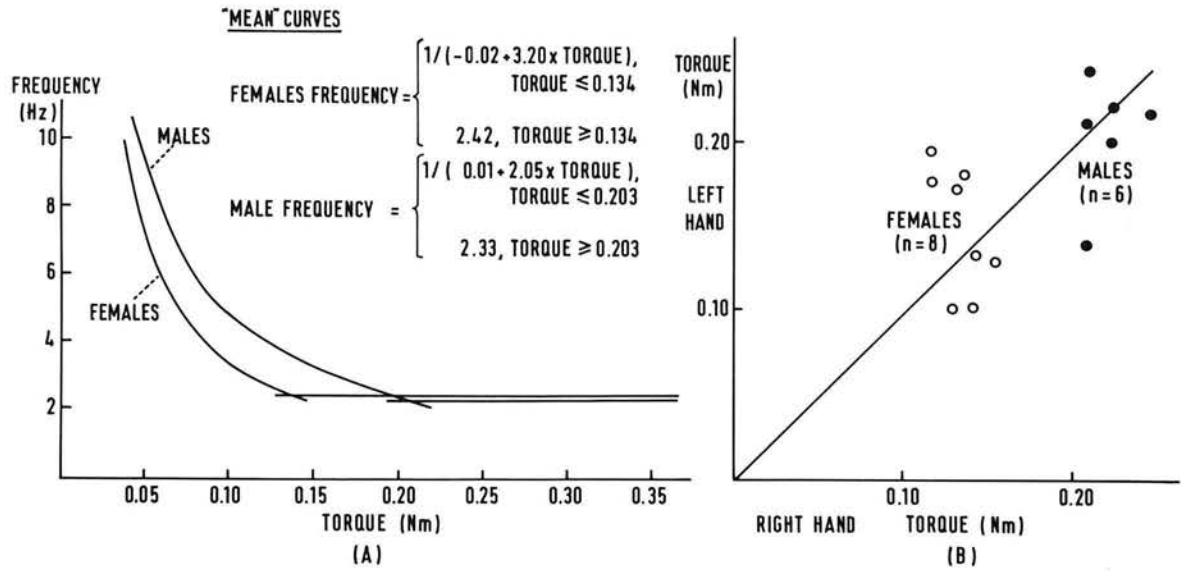


Fig. 9:3

(A) Rise in resonant frequency as torque is reduced below threshold level

(B) Torque threshold levels showing differences between men and women but no consistent difference between the two hands.

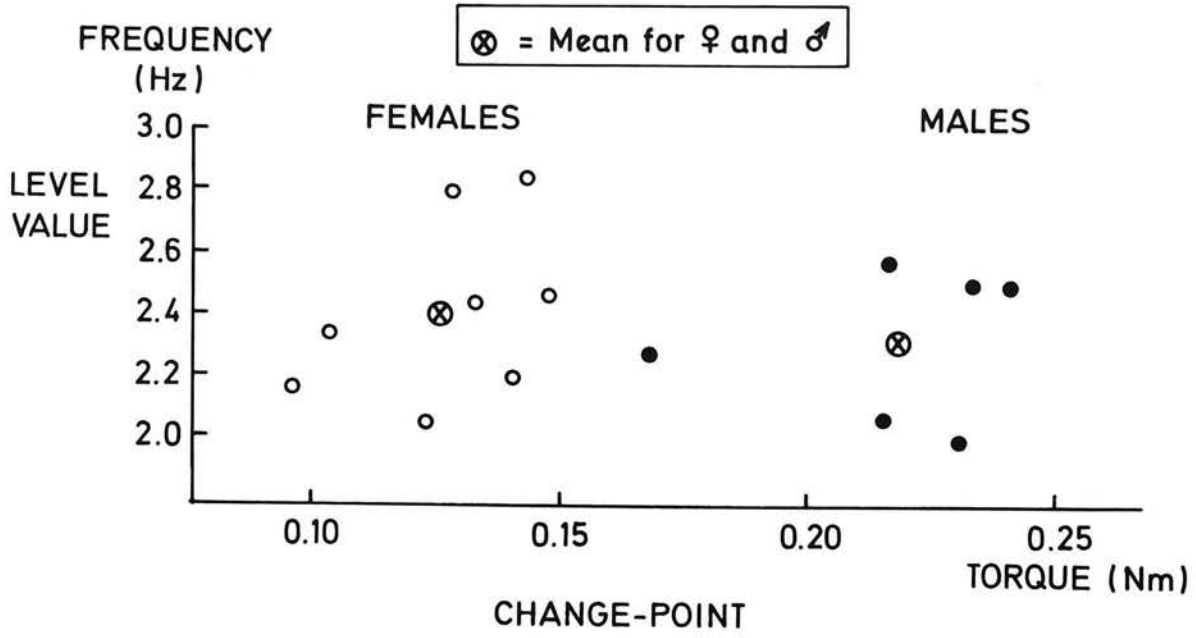


Fig. 9:4

Torque-resonance relationship between sexes. Males have a higher change-over value (threshold) than females, with no overlap in the values except for the anomalously low value for one case.

b) 1/12 octave per second (about 22 seconds per scan)

Results: 1) Effect of torque on resonance

When relaxed all subjects showed a characteristic resonance of the wrist. Above a certain force threshold this resonant frequency remained constant; there was no significant difference ($R'=36$, $P < 0.1$) between males (average resonance 2.33 Hz) and females (average resonance 2.42 Hz). Below the torque threshold value, the resonant frequency varied inversely with the torque. The threshold force value in males was 0.203 N.m. It was significantly lower in females at 0.134 N.m (at the 1% level using a Wilcoxon Rank Sum test) and there was no overlap in the values (Figs. 9:3 and 9:4). One subject, however, (WM, 29 years, male) showed an anomalously low threshold. Even so, there was no overlap with the female values. In a few cases at very high torque (0.5 N.m) the frequency deviated from its constant value at a lower level. When inertia was added to a female hand in an attempt to simulate a male hand the threshold moved in a direction opposite to that anticipated. Body build and occupation did not affect these results. The handedness of the subjects was also investigated but no consistent threshold differences were found between the two hands.

Five brothers, aged 5.5 - 13 years, were also investigated. All except the eldest showed a female resonance pattern; the latter, who was pubertal, showed a typical male pattern.

When subjects went as stiff as possible their resonant frequency was raised significantly and then torque variations had no effect on the resonance of the wrist.

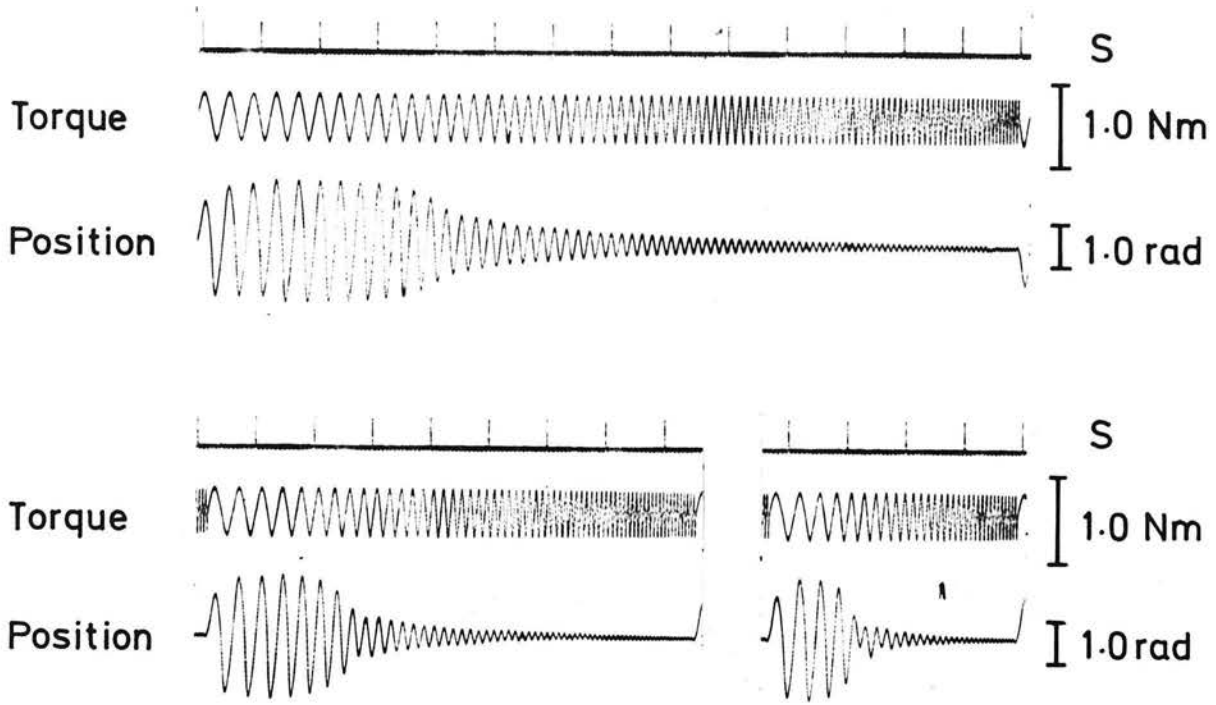


Fig. 9:5

Effect of sweep speed on resonance. By keeping the range of torque frequency constant but varying the sweep length the critical resonant frequency remains unchanged. The longer the sweep (top trace) the smoother the "envelope", whereas by reducing the sweep length (bottom traces) a sudden reduction of amplitude ("jump effect") is seen.

Results: 2) Effects of torque frequency on resonance

When two different ranges of torque frequencies were applied consecutively, one being double the other, the resonant frequency remained unchanged.

Results: 3) Effects of sweep speed on resonance

Conversely, by keeping the range of torque frequency constant but varying the sweep speed so that a scan of 1.5 - 16 Hz was applied during 5, 10 or 15 seconds the critical resonant frequency remained unchanged. The "envelope", however, was smoother when the sweep was longer (Fig. 9:5).

Discussion

It appeared from this study that the system behaves linearly with moderate torques and becomes non-linear when the torque is reduced below a threshold level which is different in men and women. This may reflect a difference in the joint itself or in the associated tendons or muscles. The observation that one small group of pre-pubertal male children showed a female pattern of reaction suggests that endocrine factors must be taken into consideration. This is to be investigated further. The fact that by loading a female's hand, its torque threshold value moved in a direction opposite to that predicted, shows that there is not a simple mechanical explanation for this.

The non-linear response of the system to low torques indicates that the system is heavily damped.

Normal subjects

1) "Jump effect"

Logarithmically modulated sinusoidal torques were applied to the wrist.

In a relaxed subject, when torques of decreasing frequencies were used at a constant level of 0.5 N.m, the amplitude of the oscillations of the displacement and velocity tracing increased smoothly and peaked at resonance. When torques of increasing frequencies were applied at a constant torque value, they started with large excursions and after the critical resonant frequency had been attained, the amplitude of the oscillations of both the position and velocity tracings was reduced by half or a third (Fig. 9:5): the so-called "jump effect" (Walsh 1974). This effect was usually produced by using large torques. The longer the sweep the more obvious was the effect. The jump effect appeared in nine out of fourteen subjects, but in a few of them it appeared in only one hand. It always appeared at torque frequencies between 2.5 - 3.0 Hz, a range just above the critical resonant frequency of the hand. The jump effect did not appear when the person went stiff voluntarily and thus increased the joint's natural frequency.

2) Resonant frequency

Sinusoidal torques of constant amplitude (0.25 N.m) and logarithmically modulated frequency (ranging from 1.5 - 21.5 Hz) were delivered to both wrists of each of the 14 volunteers. The wrist, therefore, oscillated with the same phase. Resonance of the joint was recognised when the amplitude of its movement was greatest; the torque frequency at which this occurred was recorded. The resonant frequency (RF) was measured from the "envelope" of the angular velocity trace; the higher the resonant frequency the greater the rigidity and vice versa.

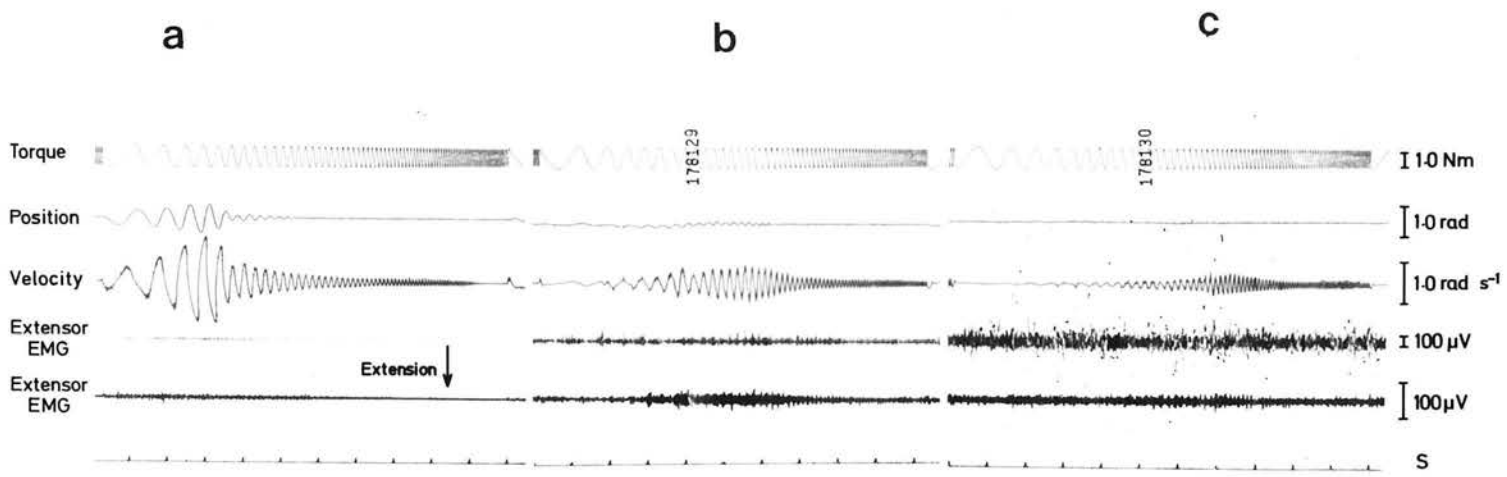


Fig. 9:6

Sinusoidal constant torques of logarithmically increasing frequency are applied to a normal wrist. Resonance of the joint is recognised when the amplitude of its movement is greatest. The resonant frequency, which is measured from the "envelope" of the velocity trace, varies with muscle tone. Increase in muscle tone by stiffening the wrist voluntarily elevated the resonant frequency, and both the extensor and flexor activity according to the degree of effort: (a) wrist fully relaxed, (b) partially stiff and (c) as stiff as possible.

Measurement of muscle tone during severe (group 1) and moderate (group 2) acute decerebrate rigidity, spontaneous relaxation of the rigidity and muscle paralysis. The resonant frequency was measured from the "envelope" of the angular velocity trace ; the higher the values the higher the degree of rigidity.

GROUP	CASE	TORQUE	RESONANT FREQUENCY (+)					INCREASE IN COMPLIANCE			
			Decerebrate rigidity	Spontaneous relaxation	Relaxation by (P)*	(D)*	(CPM)*	Spontaneous relaxation	Relaxation by (P)*	(D)*	(CPM)*
		(N.m)	(Hz)	(Hz)		(Hz)		(%)		(%)	
	B.S	0.32	10.50	3.72	1.83			684	3194		
	A.B	0.40	7.76	2.33	1.90			1008	1564		
	I.L	0.32	7.43	2.71	1.91			650	1413		
1	J.W	0.32	10.33	2.44	1.90			1689	2848		
	G.McD	0.32	11.12	2.86	1.89			1405	3357		
	D.C	0.40	8.37	3.49		2.12	2.24	471		1452	1291
	M.J	0.41	8.20	3.44		2.19		466		1298	
	S.C	0.41	4.02	2.00	1.56			320	770		
	A.N	0.33	5.51	2.59	1.88			349	758		
	G.B	0.41	4.67	2.37	1.90			288	500		
2	A.M	0.34	5.54	2.25	1.89			505	758		
	D.T	0.34	5.43	2.84	1.81			264	800		
		0.34	6.09	2.50	1.80			490	1042	788	
	N.McL	0.41	6.18	2.67			2.37	433			586

(P)* : Pancuronium bromide, (D)* : Diazepam, (CPM)* : Chlorpromazine hydrocloride
(+) : Mean resonant frequency of 20 normal wrists was 2.34 Hz (range 2.0 - 2.86); SD± 0.24

Table 9:4

When the subject was relaxed, the rate of oscillation of the joint was low, the amplitude was large and the EMG activity was absent or intermittent (Fig. 9:6). When the wrist was deliberately stiffened the rate increased, the amplitude was greatly reduced and the EMG activity became continuous and enhanced in both flexor and extensor muscles. All of these variations were proportional to the degree of effort (Fig.9:6).

The mean RF while the subjects were fully relaxed was 2.3 ± 0.2 Hz (range 2.0-2.8 Hz). When the subjects were partially stiff the mean RF increased, varying from 4.8 - 6.0 Hz; stiffening the wrist as much as possible raised the mean RF to 10.3 ± 1.3 Hz (range 8.3 - 12.5 Hz).

Patients with decerebrate rigidity

1) Resonant frequency

Sinusoidal torques of constant amplitude, 0.32 to 0.41 N.m, swept at frequencies similar to the controls, were delivered to the joint under examination.

During decerebrate rigidity the amplitude was reduced and both RF and the EMG activity increased. When a patient was relaxed (spontaneously or pharmacologically) the amplitude was great, the RF was low and the EMG showed little activity.

The RF during periods of greatest rigidity, spontaneous relaxation and paralysis is presented in detail in Table 9:4. Two groups were distinguished according to the degree of rigidity. Group 1 (cases with severe rigidity): The mean RF was 9.1 ± 1.5Hz (range 7.4 - 11.0 Hz). During spontaneous relaxation, however, the mean RF was reduced to 2.9 ± 0.56 Hz (range 2.3 - 3.7 Hz).

Group 2 (cases with moderate rigidity): The mean RF was 5.3 $\pm$ 0.8 Hz (range 4.0 - 6.1 Hz), while during spontaneous relaxation it was reduced to 2.4 $\pm$ 0.8 Hz (range 2.2 - 2.8 Hz).

The difference in the mean RF of Groups 1 and 2 during rigidity, spontaneous relaxation and "curarization" is highly significant, significant and not significant respectively (Table 9:5).

The difference between the mean RF of the control group and that of groups 1 and 2 during spontaneous relaxation is highly significant and not significant respectively (Table 9:6).

The increase in compliance of the relaxed limb as compared with the maximally rigid limb is considerable and is greatest in the paralysed limb (Table 9:4). Compliance was calculated as being proportional to the reciprocal of the square of the resonant frequency (Thomson 1964).

2) Effect of muscle relaxants on resonant frequency

In all cases (11/13) to whom it was administered pancuronium abolished decerebrate rigidity within two minutes approximately: this was tested clinically and verified on EMG. When muscle paralysis had been accomplished the RF was significantly decreased and varied from 1.3 - 1.9 Hz (mean RF 1.8 $\pm$ 0.17 Hz). The level of relaxation was significantly higher than that obtained with diazepam ($t = 2.63$, $P < 0.025$) and chlorpromazine ($t = 3.60$, $P < 0.005$). Diazepam was given in three cases whose mean RF was reduced (2.1 $\pm$ 0.14 Hz) and chlorpromazine in two cases whose mean RF was reduced to 2.25 Hz (Table 9:4). The level of relaxation achieved with both drugs was not significantly different ($t = 1.38$, $P < 0.2$) and, especially with chlorpromazine, it was unstable and the patient required frequent, repeated doses to maintain muscular relaxation.

	D.R.	S.R.	Cu
dMRF (Hz)	3.76	0.44	0.11
d.f.	12.00	12.00	9.00
t	5.87	2.30	1.07
P	0.001	0.50	0.20

Table 9:5

Difference in the mean resonant frequency (dMRF) between groups 1 and 2 during decerebrate rigidity (D.R.), spontaneous relaxation (S.R.) and "curarisation" (Cu).

	Spontaneous relaxation		
	1	2	N
MRF (Hz)	2.99	2.45	2.34
d (Hz)	0.65	0.11	
d.f.	25.00	25.00	
t	4.36	0.97	
P	0.001	0.20	

Table 9:6

Difference (d) in the mean resonant frequency (MRF) between the control (N) MRF and that of groups 1 and 2 during spontaneous relaxation following decerebrate rigidity.

DISCUSSION

LOW FREQUENCY SQUARE WAVEFORM TORQUES

Bursts of motor unit activity (8 - 12 Hz) from various skeletal muscles during voluntary contractions have been observed in EMG studies by many investigators. A physiological tremor of 8-12 Hz has been recorded during such muscle contractions from the extended third digit (Lippold 1970), the partially extended forearm (Fox and Randall 1970) and the soleus during "quiet standing" (Morri 1973). The tremor frequency may be decreased by adding mass as in the experiments of Fox and Randall (1970) or be relatively little affected by load (Robson 1959). These observations suggest that there are two types of tremor; in one the frequency is load-dependent whereas in the other it is not.

The oscillatory transients observed after sudden displacement of the wrist in the normal subjects during contraction and in the patients exhibiting decerebrate rigidity were in the range 8 - 12 Hz. It is likely that they represent a masked tremor, the mechanism of which may possibly be the same as in overt tremor. If this is the case, the tremor appears to be load dependent as it decreased on adding mass to the system. Oscillatory transients have been seen and studied extensively in mechanical servo systems subjected to sudden displacement. This effect is called "ringing" or "howling" and appears when the system becomes unstable (Bayliss 1966).

The passively displaced hand resists movement because of a) inertia; b) viscoelastic properties of its muscles and joints, (essentially what we describe as muscle tone) and c) its stretch reflex activity. The sum of these three processes

characterises the wrist compliance. As inertia remained unaltered, the wrist compliance was dependent on visco-elasticity and reflex activity. Although compliance has been widely used in mechanical systems as an index of elasticity, its measurement in complex biological systems presents problems. The great scatter of compliance values between individuals which we saw in our study is a serious disadvantage with regard to its use as an accurate and reliable index of muscle tone. Marked fluctuations in muscle tone may yet fall within the wide range of normal variation, especially as prior studies of the state of our patients were not available for comparison.

SINUSOIDAL TORQUES OF LOGARITHMICALLY VARYING FREQUENCY

A servo control system oscillates when its input is oscillated over a suitable range of frequencies. If the input amplitude is kept constant while the frequency is varied, the output amplitude increases to a maximum value, i.e. resonance occurs, when the input frequency is near the natural frequency of the oscillating system (Cunningham 1958).

Since the mass of the hand remains unchanged, its resonant frequency depends on the viscoelastic resistance with which the soft tissue of the system reacts to the displacement. This resistance, which is the muscle tone, cannot, however, be measured directly during oscillatory movements as factors such as the force required to move the mass of the hand complicate the measurement. When resonance occurs, however, the inertia due to the mass is balanced by the viscoelastic properties of the limb and the elastic resistance can be measured directly. In other words, at resonance the resonant frequency is the

"natural frequency" of the system.

The RF of the wrist in a few normal relaxed subjects, as described by Walsh (1977), varied between 2.0 and 2.5 Hz, while maximal clenching of the fist raised it to 13.0 Hz, whereas in a professional pianist it reached 16.0 Hz.

The observation that during spontaneous relaxation in cases with decerebrate rigidity the RF was higher than in normal relaxed subjects, indicates that although the muscles appear to be at rest between spasms, this is not, in fact, the case.

On mechanical ventilation and curarization the RF fell to well below 2.0 Hz, less than was seen in any of our volunteer subjects or in any decerebrate patient after either diazepam or chlorpromazine. It has been reported that in a very few normal, paralysed subjects the RF did not fall below 2.0 Hz (Walsh 1977). This suggests that pancuronium is more effective in the decerebrate patient than in the normal subject but Dr. Walsh agrees (personal communication 1978) that his findings may have been anomalous and are certainly insufficient in number for valid conclusions to be drawn.

A value of less than 2.0 Hz for the RF of the wrist thus appears to be distinctly unusual under any normal circumstances. The method may be useful in the clinical assessment of muscular hypotonia as well as of rigidity. Estimation of muscle tone by measuring the RF is reliable and reproducible, and has a theoretical basis in current concepts of neuromuscular control mechanisms.

COMPARISON OF THE TWO METHODS

A disadvantage of the resonance method as compared with applying a simple step function (square wave) is that the measurement takes longer and the system thus measured may vary its level of function during the period of measurement. This is particularly true of sharply resonant systems where a bias may be introduced if the rate of change of frequency during the sweep is too great. The duration of the sweep used in this study (8 seconds) represents a compromise between the requirements of accuracy and speed. The technique has been validated by using different sweep speeds as described.

The use of square waves allows a continuous sequence of measurements of displacement from which estimates of tone are obtained, so that in spite of the wide scatter of results useful estimates of changes in tone can be obtained. We consider that the difference in tonicity measurements obtained by the two methods is due to differences in the phenomena measured. It is unlikely that inertia or viscoelasticity will alter, so it must be a difference in stretch reflex activity; this has been shown to be produced when square waveform torques produced a sudden displacement of the hand, whereas with sinusoidal torques myotatic activity was not observed. It is known that this reflex activity is load-dependent and its threshold is much lower in spastic and decerebrate cases (Matthews and Stein 1969).

CHAPTER 10

THE EFFECT OF DECEREBRATE RIGIDITY ON INTRACRANIAL PRESSURE UNDER CONDITIONS OF ALTERED CEREBRAL ELASTANCE

INTRODUCTION

Any patient with a lesion located anywhere between the caudal thalamus and the rostral pons may show decerebrate rigidity (Walshe 1923, Nielsen 1941). Such lesions are either primary or secondary to a supratentorial space-occupying lesion (haematoma, contusion or acute hydrocephalus). In these circumstances the intracranial elastance is increased. Later, the elastance is reduced if chronic post-traumatic hydrocephalus develops.

It was shown in the cat (Chapter 8) that under conditions of normal brain elastance, mild and short-lasting spasms had no effect on the ICP; when the brain elastance, however, had been increased experimentally, similar spasms produced a marked increase in ICP.

It would appear, therefore, that the effect of decerebrate spasms on the ICP depends on the brain elastance. This has been investigated in man with a view to clarifying some of the problems posed by these difficult cases.

PATIENTS AND METHODS

Thirteen out of thirty three patients with a head injury and decerebrate rigidity were selected for study as having well-developed and similarly distributed rigidity of their peripheral and truncal musculature. Selection was based primarily on clinical assessment of the degree of rigidity; the frequency and duration of the decerebrate spasms were considered as of minor importance. It was hoped that by selecting cases with well-developed, bilateral decerebrate rigidity we would eliminate variability of the rigidity as a factor affecting the ICP.

The remaining twenty cases were excluded because:

a) Decerebrate rigidity was very mild, unilateral or affected only one limb.

b) On occasion, the Consultant in charge withheld his co-operation because of the apparently non-contributory nature of the investigation in particular patients, despite the fact that the study had been cleared by the appropriate Ethics Committee.

c) Rarely, for technical reasons satisfactory data were not obtained.

Ten of the cases were investigated in the acute stage of rigidity; this was as soon as possible after surgery and the patient had been on mechanical ventilation (IPPV) for 6 to 12 hours. When instrumentation had been set up and the arterial gas tensions had been confirmed as being within normal limits, several measurements of muscle tone, ICP, systemic arterial pressure (SAP) and intrathoracic pressure (ITP) were obtained. Relaxants were then allowed to wear off; rigidity soon developed and the measurements were repeated over a period of 30 minutes, during which time decerebrate spasms came and went and we could study their effect on the ICP, ITP and SAP. At least twenty simultaneous measurements of all parameters were obtained in each case. If, by the end of this period, technically satisfactory data had not been obtained, the patient was reparalysed and the procedure was repeated the following day.

Some cases were also studied after 3 to 8 days on IPPV.

The remaining three cases, who suffered from post-traumatic hydrocephalus, still exhibited severe decerebrate rigidity 3 to 4 weeks after injury. These were examined repeatedly and

provided the opportunity to study the effects of diazepam and chlorpromazine on both rigidity and ICP.

MEASUREMENT OF DECEREBRATE RIGIDITY

Muscle tonicity was measured by the technique called "torque-induced motion analysis" by Walsh (1974, see Chapter 9).

Two methods can be used to measure muscle tone:

a) forces of square waveform are applied and the calculated compliance of the joint used as an index of rigidity,

b) forces of sinusoidal waveform are employed, the resonant frequency of the joint measured and used as an index of rigidity.

The differences in the results obtained and possible causes for these are discussed in the previous section.

We chose to use the resonant frequency of the wrists of patients with decerebrate rigidity as an index of rigidity in this study because it gave more reproducible and consistent results over many repeated measurements on the same patient at different times and amongst the total number of patients studied.

MEASUREMENT OF VENTRICULAR FLUID PRESSURE (VFP)

The VFP was continuously measured by means of an extra-cranial physiological pressure transducer (Bell and Howell) via a rigid transparent polyethylene catheter inserted into the lateral ventricle. The pressure levels were displayed on a felt-pen recorder. (see Methodology section).

MEASUREMENT OF PRESSURE/VOLUME RELATIONSHIPS

The method of Millar (1973) was used; this has already been discussed in detail.

VFP changes were recorded on a scale which was sensitive

enough to accurately record minimal changes; this was simply achieved by adjusting the sensitivity of the pre-amplifier.

In those cases with an initially high resting level the test was performed once only to avoid a further, dangerous increase in VFP. The presence of a space-occupying lesion and the size of the ventricular system were ascertained either at operation or by arteriography, ventriculography or computerised axial tomography.

At the time of the investigation none of the hydrocephalics had been shunted. Dehydrating agents had not been administered to any patient for at least one hour before the study.

The test was repeated on each patient and the figure obtained was compared with the value obtained before the start of the measurements.

OTHER PARAMETERS

The SAP was measured every 5 minutes with a sphygmomanometer or continuously by means of a transducer and a catheter in the radial artery.

The ITP was measured by means of a latex balloon catheter in the distal oesophagus with the patient lying slightly tilted to his left side.

During the period of IPPV carbon dioxide and oxygen tensions (pCO_2 and pO_2), hydrogen ion activity (H^+) and standard bicarbonate (HCO_3) were repeatedly measured in arterial blood. Samples were taken before and during or immediately after the spasms which occurred when the relaxants were allowed to wear off.

Electroencephalograms (EEGs) were performed in four cases

throughout the period of investigation. In one other case, a so-called "cerebral function monitor" (Devices) was used (Maynard et al. 1969); this continuously records cerebral electrical activity as the integral of a two-lead EEG against time.

Muscle paralysis was induced by pancuronium bromide (Pavulon - Organon/Teknika); an initial dose of 0.08 - 0.1 mg/Kg followed by hourly supplements of 0.01 - 0.02 mg/Kg usually sufficed but some patients required more or less frequent supplements. The decay of the relaxant effect was assessed from the admittedly crude criteria of the patient's reactions to painful stimuli - withdrawal reflexes, abnormal posturing and inconstant changes in heart rate or blood pressure.

Diazepam (Valium- Roche) in repeated doses of 10 mg intra-muscularly or continuous intra-venous infusions of 5 - 10 mg/Kg body weight/24 hours and chlorpromazine hydrochloride (Largactil - May and Baker Ltd) in repeated doses of 25 - 50 mg intramuscularly were administered to a few patients for the control of rigidity.

RESULTS

DECEREBRATE RIGIDITY

Detailed data are presented in Chapter 9.

BRAIN ELASTANCE

Studies of the intracranial V/P relationships in head injured patients have shown that when consecutive measurements of the VFP differ by less than 2 mmHg per ml of fluid injected

or withdrawn the elastance may be regarded as normal; a figure greater than this signifies an abnormally high elastance.

Three groups of patients were distinguished on the basis of their intracranial elastance.

Normal elastance

Five cases showed increases in their mean VFP of 1.4 mmHg/ml (range 0.8 - 2.2 mmHg/ml)

High elastance

Five cases showed a critical P/V relationship; the mean VFP being raised by 6.8 mmHg/ml (range 3.7 - 18.5 mmHg/ml). All showed evidence of an intracranial space-occupying lesion.

Low elastance

Three cases showed little or no increase in their mean VFP of 0.2 mmHg/ml (range 0.0 - 0.4 mmHg/ml). All had post-traumatic hydrocephalus.

VFP CHANGES DURING DECEREBRATE RIGIDITY

Group A: Normal elastance (5 cases)

The mean resting VFP of 11.0 $\pm$ 2.4 mmHg was unaltered by IPPV. Allowing the relaxants to wear off had no effect provided decerebrate spasms did not develop. When these occurred the mean VFP rapidly and significantly rose to 24.5 $\pm$ 0.8 mmHg. Throughout the period of rigidity both the amplitude and frequency of the cerebral pulse wave were increased, especially at the maximum VFP. When rigidity passed off, either spontaneously or as a result of the administration of relaxants, the VFP and its waveform regained their prespasm profile (Fig.10:1). The maximum pressure recorded in any individual during rigidity

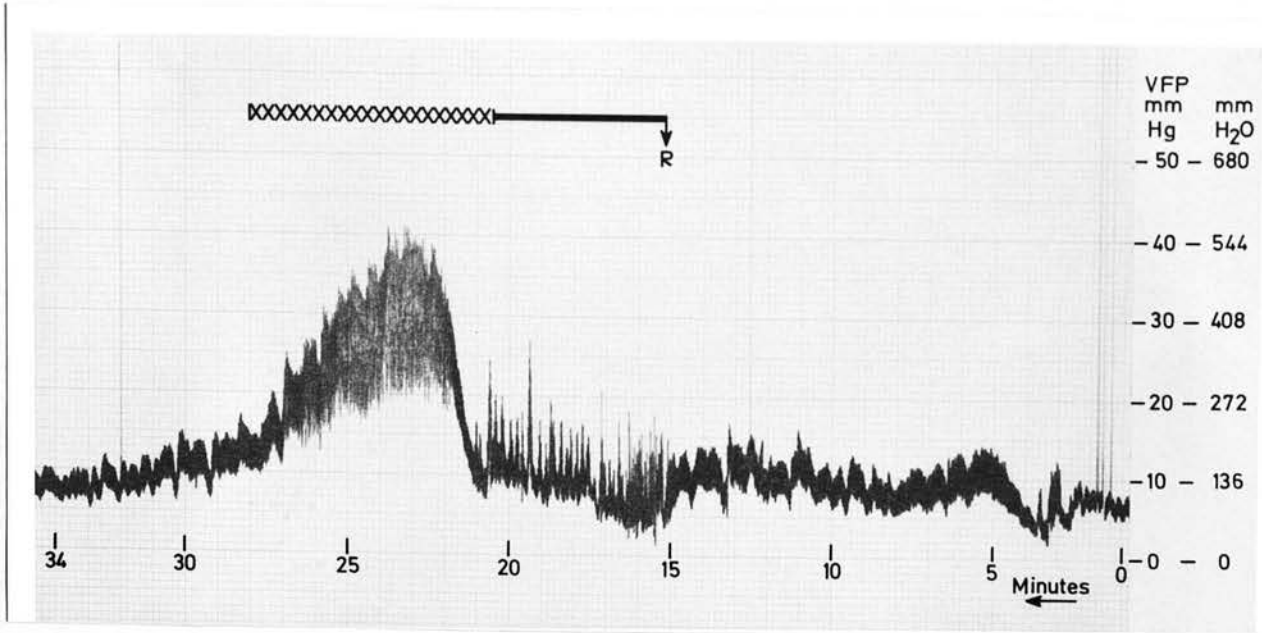


Fig. 10:1

Record of the VFP under conditions of normal brain elastance.

(xxxxxx : decerebrate spasms, R: indicated start of period during which routine recording of blood pressure, heart and respiratory rate and of temperature were made).

was 37.0 mmHg in a patient whose resting VFP was 13.0 mmHg.

Two cases developed severe and the other three moderate rigidity, the former showing the greater increase in VFP (Table 10:1).

Three cases were re-investigated at the end of a period of paralysis and IPPV when they were breathing spontaneously. Two cases showed levels comparable with those observed earlier. Two days after injury, one case (Table 10:1, case 3) showed an increased cerebral elastance, without evidence of clinical deterioration; when her relaxants were reversed the VFP rose to 36.0 mmHg.

Group B: High elastance (5 cases)

An average resting value of 26.5 $\pm$ 8.9 mmHg was recorded. During a decerebrate spasm the VFP was increased to 68.5 $\pm$ 11.6 mmHg and sustained at this level, while the amplitude and frequency of the cerebral pulse were increased. On termination of the spasm the VFP settled to its previous level and the appearance of the cerebral pulse wave was restored to normal (Figs. 10:2 and 10:3). The maximum individual rise was seen in case No. 9, in which the VFP went up to 72.0 mmHg from a resting level of 17.0 mmHg.

Three cases who had severe rigidity showed a greater rise in VFP than the two who developed only moderate rigidity (Table 10:1).

Only two cases could be re-investigated (the others had died), after 2 and 4 days. One case showed a rise in VFP, rigidity and elastance similar to that seen when first examined. The second case showed a significant reduction of the mean VFP to 44.0 mmHg, a significant reduction in rigidity to 6.1 Hz and an almost normal elastance.

The mean ventricular fluid pressure(VFP) and intrathoracic pressure(ITP) during mechanical ventilation(IPPV), spontaneous relaxation and maximal decerebrate rigidity under conditions of normal(A), increased(B), and decreased(C) cerebral elastance(E).

E	CASES	Mean V F P				Mean I T P			
		SPONTANEOUS RELAXATION (mmHg)	MAXIMAL RIGIDITY (mmHg)	INCREASE (mmHg) (%)		I P P V (mmHg)	SPONTANEOUS RELAXATION (mmHg)	MAXIMAL RIGIDITY (mmHg)	INCREASE (mmHg) (%)
A	G.B	9.0	16.0	7.0 (78)		+6	-3	+13	+16 (533)
	A.M	15.0	22.5	7.5 (50)		+5	-5	+14	+19 (380)
	D.T	11.0	19.5	8.5 (77)		+5	-4	+27	+31 (675)
	J.W	9.0	27.5	18.5 (205)		+6	-4	+30	+34 (750)
	G.McD	12.0	37.0	25.0 (209)		+6	-4	+32	+28 (700)
	MEAN	11.0	24.5	13.5 (123)					
	SD±	2.4	8.0						
B	S.C	22.5	61.0	38.5 (171)		+6	-3	+20	+23 (767)
	A.N	22.0	52.5	30.5 (139)		+6	-4	+12	+16 (400)
	B.S	36.0	83.0	47.0 (131)		+6	-3	+23	+26 (866)
	A.B	17.0	72.0	55.0 (324)		+5	-4	+42	+46 (1150)
	I.L	36.0	74.5	38.5 (107)		+6	-4	+27	+31 (775)
	MEAN	26.5	68.5	42.0 (159)					
	SD±	8.9	11.6						
C	N.McL	8.5	9.5	1.0 (12)			-3	+17	+19 (633)
	D.C	7.0	8.5	1.5 (21)			-4	+36	+39 (975)
	M.J	7.5	11.0	3.5 (46)			-3	+26	+29 (967)
	MEAN	8.0	10.0	2.0 (25)					
	SD±	0.8	1.3						

Table 10:1

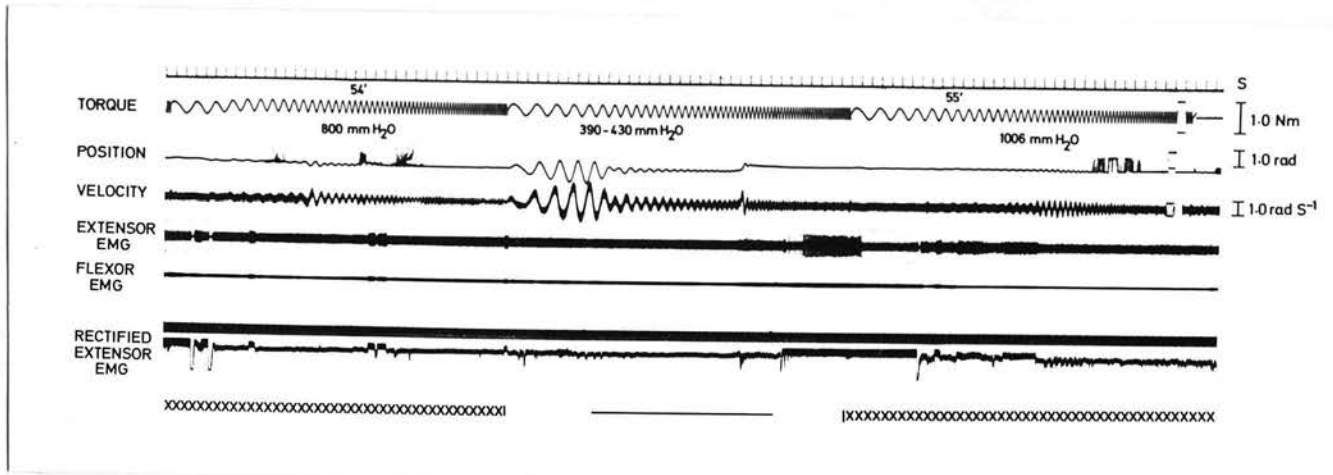


Fig. 10:2

Record of muscle tone and VFP under increased brain elastance in a head injured patient. (VFP in mmH_2O presented over the resonance "envelopes" during periods of maximum rigidity (xxxxxxx) and spontaneous relaxation (———)).

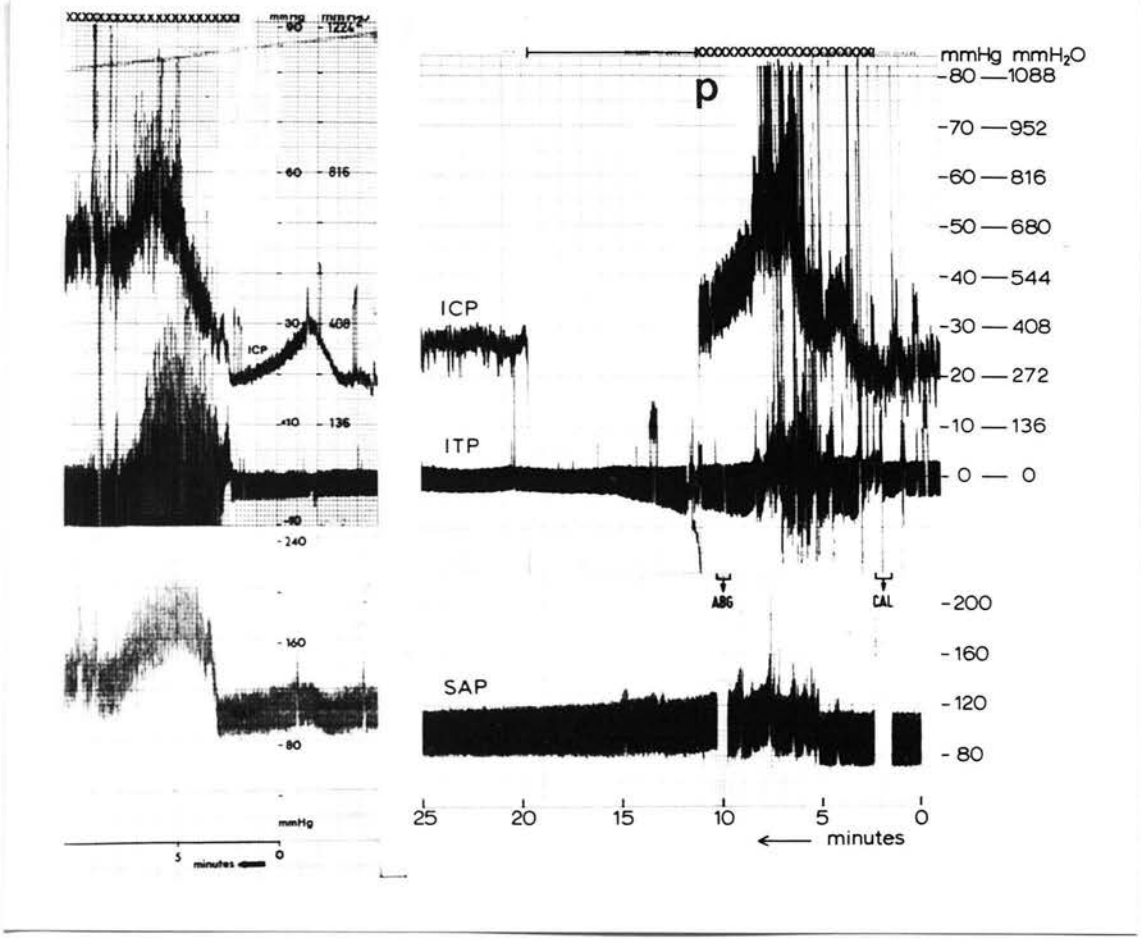


Fig. 10:3

Recording of the ICP, ITP and SAP during the onset of decerebrate spasms (xxxx). Despite the low speed of chart recording and the marginal time difference at which the parameters begin to alter with the onset of decerebrate rigidity, it seems that the ITP rises first and is followed by the ICP and SAP.

ABG: arterial blood sample withdrawn for blood gases.

CAL: calibration and zero checked.

(——):period of muscle paralysis and mechanical ventilation

P: pancuronium bromide.

Group C: Low elastance (3 cases)

These patients were repeatedly tested on different dates; the results were always much the same, a mean resting VFP of 8.0 ± 0.8 mmHg being recorded. Decerebrate spasms produced insignificant rises in the mean VFP (to 10.0 mmHg). The greatest rise in any one case was 4 mmHg above the resting level of 7.5 mmHg (Table 10:1).

From these results it appears that the two main determinants of the magnitude of the increase in VFP during decerebrate rigidity are the brain elastance and muscle hypertonicity. The relationship between the three parameters is graphically displayed in Figs. 10.4 and 10.5.

We undertook a statistical analysis of the relative importance of these factors in elevating the VFP, using a logarithmic scale for the VFP in order to equalise the variability within each elastance group. In each of the elastance groups the rise in VFP from rest to spasm was plotted against decerebrate rigidity (in Hz). Multiple regression analysis was applied to determine the influence of resting VFP, elastance and rigidity on the rise in VFP. The resting value of the VFP did not significantly influence the increase in this parameter when the other two factors were taken into account. The effect of elastance was highly significant ($F = 63.23$ with 2 and 9 d.f.) while that of rigidity was also significant ($t: 2.42$ with 9 d.f.). There was no significant difference in the slope of the lines ($F = 1.60$ with 2 and 7 d.f.); they were, in fact, parallel (Fig. 10:6). A significantly better fit was not obtained with lines of different slope

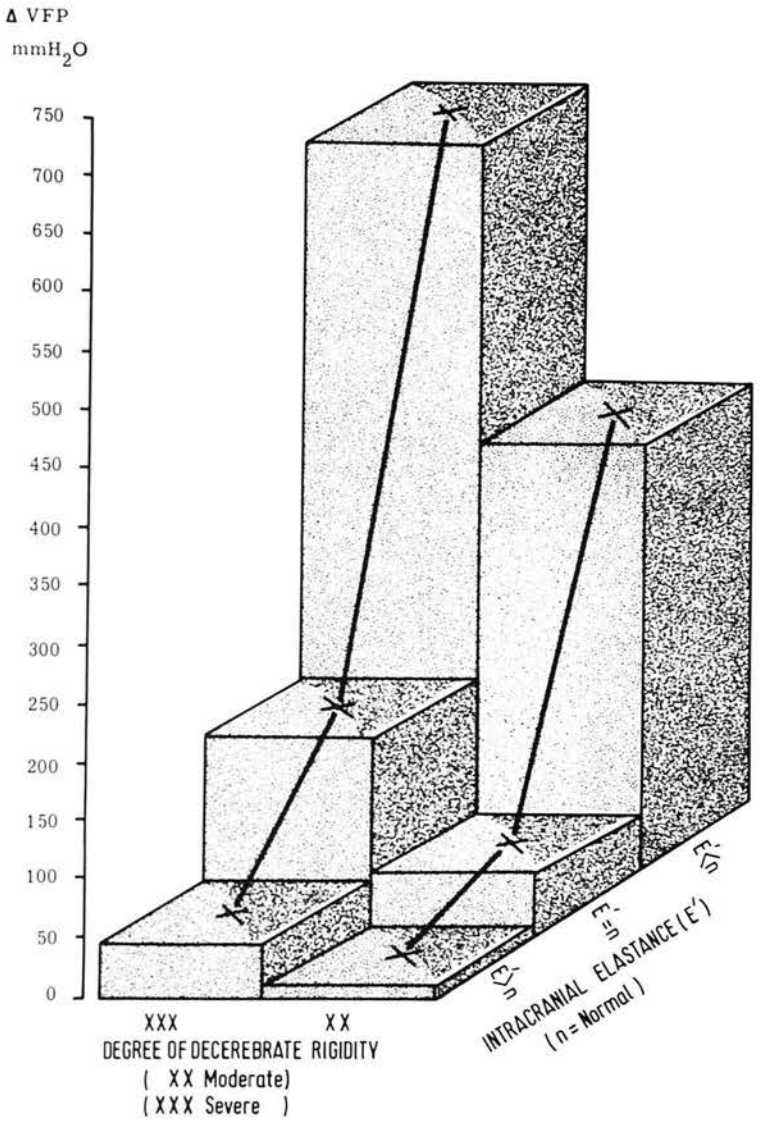


Fig. 10:4

Changes in VFP are shown as affected by the degree of rigidity and brain elastance.

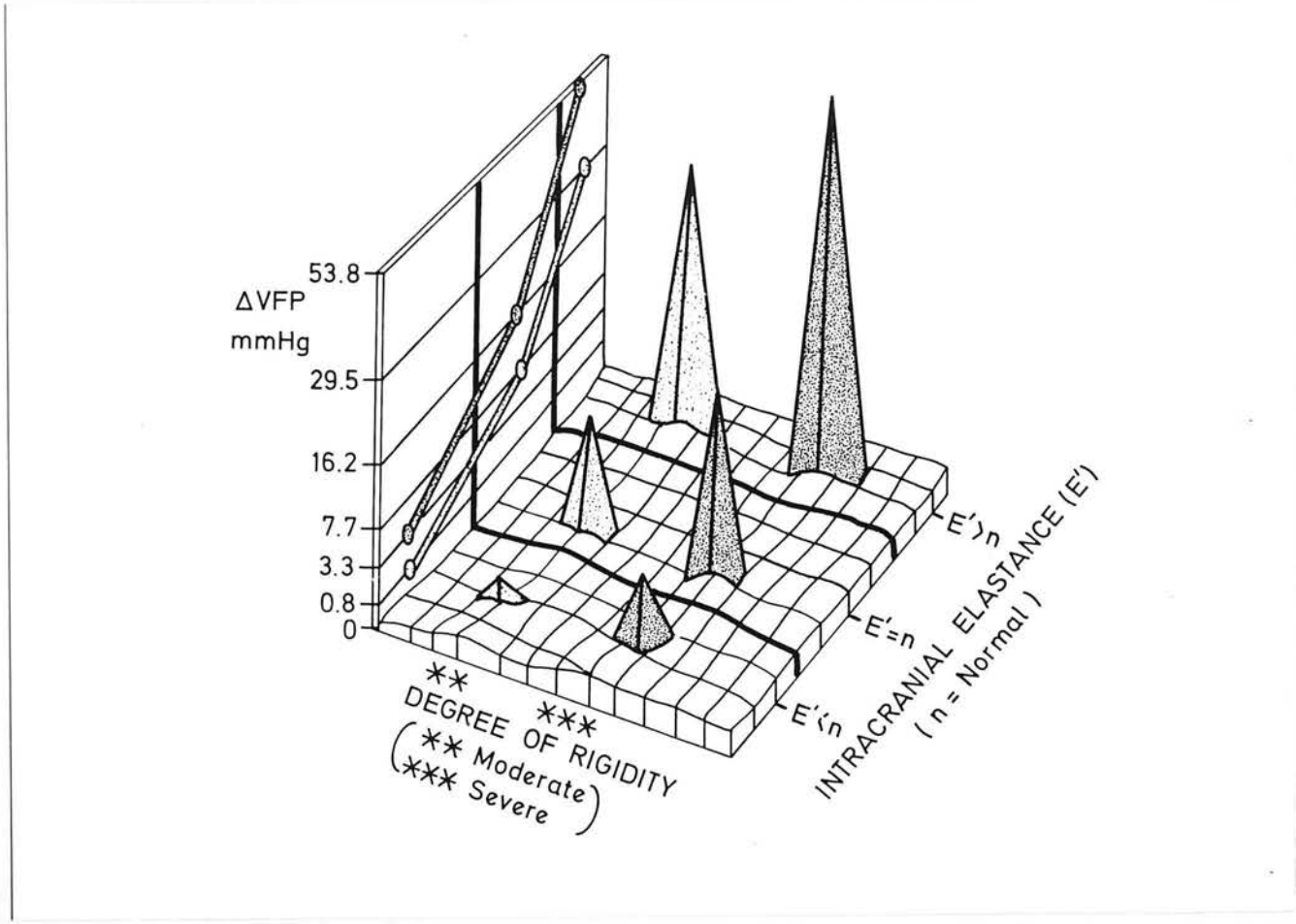


Fig. 10:5

A three dimensional representation of the changes in VFP during moderate and severe decerebrate rigidity and under conditions of altered cerebral elastance. The continuous fluctuations of the VFP are expressed by the wavy base; heavy dotted peaks show VFP changes during severe (xxx) and lightly dotted peaks show VFP changes during moderate (xx) decerebrate rigidity with differing cerebral elastance (E). The peaks are plotted on a calibrated board. It is apparent that the higher the rigidity and elastance the greater the rise in VFP.

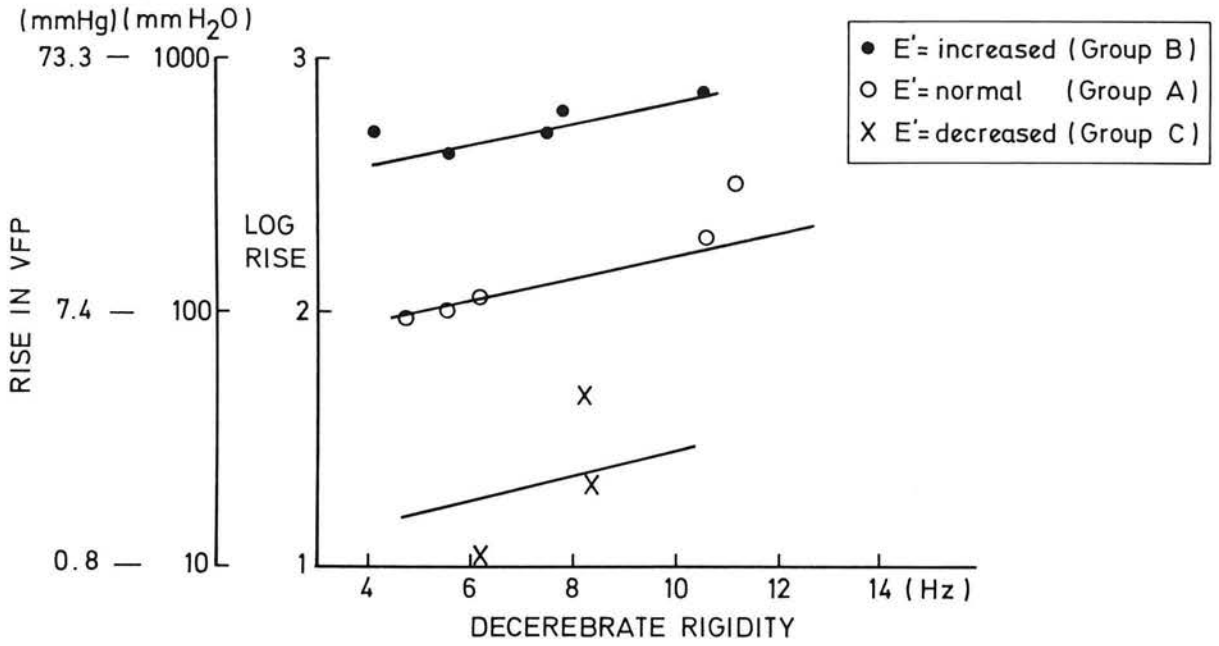


Fig. 10:6

The diagram shows the rise in VFP from rest to spasm plotted against decerebrate rigidity in three groups of patients (A, B and C) with differing brain elastance (E). A logarithmic scale for the VFP is used to equalise the variability within each group.

through the three sets of points, and therefore, the simpler model of parallel lines was preferred. The formulae for the lines were:

$$\log \text{rise} = \text{constant} + 0.038 \times \text{rigidity}$$

where the constant was 1.84, 2.47 or 1.05 for Groups A, B and C respectively.

For each elastance group the increase in VFP from rest to maximum spasm was plotted against its resting level and a line computed to best fit the points for each elastance group. If the three lines thus obtained were displayed on a single graph (Fig. 10:7), a significantly greater rise in VFP was found in severe rigidity than in moderate rigidity ($t = 4.27$ with 7 d.f.).

EFFECT OF MUSCLE RELAXANTS ON VFP

The elevated VFP seen during decerebrate spasms was reduced in all patients after the administration of muscle relaxants. In patients with normal and reduced elastance the raised VFP returned to its previous level and the deeper the relaxation, the quicker and more lasting was the reduction (Fig. 10:8). Both diazepam and chlorpromazine would temporarily reduce the VFP to its normal value but the spasms, although greatly reduced in number and severity, were not entirely abolished and elevations in VFP could still occur (Fig. 10:9). Rises in VFP could be prevented only by complete paralysis with pancuronium. In patients with an increase in both elastance and resting level, paralysis returned the VFP to its previous abnormal resting level.

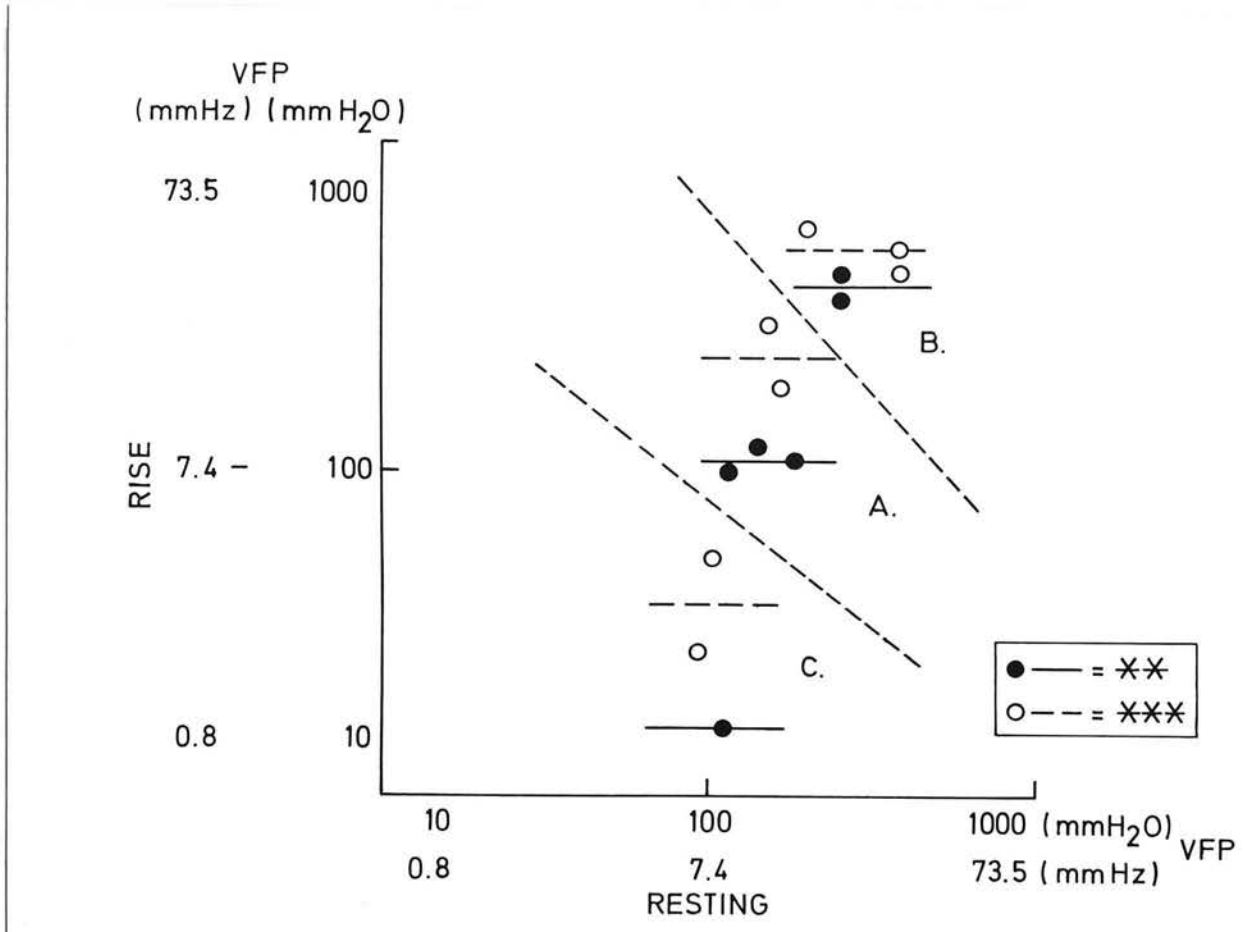


Fig. 10:7

The diagram shows the rise in VFP from rest to spasm plotted against the resting VFP level in the three groups of patients with differing elastance - A, B and C. In each elastance group the greater the rigidity the higher the rise in VFP. A logarithmic scale is used on both axes in order to equalise the variability within groups of points.

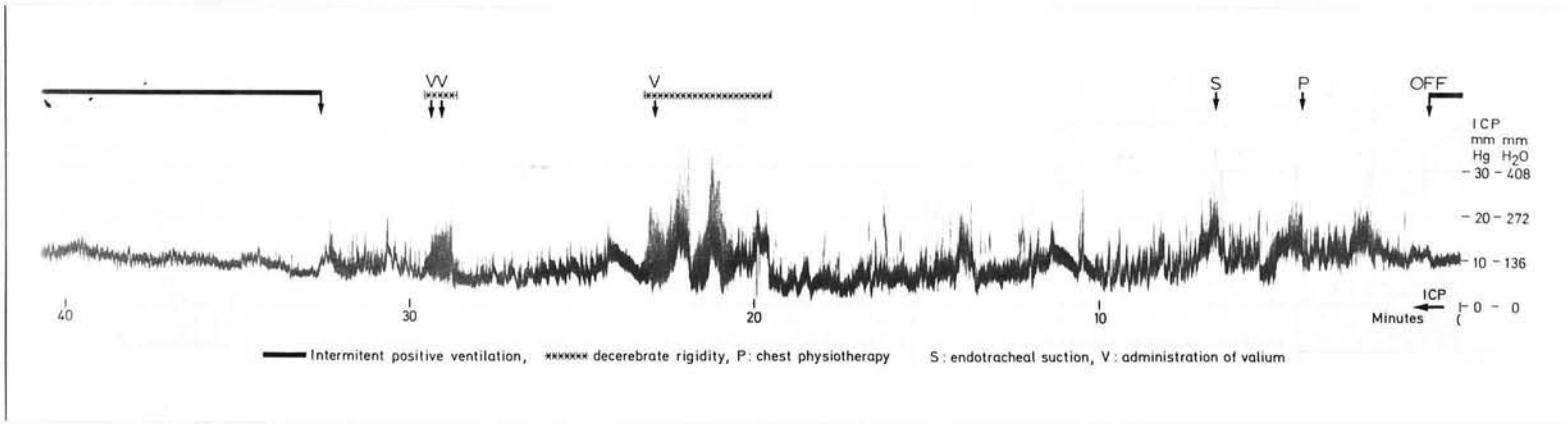


Fig. 10:8

Record of the VFP during decerebrate rigidity. Administration of diazepam to control spasms failed and paralysis by pancuronium and mechanical ventilation were re-established (Brain injury with normal brain elastance).

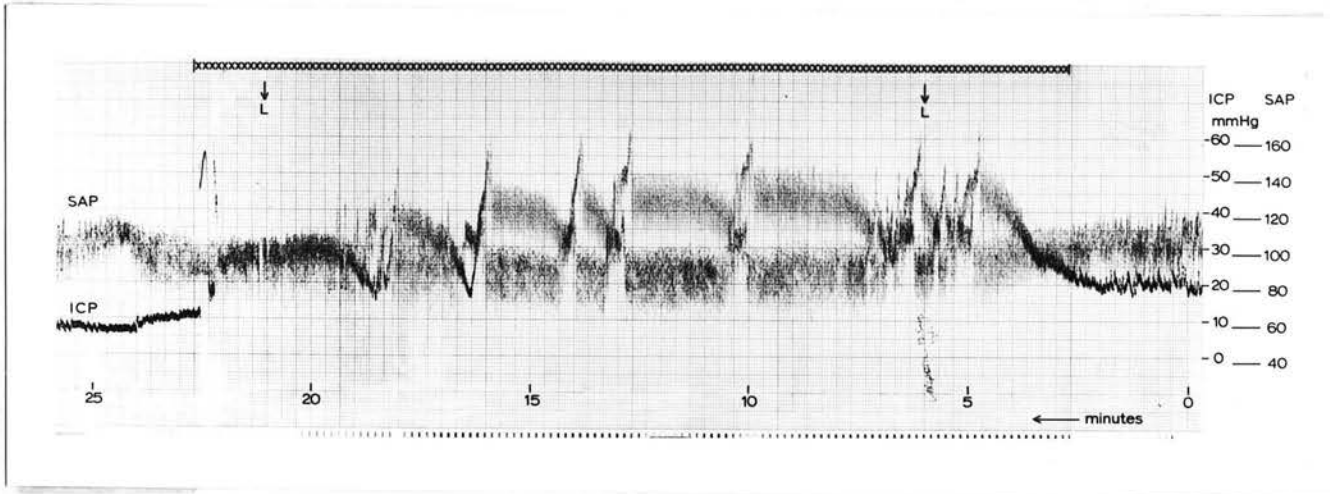


Fig. 10:9

Marked rises in ICP during decerebrate spasms whereas the simultaneously monitored SAP remained virtually unchanged. Some slight, short-lasting rises in SAP followed the sudden elevation in ICP at the onset of each intensification of the spasm. Administration of Largactil (L) took some time to reduce the severity of spasms but it never abolished them.

ASSOCIATED PHENOMENA: THEIR RELATIONSHIP TO VFP ALTERATIONS

Cardiovascular changes

1) Heart rate (HR)

The heart rate before and during spasms during spontaneous breathing and IPPV is shown in Table 10:2.

During IPPV the average HR was 105 $\pm$ 20/min; all showed a slight tachycardia except for one who developed a bradycardia which was cured with atropine. The mean rate settled to normal as soon as spontaneous breathing was restored. The average HR during relaxation on spontaneous ventilation (SV) was 108 $\pm$ 17/min; essentially the same as on IPPV. During spasms a significant tachycardia (mean 140 $\pm$ 20/min) was always present. The rise was proportional to the severity of spasms but bore no relationshp to the intracranial elastance (Fig. 10.10).

2) Systemic arterial pressure (SAP)

Data for systolic (syst SAP) and diastolic (diast SAP) arterial pressures during IPPV and spontaneous breathing while the subjects were relaxed or rigid are shown in Table 10:2. The average pressure during IPPV was 118.5 $\pm$ 14/79.0 $\pm$ 13 mmHg. When paralysis wore off the mean figures were 130.0 $\pm$ 17/ 79.5 $\pm$ 12 mmHg; the increase in systolic pressure, although statistically significant ($t : 3.87$, $P < 0.005$), was of no clinical significance. The average diastolic remained essentially unchanged.

During decerebrate spasms both pressures were greatly increased, particularly the former, average values being 156.0 $\pm$ 22/90.0 $\pm$ 17 mmHg. Again, although this increase was significant (syst SAP, $t:8.32$, $P < 0.001$ and diast SAP, $t:5.13$, $P < 0.001$), it was clinically insignificant. A very wide

PATIENT	PULSE RATE (beats/min)				SYSTOLIC BLOOD PRESSURE (mm Hg)				DIASTOLIC BLOOD PRESSURE (mm Hg)			
	IPPV	S.R.	M.R.		IPPV	S.R.	M.R.		IPPV	S.R.	M.R.	
G.B.	125	125	140	(+ 15)	110	125	135	(+ 10)	60	60	65	(+ 5)
A.M.	100	94	120	(+ 26)	100	130	148	(+ 18)	65	70	80	(+ 10)
D.T.	95	92	120	(+ 28)	115	130	135	(+ 5)	80	86	90	(+ 4)
J.W.	95	110	152	(+ 42)	120	125	170	(+ 35)	85	80	95	(+ 15)
G.McD.	110	128	170	(+ 42)	110	130	166	(+ 36)	80	80	95	(+ 15)
S.C.	130	118	135	(+ 17)	130	140	145	(+ 5)	90	80	80	(0)
A.N.	65	118	150	(+ 32)	135	145	156	(+ 11)	80	80	90	(+ 10)
B.S.	125	134	180	(+ 46)	100	120	165	(+ 45)	60	70	95	(+ 25)
A.B.	110	115	150	(+ 35)	135	148	180	(+ 32)	100	100	120	(+ 20)
I.L.	90	106	132	(+ 26)	130	175	210	(+ 35)	90	110	120	(+ 10)
N.McL.		98	130	(+ 32)		108	120	(+ 12)		70	72	(+ 2)
D.C.		90	126	(+ 36)		115	140	(+ 25)		70	80	(+ 10)
M.J.		80	115	(+ 35)		125	145	(+ 25)		80	90	(+ 10)

Table 10:2

The mean pulse rate, systolic and diastolic arterial pressures during mechanical ventilation (IPPV), spontaneous muscle relaxation (S.R.) and maximal decerebrate rigidity (M.R.) of head injured patients.

(+) = increase in mean value.

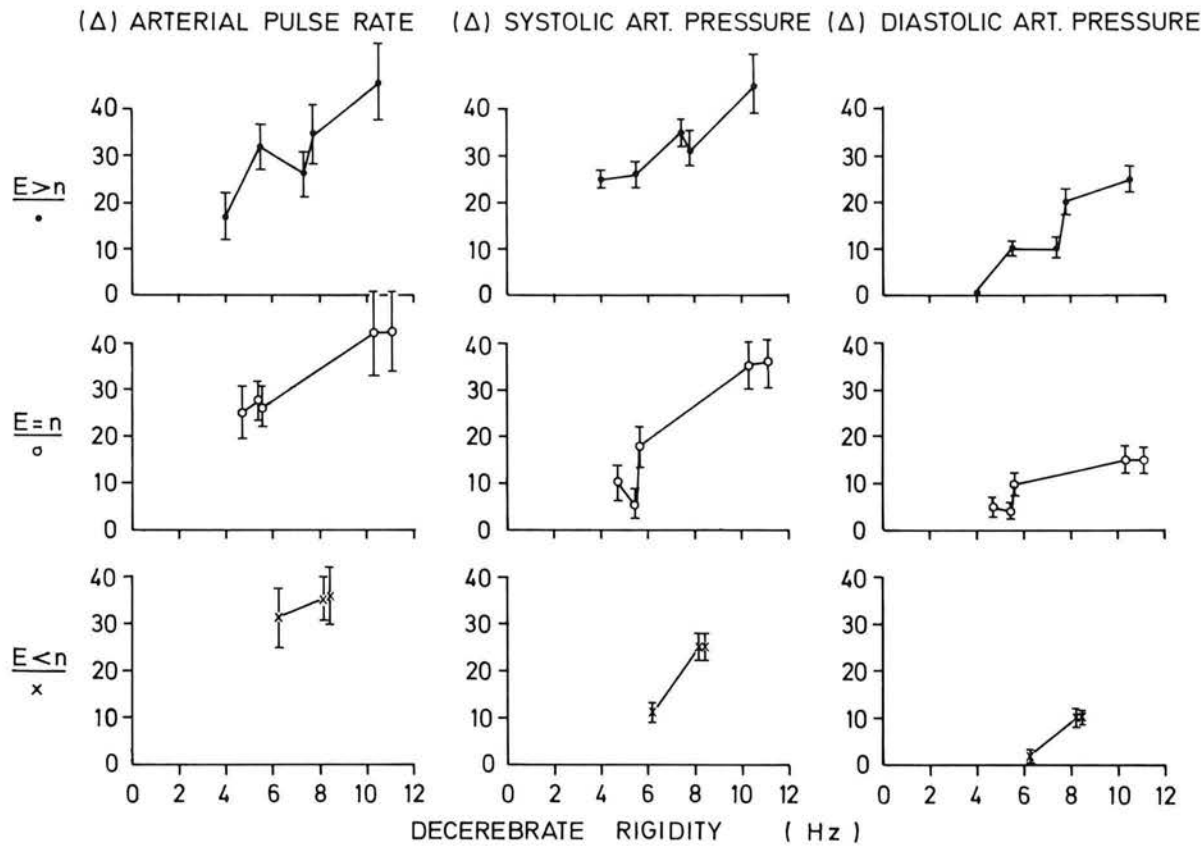


Fig. 10:10

Changes in the systolic, diastolic pressure and pulse rate plotted against degree of rigidity (in Hz) within each elastance group. A rise in all these parameters is proportional to the severity of spasms but is unrelated to the brain elastance.

individual variation was seen in the elevation of both syst SAP and diast SAP (Fig. 10:10).

A rise in SAP coincided with the onset of a spasm, lasted as long as it did and returned to its previous value immediately on termination of the spasm.

There was no apparent correlation between levels of SAP and elastance.

Changes in respiration and intrathoracic pressure (ITP)

The ten cases on IPPV had a mean ITP of +6 mmHg. All cases who were breathing spontaneously had a negative ITP of -3 ± 1.0 mmHg.

Pulmonary hyperventilation occurred during decerebrate rigidity, as seen on the ITP tracing. During spasms, the average ITP increased to 27.0 ± 12 mmHg (Table 10:1) which is both statistically and clinically significant. This rise was unrelated to intracranial elastance but was directly proportional to the severity of decerebrate rigidity. The rises in ITP observed in patients with severe rigidity were very significantly greater than those in patients with moderate rigidity ($t: 3.82$, $P < 0.005$).

When the ITP was elevated increases in the VFP were observed; when pulmonary hyperventilation was uncomplicated by an increase in ITP the VFP was unchanged but its waveform increased in amplitude and frequency in proportion to the severity of the hyperventilation.

When the chart speed was fast enough it could be seen that the ITP was the first parameter to change (Fig. 10:3).

Arterial blood gases and acid-base balance

Arterial blood gases and acid-base determinations during spontaneous relaxation and spasm showed no significant differences between the moderate and severe decerebrate rigidity groups. Data were, therefore, pooled and are graphically presented in Fig. 10:11.

Arterial H^+, pCO_2 pO_2 and HCO_3 were within accepted physiological limits while the patients were on IPPV; mean values shown in Table 10:3.

During relaxation between spasms these parameters remained within normal limits throughout; values are presented in Table 10:3. Samples taken during or immediately after a spasm showed values which did not differ statistically from those seen during relaxation (Table 10:3).

Cerebral electrical activity

Episodes of decerebrate rigidity may be associated with epileptic fits. The possibility of their occurrence was explored in four cases by recording EEGs during decerebrate spasms; the tracings were comparable with those of comatose patients and showed no epileptic features (Fig. 10:12).

In one case the cerebral electrical activity was monitored continuously with a "cerebral function monitor" before, during and after decerebrate spasms; no change in activity was found during even severe spasms and no fits were observed (Fig. 10.13).

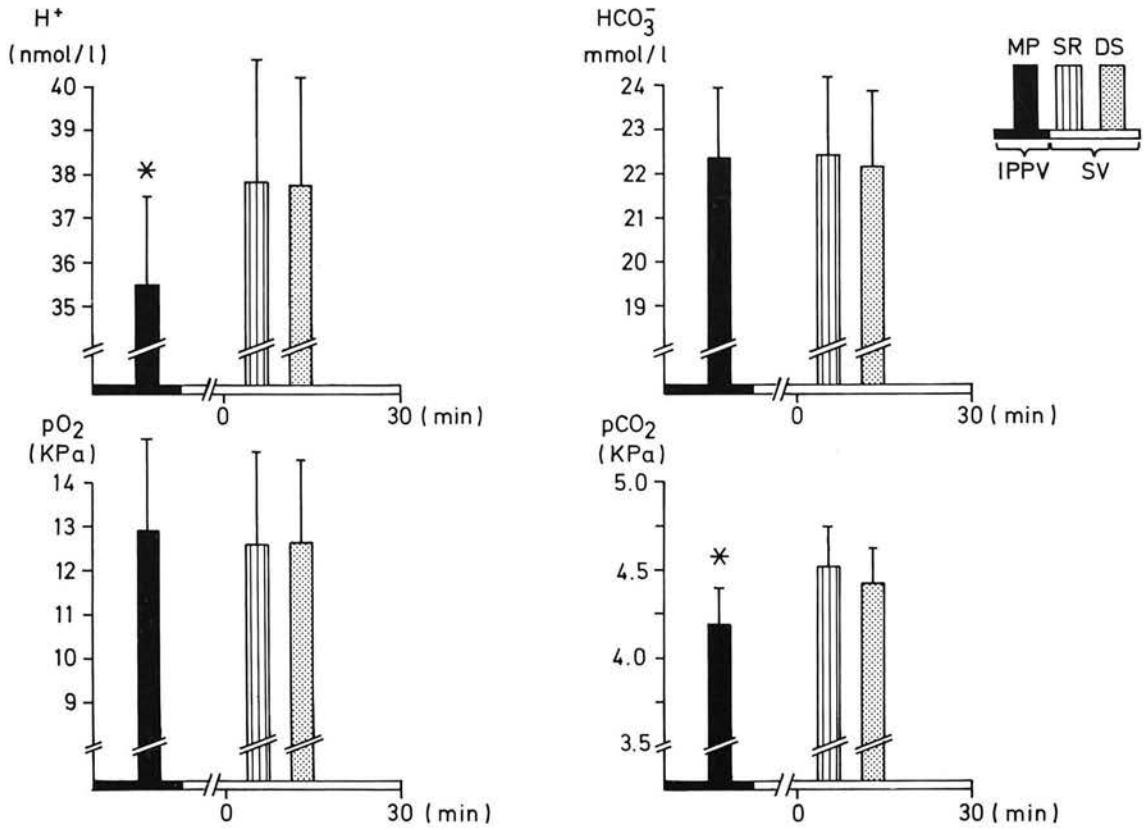


Fig. 10:11

Arterial blood gases and acid-base balance values showed no significant differences between spontaneous relaxation and rigidity. (IPPV: mechanical ventilation; SV: spontaneous ventilation; MP: muscle paralysis; SR: spontaneous respiration; DS: decerebrate rigidity)

The arterial H^+, pCO_2, pO_2 tensions and standard HCO_3 during IPPV, spontaneous relaxation (SR) and decerebrate rigidity (DR) .

PATIENT	H^+ (nmol/l)			pCO_2 (KPa)			pO_2 (KPa)			HCO_3 (mmol/l)		
	IPPV	SR	DR	IPPV	SR	DR	IPPV	SR	DR	IPPV	SR	DR
G.B	37.5	37.0	38.0	3.9	4.4	4.5	14.5	14.5	14.5	22.0	21.5	21.5
A.M	38.5	39.5	39.0	4.2	4.3	4.4	13.4	12.6	10.8	20.5	20.0	20.5
D.T	34.0	35.0	34.0	4.0	4.4	4.2	11.0	11.2	10.8	23.5	23.5	24.0
J.W	34.0	36.5	37.0	4.0	4.6	4.5	11.2	12.3	11.9	23.0	23.0	22.0
G.McD	33.0	35.0	35.0	4.4	4.8	4.8	10.8	11.3	11.5	25.0	26.0	26.0
S.C	37.5	41.0	40.5	3.9	4.5	4.4	16.2	16.6	16.3	18.5	19.5	19.5
A.N	35.0	34.0	34.0	4.1	4.2	4.2	11.5	10.6	10.8	21.5	22.5	22.0
B.S	38.5	39.5	37.5	4.4	4.7	4.6	13.0	11.8	12.1	20.5	20.5	22.0
A.B	33.0	37.0	36.0	3.8	4.6	4.3	16.1	15.5	15.0	21.5	22.0	22.0
I.L	35.5	36.0	34.5	4.0	4.3	4.1	13.8	13.0	13.3	23.0	22.5	22.5
N.McL		35.5	36.0		4.5	4.6		12.6	12.8		24.0	24.0
D.C		35.0	34.5		4.8	4.6		13.0	13.0		26.0	26.0
M.J		38.0	37.0		4.9	4.8		12.4	12.4		23.5	23.5

Table 10:3

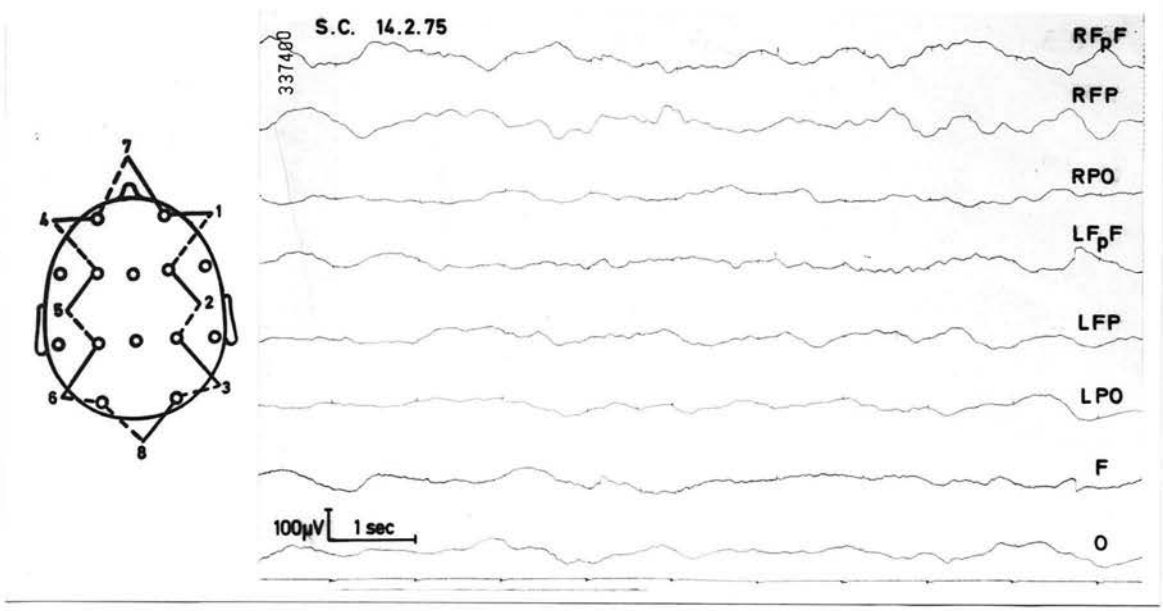


Fig. 10:12

EEG showing diffuse low-voltage irregular slow trace.
Note absence of epileptic features.

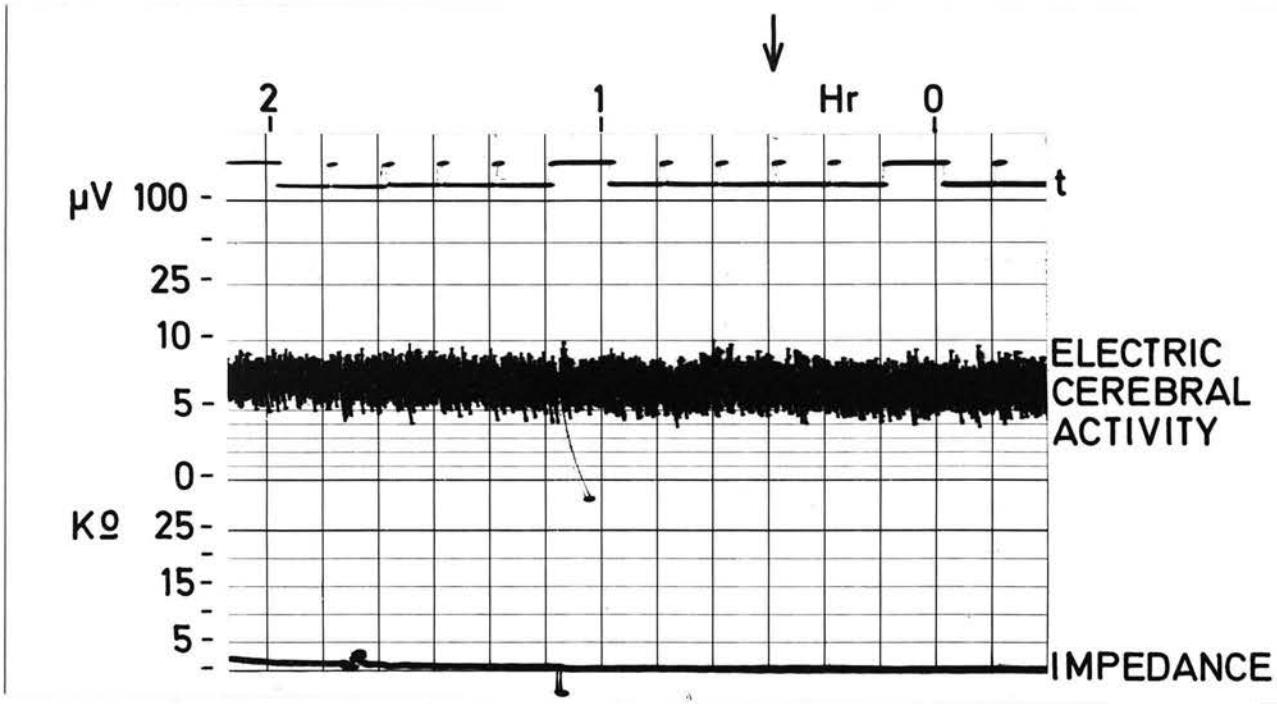


Fig. 10:13

Cerebral electrical activity during rigidity and periods of relaxation as recorded by a cerebral function monitor. The activity remains unchanged during rigidity.

DISCUSSION

It appeared from this study that well developed decerebrate spasms were accompanied by an increase in the VFP. Two main factors appeared to be responsible; muscle hypertonicity and high cerebral elastance. The relationship was direct; the greater the rigidity or the elastance the greater the rise in VFP and vice versa.

DECEREBRATE RIGIDITY

The rigidity of most linear systems may be determined by an isolated measurement of the displacement/force ratio; the rigidity, however, of a non-linear system such as the musculoskeletal apparatus, which possesses intrinsic adaptive mechanisms, is a continuous variable. Each articulation appears to have its own natural frequency. Valid information regarding the operation of the control system can only be obtained by non-intrusive methods; traditional methods do not fulfil this criterion and any conclusions based on data so obtained are of limited value.

The continuous measurement of the resonant frequency, i.e. the natural frequency of the wrist, during decerebrate rigidity by the technique of torque-induced motion analysis provided a most reliable continuous measure of rigidity and made possible its correlation with the alterations in VFP.

CAUSATION OF INTRACRANIAL HYPERTENSION DURING DECEREBRATE RIGIDITY

Systemic hypertension alone is known not to increase the ICP. Even the severe hypertension induced by vasopressin (Sokoloff 1959) or by norepinephrine (Moyer and Morris 1954, Langfitt et al.

1966) had no effect on the cerebral blood flow and volume in either man or animals.

Experimentally, severe systemic hypertension induced by the injection of norepinephrine was effective in causing brain swelling (i.e. an increased cerebral blood volume) only after an open or closed head injury, possibly because of a loss of autoregulation. The blood pCO_2 and pO_2 tensions were known to be normal in those with closed injuries (Langfitt et al. 1968).

Reivich et al. (1969) attributed the increase they saw in human CBF following a head injury to impaired control of the cerebral vasoconstrictor tone. Lewis et al. (1974) showed a 4-fold increase in the human cerebral blood volume 30 minutes after an injury; they, also, suggested that this was due to cerebral vasodilatation. Hypertension, then, has no effect on the cerebral blood volume unless homeostasis is defective. When defective homeostasis and systemic hypertension co-exist the volume of the cerebral vascular bed is greatly increased.

Most of our cases, normotensive at rest, showed arterial hypertension and tachycardia during decerebrate spasms; the argument that these are due to sympathetic overactivity is best supported by the occasional occurrence of lacrymation and skin pallor. The situation is complicated by the fact that a rise in both ITP and IAP, or IAP alone, raised the SAP, possibly by increasing the venous return; paradoxically a very large rise in ITP alone <u>decreased</u> it dangerously (Tsementzis et al. 1979). The suggestion that arterial hypertension might be dependent upon thoraco-abdominal dynamics gains support from

the observation that the rise in SAP was proportionate to the degree of rigidity and to the rise in ITP and IAP.

Evidence for the integrity of cerebral vasomotor tone at the time of this study was provided by the inter-relationship between the SAP and the ICP during decerebrate spasms:

1) Intracranial hypertension showed no constant relationship to the systemic.
   a) most (11 cases) showed moderate systemic hypertension; some individual levels, however, remained unchanged and did not correlate with the observed levels of ICP.
   b) two (2 cases) showed no rise in SAP while their ICP was elevated.
2) All rises in SAP were concomitant with or followed the rises in ICP during the spasms and both returned to their previous values when the rigidity passed off.
3) The electrical activity of the brain is known to reflect changes in the cerebral perfusion pressure (Branthwaite 1975). The only patient so studied showed no change in the amplitude or frequency of the tracing despite the occurrence of systemic hypertension during the spasms. If auto-regulation were impaired even small rises in SAP should produce an increase in ICP out of all proportion to the amount of muscle activity. Langfitt et al. (1966) showed that when autoregulation became defective, increases in ICP and SAP occurred simultaneously; from its resting level the ICP increased rapidly to reach a level equal to the mean arterial pressure.

Cerebral vasodilatation might also have resulted from hypercapnia or hypoxia, both of which are frequently found in

patients with a head injury, especially those with respiratory irregularities. Brown (1971) showed that although hypocapnia and hypoxia were seen in such patients with decerebrate rigidity and hyperventilation there were no changes in the acid-base balance of the arterial blood until at least several hours after injury. The patients in this study had been stabilised on IPPV for several hours before investigation. Throughout the period of study, even when the relaxants had worn off and the patient was self-ventilating, the arterial gases and acid-base balance remained within normal limits, whether the patient was at rest or in spasm. Despite the fact that severe spasms produced a marked rise in ITP, even at its maximum hyperventilation continued and respiratory arrest never occurred. Once the study had been completed a tendency towards reduction in pO_2 was observed but this was within physiological limits.

Another possible cause of cerebral vasodilatation and hypertension is an increase in cerebral metabolic rate and the accumulation of metabolites, as in epileptic fits (Meyer et al. 1966, Plum and Wasterlain 1970). In this study fits were not observed in the EEG of the several patients thus examined and fluctuations in ICP rapidly and precisely followed variations in muscle activity, an observation difficult to explain on the grounds of metabolite accumulation. Minns and Brown (1978) have recently shown that the intracranial hypertension seen in tonic fits might be sustained for as long as 20 minutes after cessation of the fit.

We would argue that intracranial hypertension is caused by an increase in the craniospinal venous blood volume. Raising the pressure in the superior vena cava would increase the ICP

by "backing up" the cranial venous blood. Meyrson and Loman (1932) and Bedford (1935) showed that the increased ICP which followed bilateral internal jugular vein ligation was transient, and that rapid restoration of the normal level occurred, presumably by diversion of the cerebral venous blood into the spinal epi- and subdural veins. Batson (1940) demonstrated the communication of these veins with the venae cavae through the azygos and hemiazygos veins and petrosal sinuses and pointed out that as this system is valveless blood could flow freely in either direction. Hamilton et al. (1936) showed that both coughing and straining increased the ITP by about 50 mmHg in normal subjects and in those with an artificial pneumothorax and that this was accompanied by an increase in CSFP and SAP; they postulated that the systemic hypertension was due to an increase in CVP. We have shown that in animals an "isolated" increase in either ITP or IAP results in only a moderate increase in ICP, whereas simultaneous increases in the ITP and IAP produce an exponential elevation in ICP.

If this experimental finding is indeed applicable to the clinical situation, the intracranial hypertension of decerebrate rigidity is an indirect result of truncal muscle spasm; this triggers off sequential increases in the IAP, ITP and CVP and finally the cranio-spinal venous bed. The relationship between rigidity and ICP is linear.

From the present study it was evident that:

a) When the ITP was elevated the ICP was always elevated also and these changes were always proportional to one another.

b) The waveform of the ITP tracing was phase-locked with that of the ICP; i.e. the amplitude and frequency of the cerebral

pulse varied in parallel with the respiratory excursions which, as discussed earlier, are reflected in central venous pulsations.

Although conclusive evidence is lacking so far, most investigators believe that cerebral pulsations are of arterial origin and are modified by respiration (Bering 1955, Dunbar et al. 1966). Hamit et al. (1965), however, showed that CSF pulsations follow the contour of venous rather than arterial pulsation and they suggested that the static CSF pressure is maintained by the SAP whereas the phasic changes are effected mainly through venous channels.

c) The rise in ITP preceded the occurrence of either systemic or intracranial hypertension.

While increased production and decreased absorption of CSF may have played a small additive role, the rapid and dynamic changes in the ICP which were observed cannot reasonably be attributed to such alterations.

An increase in the brain tissue volume by means of water uptake (oedema) is unlikely to play a major role in such a sudden increase in ICP; it is difficult to envisage such a very rapid development of oedema but if this had indeed occurred, one would then have expected the elevation in ICP to remain uninfluenced by the cessation of the decerebrate spasms.

CEREBRAL ELASTANCE

The craniospinal tissue and fluid volumes are rigidly enclosed and are protected from alterations in pressure by adjustments of the latter. The reciprocal relationship between the intracranial pressure and volume depends on the elastic properties of the system, i.e. the fluid components plus the

brain, cord and their immediate surroundings.

Rapid changes in the volume of CSF are primarily compensated by alterations in the volume of the venous blood channels. Ryder et al. (1953) showed that measured changes in the CSF volume had a minimal effect on the CSF pressure when it approximated to that of the systemic veins and when the intracranial venous pressure was elevated the elastance was increased. This has been confirmed in later studies by Löfgren (loc.cit.). The contribution of the arterial bed to the total elastance is minimal because of its relative "stiffness", which is a reflection of its thick walls, high tone and high intraluminal pressure. An increase in the SAP indirectly impairs the elasticity of the system; in dogs a rise in mean SAP of between 25 - 200 mmHg produced a 5-fold increase in the brain elastance (Löfgren loc.cit.). This distensibility of the spinal membranes contributes to the elasticity of the system only at CSF pressures of less than 10 - 20 mmHg.

The elastic properties of the craniospinal system become "stiffer" or "softer" under certain pathological conditions. A space-occupying lesion decreases the elasticity and will, therefore, increase the stiffness of the system, while in chronic hydrocephalus and cerebral atrophy the elasticity increases and the system becomes softer. We have confirmed that the magnitude of the CSFP response to volumetric changes in any of the craniospinal components depends primarily on the cerebral elastance. For a given degree of rigidity cases with increased elastance showed much greater rises in ICP than those with decreased elastance. The concomitant elevation in SAP seen during the spasms influenced the degree of intracranial hypertension only in so far as it increased the cerebral elastance.

CHAPTER 11

THE EFFECT OF FOCAL TWITCHING ON THE INTRACRANIAL PRESSURE DURING MECHANICAL VENTILATION: ITS PROGNOSTIC VALUE

INTRODUCTION

Post-traumatic epilepsy is a well recognised complication of head injuries. Of 1000 consecutive, unselected, closed head injuries, 5% had a fit or fits during the first week, whereas only one of these fitted during the subsequent three month period; this "early" epilepsy was of focal nature, commoner under the age of 5 years and 30 times commoner than the epilepsy developed at a later date (Jennett 1972).

During epileptic seizures in man and animals major cariovascular changes, respiratory arrest and consequent hypercapnia and hypoxia, increase of cerebral venous pressure and brain metabolism are all known to occur. Any one of these changes might be responsible for the marked elevation in ICP which is known to occur during fits. White et al. (1961) attributed the elevation in ICP to the cardiovascular changes observed. Meyer et al. (1966) suggested that intracranial hypertension represented the combined effects of hypercapnia, hypoxia, acidosis and systemic hypertension. More recently Minns and Brown (1978) have postulated that the intracranial hypertension was due to cerebral hyperaemia caused by the accumulation of cerebral metabolites.

Three patients with head injuries are described who developed focal twitching while being mechanically ventilated. Their arterial gases and acid-base balance were normal before and during the fits and cardiovascular changes were minimal. Changes in their intracranial pressure are described.

PATIENTS AND METHODS

These patients had been treated by IPPV for 3 to 8 days when they developed focal twitching; in two of them it was successfully treated with anticonvulsants but, in the third, it was uncontrollable despite vigorous treatment.

CLINICAL SUMMARIES

Case 1

A 13 year old boy sustained a left temporo-parietal fracture which extended into the base of the skull. Although unconscious from the time of injury, to begin with he responded purposefully to stimulation, but within a few hours developed severe decerebrate rigidity. Burr-holes disclosed only bilateral cerebral swelling and a ventricular catheter was inserted for continuous recording of the ICP. He was paralysed and mechanically ventilated for 4 days, but when, at the end of this period, neuromuscular paralysis was reversed, continuous grand mal seizures were seen to affect all limbs except the right leg.

He was reparalysed and treated with Epanutin 100 mg t.i.d. A few hours later episodic intracranial hypertension developed; each episode lasted for 10-15 minutes and recurred every 10-15 minutes. Close observation of the patient's face revealed bilateral twitching of the lower eyelids and cheeks. The onset and termination of the twitching coincided with the take off and return to previous profile of the ICP tracing (Fig.11:1). These facial twitches were completely controlled by a single oral dose of 15 mg of diazepam and subsequently by phenobarbitone 30 mg t.i.d. The patient survived the initial injury.

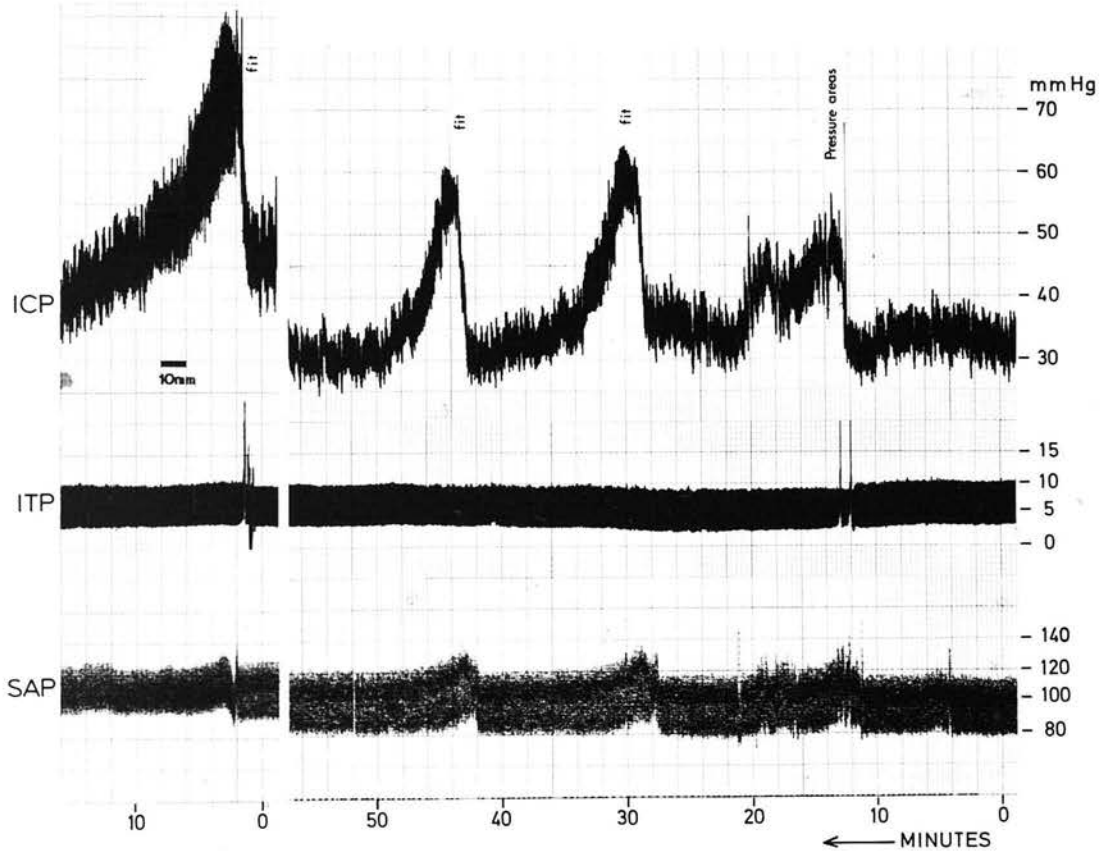


Fig. 11:1

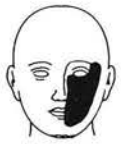
Simultaneous recordings of the ICP, ITP and SAP in a head injury paralysed and mechanically ventilated. Marked increases in the ICP during facial twitching; slight increases in SAP are seen while the ITP remained unchanged.

Case 2

A 7 year old boy was struck by a car and rendered unconscious immediately. At the local hospital he was noted to have muscle rigidity and before his transfer to neurosurgical care he was given 200 ml of 20% mannitol and 4 mg dexamethasone parenterally. On admission to the Royal Infirmary, Edinburgh he was unconscious and exhibiting severe decerebrate spasms. Whilst being examined he vomited and his right pupil gradually dilated. Meanwhile skull X-rays and an echoencephalogram had shown no abnormality. Burr-holes showed no evidence of haemorrhage but there was generalised brain swelling. A right ventricular catheter was inserted for ICP monitoring and he was put on IPPV. On the 7th day, however, his right pupil became widely dilated and showed no response to light. An echoencephalogram showed a minimal right to left shift and as his condition deteriorated throughout the day an angiogram was performed but this did not confirm the shift. On the evening of that day he had three episodes of acute intracranial hypertension, each lasting for about 2-3 minutes, and during these close observation revealed twitching of the left lower eyelid, left cheek and left corner of mouth; the ICP was seen to rise during the period over which these twitches were observed. Fits were abolished by injecting diazepam (an initial dose of 3 mg and then an infusion of 2 mg diazepam in 60 ml/hour). His condition deteriorated further and he died two days later.

Case 3

Following a road traffic accident this 27 year old male had a temporal burr hole made at a peripheral hospital and a subdural clot was partially evacuated. He was then transferred

	CHARACTISTICS OF FITS				ARTERIAL BLOOD GASES						INTRACRANIAL PRESSURE (mmHg)				ARTERIAL PRESSURE (mmHg)			
AGE, SEX	LOCATION	FREQUENCY (No/min)	DURATION (min)	TOTAL No	H^+ I	H^+ II	pCO_2 I	pCO_2 II	pO_2 I	pO_2 II	HCO_3 I	HCO_3 II	I	II	$\bar{X}_1 - \bar{X}_2$	RISE %	I	II	$\bar{X}_1 - \bar{X}_2$	RISE %
13, ♂		1/ 10-15	10-15	6	35	35	3.8	3.8	11.5	11.5	20.0	20.0	$\bar{X}_1$ 31.0 Mx 35.5±3.8 Mn 28.5±1.9	$\bar{X}_2$ 60.0 68.3±4.2 56.0±3.4	29.0 ** (t 4.26 P<0.01)	94	$\bar{X}_1$ 93.0 Mx 108.0±3.0 Mn 79.7±1.2	$\bar{X}_2$ 103.0 138.0±3.0 86.0±1.7	10.0 (t 0.39 P>0.5)	11
		1/ 90 +	4 +	1 +																
7, ♂		1/ 60	3-4	3	36	36	3.5	3.5	10.8	11.0	20.0	20.0	$\bar{X}_1$ 19.0 Mx 25.0±2.4 Mn 15.9±3.0	$\bar{X}_2$ 34.0 38.4±3.7 31.4±3.2	15.0 * (t 3.22 P<0.05)	79	$\bar{X}_1$ 101.0 Mx 123.7±2.6 Mn 90.4±3.1	$\bar{X}_2$ 110.0 137.2±3.1 96.0±1.9	9.0 (t 0.36 P>0.5)	9
26, ♂		1/ 12-16	5-8	Major Status	33	34	3.8	3.7	11.6	12.5	21.0	21.0	$\bar{X}_1$ 23.0 Mx 27.1±2.7 Mn 21.0±1.9	$\bar{X}_2$ 46.0 52.6±2.7 42.7±1.6	23.0 ** (t 4.06 P<0.001)	100	$\bar{X}_1$ 100.0 Mx 130.9±2.5 Mn 84.0±3.0	$\bar{X}_2$ 115.0 157.5±3.4 93.5±3.0	15.0 (t 0.45 P>0.5)	12
		1/ 50 +	10-12 +	5 +																
		1/ 25-30 +	4-10 +	Major Status																

$\bar{X}$ = Mean, Mx = Maximum level, Mn = Minimum level, I : Before fits, II : During fits,
+ = After treatment, * = Significant, ** = Very significant.

Table 11:1

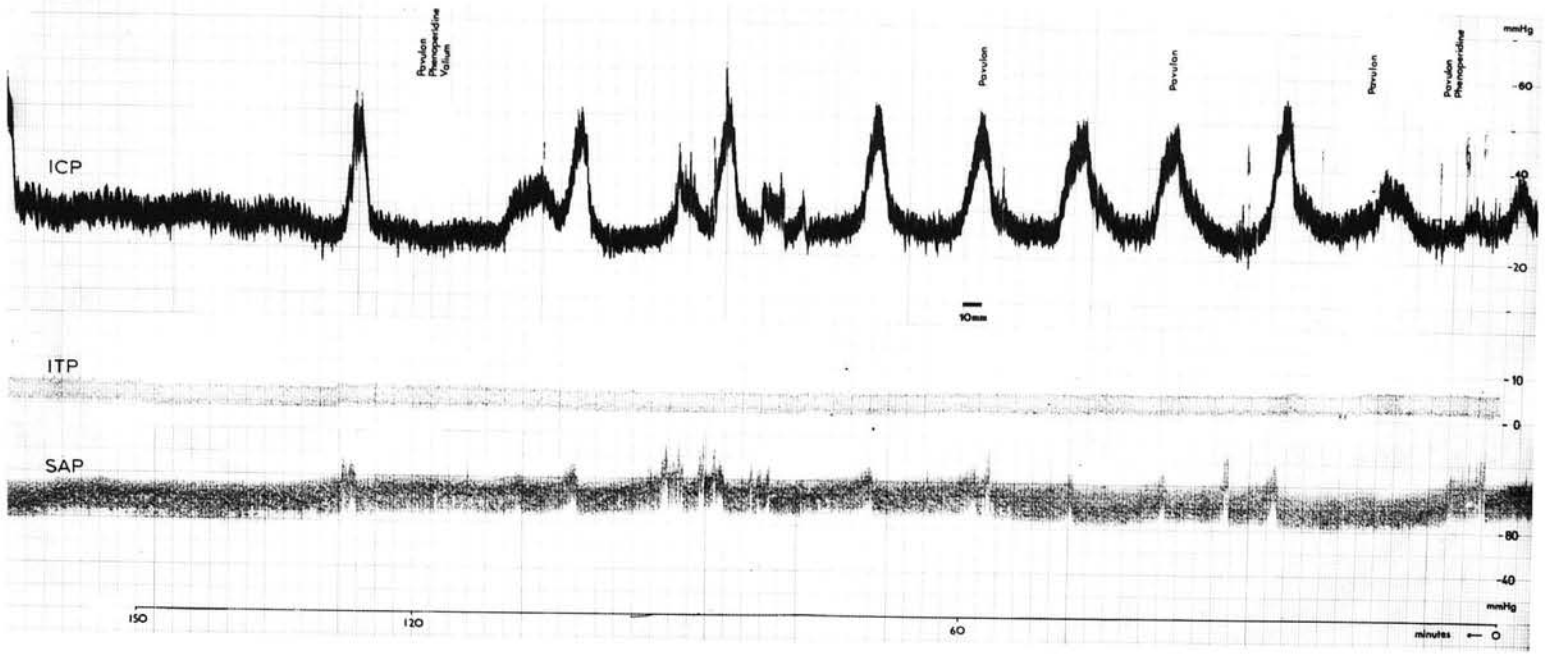


Fig. 11:2

Rises in ICP during subclinical status epilepticus which was uncontrolled by the administration of pancuronium and diazepam. The ITP remained unaltered whilst the SAP was slightly elevated.

to neurosurgical care. He was comatose, had marked extensor rigidity in all extremities, his pupils were slightly dilated (L < R) and responded poorly to light. A massive subdural haematoma was evacuated through an extensive craniotomy and the sagittal sinus and its bridging veins were packed with gelfoam to control the haemorrhage. A ventricular catheter was inserted and artificial ventilation started.

Three days after operation he developed slight, intermittent twitching of the right side of his face; marked increases in ICP corresponded with the onset and termination of these twitches. Epanutin 100 mg/t.i.d. was ineffective in controlling these and they spread to affect the homolateral thumb and index fingers (Table 11:1). Each twitching episode was associated with very marked increases in ICP (Fig. 11:2). Supplements of pancuronium had no effect on either the twitching or the intracranial hypertension. Intermittent doses of diazepam did reduce the frequency and duration of the twitches but failed to stop them; two days later both pupils became fixed and dilated and he died.

The ICP was measured in the right lateral ventricle by a polyethylene catheter and a Bell and Howell transducer (see Chapter 3). The intrathoracic pressure was measured in the distal oesophagus by a balloon catheter and transducer. The SAP was measured directly by a catheter in the radial artery and the same type of transducer. All data were displayed on a felt-pen recorder (see Chapter 3).

RESULTS

Values for the ICP, SAP, ITP and the blood gases and acid-base balance before and during twitching in all three cases are summarised in Table 11:1.

INTRACRANIAL PRESSURE

Case 1

The mean resting ICP was 31.0 mmHg; during the twitching episodes the mean rose to 60.0 mmHg, which is very significant statistically. The onset, duration and termination of the intracranial hypertension coincided with those of the twitching. An increase in the amplitude of the ICP tracing was observed at the peak rise.

Case 2

From a mean resting ICP of 19.0 mmHg, the level rose to a significant value of 34.0 mmHg, a statistically significant increase. These rises coincided with the onset, duration and termination of the twitching.

Case 3

A statistically very significant increase of 23.0 mmHg from the mean resting ICP of 23.0 mmHg was recorded during twitching.

For a short time only, the post-ictal resting ICP in all cases was lower than that of the pre-ictal period.

SYSTEMIC ARTERIAL PRESSURE

Small increases in the systolic and diastolic pressures were recorded during twitching. These were not statistically significant; values are shown in Table 11:1.

INTRATHORACIC PRESSURE

There was no apparent change in the respiratory pattern before and during the twitching. Respiratory excursions, as judged by the amplitude and frequency of the ITP tracing, were unaltered.

The arterial blood gases remained unchanged throughout the episodes. Values are displayed in Table 11:1.

DISCUSSION

These results confirm that intracranial hypertension occurs during epileptic fits in patients with head injuries. While pressure increases of 50 mmHg or more have been measured during major convulsions, local or limited epilepsy has been shown to have less effect on the ICP (Minns and Brown 1978). Rather to our surprise, focal twitching could be associated with an extreme degree of intracranial hypertension (> 65 mmHg), the rises ranging from 79 - 100% of the resting values. These acute increases in ICP drew attention to the possibility of a seizure taking place. The rapidity of their onset and their reversibility differentiated them from progressive intracranial hypertension due to swelling and oedema. It may be that in Case 3 epileptic phenomena were missed because of the adequacy of muscle paralysis and that by the time the ICP showed the characteristic rise, a self-sustained, uncontrollable status epilepticus had already been established.

Corsellis (1971) has emphasised that status epilepticus in man is a dangerous condition which may result in extensive brain damage or death.

Although the cause of intracranial hypertension during a fit is generally accepted to be an increase in cerebral blood flow due to vasodilatation, this is still debatable.

Gibbs et al. (1934) suggested that the great increase in CBF they observed in man during a seizure was due either to the rise in SAP or to the accumulation of carbon dioxide from the arrest of respiration. Penfield et al. (1939) disagreed and attributed the 4-fold increase in CBF they observed 3 minutes after termination of a seizure to the accumulation of cerebral metabolites. White et al. (1961) believed that the cerebral vasodilatation induced by epilepsy in man was due to the observed huge increase in blood pressure and cardiac output. Meyer et al. (1966) attributed the great increase in CBF which occurred during both spontaneous and induced seizures in known epileptic volunteers to the synergistic action of systemic and cerebral hypercapnia, hypoxia, systemic and cerebral acidosis and systemic hypertension. They stressed that none of these factors alone could sufficiently explain the great increase in CBF and ICP.

Plum et al. (1968) showed that in rats cerebral auto-regulation was lost for half an hour after the onset of a seizure, and that the blood pressure and CBF increased immediately and in parallel with one another. The CBF showed a 3-fold increase and there was an even greater increase in cerebral metabolic rate as judged by arterio-venous oxygen and carbon dioxide gradients across the brain. During seizures induced in rats paralysed by succinylcholine and artificially ventilated the CBF can be doubled even if no change occurs in oxygen or carbon dioxide tensions, (Plum and Wasterlain 1970).

We suggest that the abrupt onset and termination and the short duration of these episodes of intracranial hypertension during the twitching in our cases are explicable only if transient periods of cerebrovascular dilatation occurred, an argument in line with the above experimental evidence from man and animals. The systemic arterial carbon dioxide and oxygen tensions were normal so abnormalities of these were not responsible for the episodes. Systemic hypertension is known to produce cerebral hyperaemia and swelling only if auto-regulation has broken down, as seems to happen during fits. The arterial hypertension, however, was so minimal that it would be unlikely to account for the ICP elevations; some contributory effect, however, cannot be excluded. Furthermore since the ITP remained normal it is unlikely that venous hyper-tension, cerebral or systemic, occurred which in turn might have caused the ICP elevation.

The oxygen-carrying capacity of the blood cannot be increased to meet the increased metabolic demand of neural tissue during fits; the only way of meeting this demand, therefore, is by increasing the CBF. This may occur rapidly, within 1-2 seconds after the onset of a seizure. If hypoxia supervenes the high energy reserves in blood are depleted and lactate accumulates in the brain. Lactic acidosis is known to occur during seizures in spontaneously breathing animals; in ventilated and paralysed animals, however, Plum and Wasterlain (1970) did not see post-ictal acidosis. Recent studies of brain tissue rapidly frozen within 5 seconds of a fit have demonstrated a 6-fold increase in tissue lactate (Bolwig and Quistorff 1973). Local acidosis induced by direct

cerebral vasodilatation seems the most likely explanation of the intracranial hypertension which accompanies these minor twitchings.

In subjects breathing spontaneously and allowed to convulse it is reasonable to postulate that tissue acidosis, hypercapnia, hypoxia and marked systemic hypertension all act synergistically to raise the ICP.

How much the ICP increases depends also upon the elastance of the craniospinal system; this is known to decrease in hydrocephalics and increase in cases with a space-occupying lesion. The case of a young girl with normotensive hydrocephalus is cited as an example. While the patency of her AV shunt was being tested by continuously monitoring the ICP she had two major fits, during which the ICP remained quite unchanged. Probably her greatly reduced elastance compensated for the increased cerebral blood volume by cerebrospinal or venous displacement of intracranial volume; perhaps increased absorption via her shunt also occurred, indirect evidence of its patency.

CHAPTER 12

PROGNOSTIC VALUE OF THE EFFECT OF "NURSING CARE STIMULI" ON INTRACRANIAL PRESSURE IN PATIENTS PARALYSED AND MECHANICALLY VENTILATED

INTRODUCTION

Patients with severe head injuries frequently need mechanical ventilation either because of respiratory insufficiency as a result of a brain stem injury (primary or secondary) or in order to prevent or control the development of brain swelling. A good outcome in these cases depends not only on prompt and effective treatment but also upon alert, expert and "affectionate" nursing supervision.

It is not possible to make a detailed neurological examination of a paralysed and mechanically ventilated patient. His progress must, of necessity, be followed largely by nursing observation and the charting of "vital signs": blood pressure, pulse and respiration rates and the reaction of the pupils to light.

The patency of the airway is of prime concern and is achieved by regular endotracheal suction and chest physiotherapy. Most neurosurgeons have seen at operation the brain swelling and cortical venous haemorrhages which result from acute respiratory obstruction; these observations have been amply confirmed in dogs by Lafia et al. (1960).

Many nursing procedures such as the injection of drugs, postural changes and bathing are vital to the well-being of the patient.

There is evidence that each of these unquestionably justified procedures may, on occasion, result in disproportionate and even lethal intracranial hypertension in patients treated by paralysis and mechanical ventilation (IPPV).

PATIENTS AND METHODS

The thirty-nine head injuries who developed decerebrate rigidity in the traumatic head and spinal unit of the Royal Infirmary over a 4 year period were studied. All were ventilated after early operation which varied from exploratory burr holes to extensive craniotomies. At times the only operation was a single burr hole made for insertion of the ventricular catheter for continuous measurment of the ICP.

The "nursing care stimuli" (NCS) considered in this study were: endotracheal suction, with or without chest physiotherapy, testing the pupillary light reflex, clanking two metal rods or striking the metal bed-frame, taking the blood pressure using a sphygmomanometer, taking the rectal temperature, inserting a nasogastric tube (N/G) and performing oral or skin hygiene.

The ICP during NCS was monitored for anything from 24 hours to 10 days while the patients were paralysed and sedated. The intrathoracic (ITP) and systemic arterial pressure (SAP) were also recorded throughout. The magnitude of the effect was measured in terms of the peak increase in ICP. The mean of these measurements was then calculated.

Measurement of the VFP in real "normals" is clearly impossible and, therefore, sixteen selected non-traumatic cases were studied. Fifteen had hydrocephalus or a tumour or both but had no signs of raised ICP. One, a case of aneurysm, clinically Grade I (Botterell scale) with ventricles of normal size as seen in the CAT scan was considered as "normal". The alterations in ICP in response to the same stimuli and during voluntary stiffening and muscular exercise while lying in bed

were recorded and compared with those seen in the head injury group. All stimuli could not be applied to all controls because of the exigencies of the clinical situation.

MEASUREMENT OF INTRACRANIAL PRESSURE

In most cases a transparent polyethylene catheter was inserted into the right lateral ventricle for continuous recording of the ICP. In a few hydrocephalics, however, it was measured through a green Luer needle (G 18) in a Rickham's reservoir which had been implanted for repeated measurements of the ICP in order to help decide whether a shunt was indicated.

MEASUREMENT OF THE INTRATHORACIC PRESSURE

This could be measured only in the head injuries. When attempted in two of the control group it had to be abandoned because the patients could not tolerate the intraoesophageal catheter and their restlessness invalidated the record.

MEASUREMENT OF THE SYSTEMIC ARTERIAL PRESSURE

The SAP was measured directly through a catheter in the radial artery in twenty-two (22) head injuries whereas in the remaining seventeen (17) and in the controls it was measured indirectly using a cuff sphygmomanometer.

Details of the methods of measuring the ICP, ITP and SAP are given in Chapters 3 and 5.

Muscle paralysis was achieved with the regime of pancuronium bromide which has already been described. Sedatives, such as phenoperidine were always used in addition to the relaxants.

STATISTICAL ANALYSIS

The results were analysed using a Student's t-test; values of $P < 0.05$, $P < 0.01$ and $P < 0.001$ were considered as significant, very significant and highly significant respectively.

In addition, a two-factor analysis of variance (patients vs stimuli) was applied to the data from the group of head injuries which had shown an abnormally high ICP in response to each NCS (Group II).

RESULTS

CONTROLS

Nursing stimuli

All cases showed a normal resting ICP during the recording. As might have been anticipated, chest physiotherapy was the ONLY effective stimulus, but the elevation of ICP seen in the six cases to whom it was applied was insignificant.

Physiological activities

1) Straining

All eleven (11) cases who were observed during straining on a bed-pan showed an increase in ICP, but it was significant in only six of them. Three cases (one aneurysm, one apparently cured astrocytoma with only slight ventricular enlargement and a clivus chordoma with involvement of the brain stem) showed very significant elevations, whereas the other three cases (all normotensive hydrocephalics with or without a tumour) showed only significant elevations.

2) Muscular exercise

This was without effect on the ICP.

HEAD INJURIES

These were divided into two groups on the basis of the level of intracranial hypertension and its response to treatment by relaxants:

Group I: a) No significant rise in ICP was observed and
b) this rise was readily controlled by supplementary doses of relaxant.

Group II: a) Significant intracranial hypertension was seen which
b) was uncontrollable by the use of muscle relaxants.

Group I (33 cases)

Intracranial pressure

Nineteen (19) cases showed no alteration in their ICP during any NCS. The remaining fourteen (14) showed only a minimal increase in ICP during endotracheal suction (range of means 1.4 - 6.5 mmHg); of these, two also showed an increase during insertion of a N/G tube (range of means 0.5 - 2.0 mmHg), two during intramuscular injection (range of means 1.7 - 3.8 mmHg) and one during pinching of the skin (mean rise by 0.8 mmHg). None of these increases was significant, either statistically or clinically. At the peak rise the amplitude of the ICP tracing was greatly increased; on cessation of the stimulus both the level and waveform of the ICP rapidly returned to their prestimulus profile.

Intrathoracic pressure

This rose simultaneously with the ICP and the increase was proportional to it, coincided with the application of the stimulus and lasted for its duration.

TABLE 12:1a

NO.	SEX	AGE (YRS)	ICP (mmHg) RESTING PRESSURE Mn	Mx	$\bar{x}$	"NURSING CARE STIMULI"	ICP (mmHg) NET INCREASE PRESSURE Mn	Mx	$\bar{x}$
1)	♂	7	13.3 ± 1.2	16.7 ± 1.5	15.6	BP	21.0 ± 1.4	27.5 ± 0.7	25.3
			13.0 ± 1.1	18.0 ± 2.0	14.7	HYGIENE	20.5 ± 2.0	26.5 ± 2.6	22.5
			14.0 ± 0.8	22.0 ± 2.4	16.7	INJECTION	23.5 ± 3.8	30.0 ± 3.5	25.7
			13.0 ± 0.9	19.0 ± 1.4	17.0	LIGHT	33.4 ± 2.2	40.6 ± 3.0	38.2
			13.5 ± 1.6	20.8 ± 1.8	16.0	N/G	27.5 ± 3.4	36.4 ± 3.1	30.5
			13.0 ± 1.0	18.5 ± 1.5	14.8	SOUND	-	-	-
			13.5 ± 1.3	17.5 ± 1.7	16.2	SUCTION	49.2 ± 5.5	59.0 ± 7.2	55.7
2)	♀	18	35.0 ± 1.0	39.8 ± 0.9	36.6	BP	6.8 ± 2.0	11.6 ± 1.7	8.4
			32.5 ± 1.5	40.0 ± 1.3	35.0	HYGIENE	6.5 ± 1.8	12.0 ± 1.5	8.3
			32.0 ± 0.9	36.8 ± 1.2	33.5	INJECTION	6.5 ± 1.8	14.5 ± 2.0	9.2
			32.5 ± 0.7	38.0 ± 1.4	36.2	LIGHT	16.0 ± 1.4	19.0 ± 1.4	18.0
			35.3 ± 0.6	41.7 ± 1.2	39.6	N/G	8.3 ± 1.5	17.0 ± 3.0	14.1
			32.0 ± 0.6	37.8 ± 1.8	35.9	SOUND	1.5 ± 0.4	8.2 ± 1.0	3.8
			31.0 ± 1.4	37.0 ± 1.4	35.0	SUCTION	16.5 ± 2.1	23.0 ± 2.8	20.1

TABLE 12:1b

NO.	SEX	AGE (YRS)	ICP (mmHg) RESTING PRESSURE Mn	Mx	$\bar{x}$	"NURSING CARE STIMULI"	ICP (mmHg) NET INCREASE PRESSURE Mn	Mx	$\bar{x}$
3)	♀	32	8.0 ± 1.5	11.0 ± 1.7	9.0	BP	1.6 ± 0.2	4.0 ± 0.2	2.4
TIME SINCE ADMISSION 0-24 HOURS			10.5 ± 1.8	14.0 ± 2.7	11.7	HYGIENE	-	-	-
			8.0 ± 1.5	11.0 ± 1.7	9.0	INJECTION	4.2 ± 0.2	9.0 ± 0.6	5.8
			7.7 ± 2.1	11.0 ± 1.7	8.8	LIGHT	8.5 ± 2.1	15.0 ± 1.4	10.7
			10.5 ± 1.8	14.0 ± 2.3	11.7	SOUND	-	-	-
			12.3 ± 2.5	17.0 ± 1.0	13.8	SUCTION	9.5 ± 2.1	17.5 ± 2.1	12.2
TIME SINCE ADMISSION 48-72 HOURS			22.0 ± 2.8	26.0 ± 3.8	23.3	BP	10.3 ± 3.0	16.3 ± 3.0	12.3
			22.0 ± 3.0	27.3 ± 2.4	23.8	INJECTION	12.0 ± 2.5	19.0 ± 2.8	14.3
			22.0 ± 3.0	25.5 ± 2.6	23.8	N/G	12.0 ± 2.5	18.0 ± 3.3	14.0
			25.0 ± 1.1	30.5 ± 1.5	26.8	LIGHT	15.0 ± 1.2	20.0 ± 1.2	16.7
			21.5 ± 2.0	26.0 ± 3.0	31.7	SOUND	-	-	-
			32.5 ± 0.7	39.0 ± 1.4	34.5	SUCTION	24.5 ± 0.7	36.5 ± 0.7	28.5
TIME SINCE ADMISSION 72-96 HOURS			44.5 ± 6.0	55.0 ± 5.3	48.0	BP	19.5 ± 6.2	26.5 ± 3.5	23.3
			44.0 ± 6.2	54.5 ± 6.0	47.5	HYGIENE	16.8 ± 4.5	22.0 ± 5.1	18.5
			40.8 ± 8.0	48.0 ± 7.4	43.2	INJECTION	21.8 ± 8.2	29.0 ± 7.3	24.2
			42.3 ± 8.1	49.8 ± 8.1	43.8	N/G	24.0 ± 6.0	35.4 ± 5.5	27.8
			51.8 ± 8.8	62.7 ± 6.4	54.4	LIGHT	27.4 ± 5.9	39.6 ± 6.5	31.5
			47.5 ± 5.4	58.0 ± 6.5	51.0	SOUND	-	-	-
			48.2 ± 3.4	56.0 ± 4.1	50.8	SUCTION	32.4 ± 3.9	42.0 ± 5.5	35.7

TABLE 12:1c

NO.	SEX	AGE (YRS)	ICP (mmHg) RESTING PRESSURE Mn	Mx	$\bar{x}$	"NURSING CARE STIMULI"	ICPP(mmHg) NET INCREASE PRESSURE Mn	Mx	$\bar{x}$
4)	♀	40	17.3 ± 1.6	20.5 ± 1.6	18.6	BP	11.2 ± 1.6	14.7 ± 1.6	12.4
			17.2 ± 1.5	20.2 ± 1.4	18.2	HYGIENE	9.0 ± 1.2	12.6 ± 1.7	10.2
			17.3 ± 1.6	19.8 ± 1.7	18.1	INJECTION	18.0 ± 1.8	27.9 ± 3.1	21.3
			17.7 ± 1.6	20.6 ± 1.6	18.7	LIGHT	20.5 ± 2.4	29.3 ± 2.6	23.4
			18.0 ± 1.8	20.0 ± 1.7	18.9	N/G	13.0 ± 1.4	19.3 ± 1.5	15.1
			17.7 ± 1.6	20.2 ± 1.8	18.3	SOUND	-	-	-
			17.7 ± 1.7	20.7 ± 1.6	18.7	SUCTION	29.4 ± 2.5	41.3 ± 3.0	33.4
5)	♀	29	17.4 ± 1.0	19.5 ± 2.0	18.1	BP	24.7 ± 1.5	30.3 ± 2.5	26.7
			18.0 ± 2.3	22.1 ± 2.4	19.4	HYGIENE	24.5 ± 1.3	28.8 ± 2.0	26.0
			18.0 ± 2.0	19.7 ± 2.5	18.6	INJECTION	26.3 ± 2.0	29.8 ± 2.0	27.5
			18.0 ± 0.6	20.0 ± 1.8	18.9	LIGHT	29.3 ± 2.5	35.0 ± 3.0	31.2
			18.2 ± 1.5	21.1 ± 2.2	19.8	N/G	25.6 ± 1.9	29.4 ± 2.4	26.7
			18.3 ± 1.2	21.0 ± 2.0	19.2	SOUND	-	-	-
			18.0 ± 1.8	20.8 ± 2.5	19.0	SUCTION	29.7 ± 1.8	37.0 ± 2.0	32.1
6)	♂	17	21.3 ± 0.9	26.5 ± 2.0	23.0	BP	15.5 ± 2.0	21.6 ± 2.7	17.6
			21.3 ± 1.0	27.3 ± 1.8	23.3	LIGHT	20.0 ± 4.0	29.6 ± 2.5	23.2
			27.6 ± 2.4	34.0 ± 4.6	29.7	SOUND	-	-	-
			26.8 ± 0.9	32.3 ± 1.7	28.7	SUCTION	22.4 ± 3.0	30.0 ± 4.2	24.9

When supplements of pancuronium were administered, the same stimuli were no longer effective in raising either the ICP or ITP.

The cases which showed a rise in ITP were those (14 cases) which also reacted with an increased ICP.

Systemic arterial pressure

The seventeen (17) cases in whom it was continuously measured showed only a minimal increase (12 cases) or decrease (5 cases) during suction, intramuscular injection and insertion of a N/G tube, all other stimuli leaving the SAP unaffected; these changes were not statistically significant. All increases in SAP in this group occurred immediately on application of the stimulus and in several had decayed before the stimulus itself was withdrawn. They were resistant to treatment with relaxants.

Group II (6 cases)

Intracranial pressure

The resting level fluctuated between 11.0 to 52.0 mmHg (detailed data are given in Table 12:1). All stimuli but one, clanking metal (auditory), produced an elevation in ICP which was at least significant and often very much so.

Analysis was carried out for each of the three measurements of the net increase in ICP (min., mean and max.) shown by five patients (M - 7; F - 18; F - 32; F - 29; F - 40) for whom complete data were available, and for six stimuli (ignoring "sound", for which very little increase occurred).

The mean net increase in pressure (over the five patients), in order of magnitude, were:

	Hygiene	BP	Injection	N/G	Light	Suction
Min. :	15.46	16.64	19.22	20.36	24.64	31.44
Mean :	17.10	19.22	21.58	23.58	27.72	35.40
Max. :	20.38	22.12	26.24	28.34	31.86	40.46

A two-factor analysis of variance (patients vs stimuli) on each measurement showed a highly significant difference between stimuli ($P < 0.001$). On follow-up tests it was found that the "suction" mean was significantly greater than all the others, and that the "light" mean was significantly greater than those for "hygiene" and "BP" (each at 1% level, all other pairs of means not significantly different). There also appeared to be no relationship between resting level and increase among the different patients.

The relationship between the mean net increase in ICPs for each of the three ICP measurements and the stimuli is shown in Fig. 12:1.

These increases in ICP were totally resistant to treatment with supplementary doses of pancuronium.

Case No. 4, to whom suction and light were applied consecutively showed characteristic intracranial plateau waves which were apparently triggered by both these stimuli. Both pupils were normal before the plateau waves developed; the right pupil then progressively dilated and became unresponsive (Fig. 12:2). These waves disappeared on withdrawal of the stimulus and the pupil regained its normal size and reactivity.

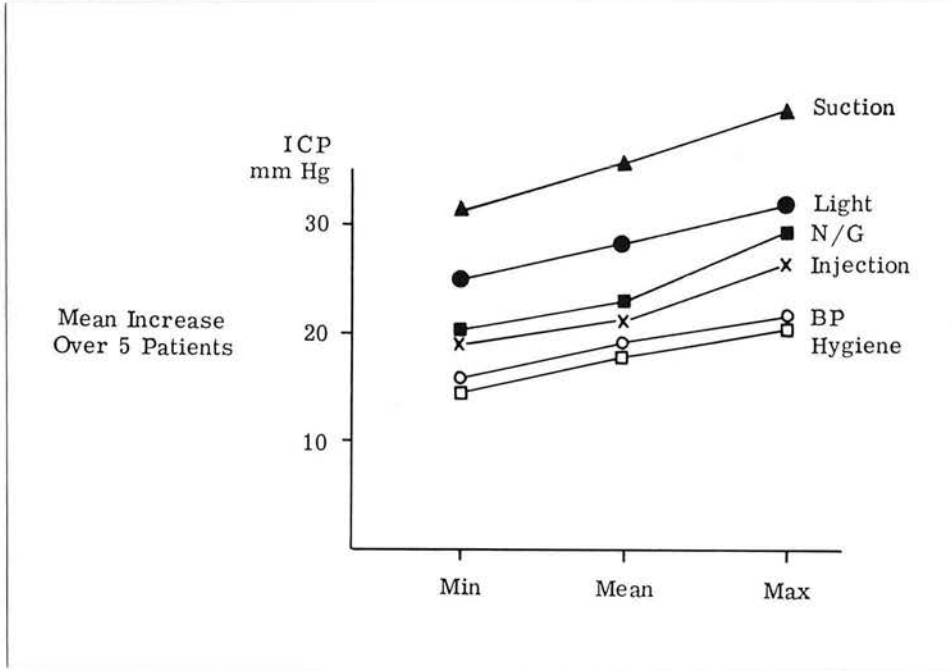


Fig. 12:1

Relationship between the mean net increase in ICP for each of the three ICP measurements (maximum, mean and minimum) and the nursing care stimuli.

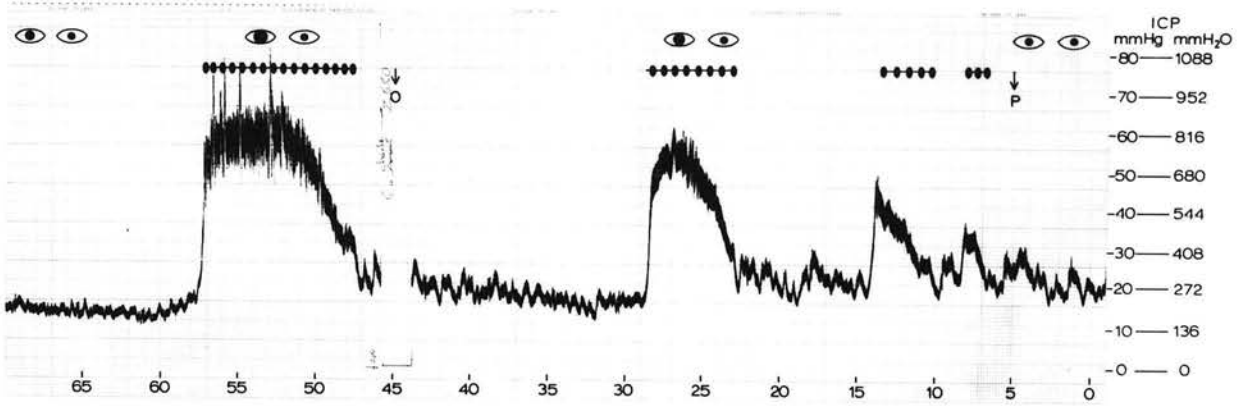


Fig. 12:2

Development of intracranial plateau waves, as seen in the ICP tracing, during endotracheal suction (eeeee) associated with progressive dilatation of one pupil.
(P : administration of Pancuronium, O : hydraulic zero checked out).

In case No. 3 exponential increases in ICP were seen; as the patient deteriorated clinically, the same stimuli resulted in a progressively greater, disproportionate and uncontrollable (in fact, lethal) elevation of ICP.

In case No. 1, following prolonged suction and physiotherapy, a progressive increase in the resting ICP level occurred; the pupils gradually dilated and became unresponsive. A partial temporal lobectomy proved to be life-saving and the child made an excellent recovery.

Shining a light into the eyes precipitated an immediate rise in ICP and when the stimulus was discontinued restoration of the prestimulus ICP level and profile was delayed by 1-2 minutes (Fig. 12:3).

In one patient whose intracranial hypertension had reached a steady level it was not reduced by either CSF drainage (simply because there was no CSF in the ventricular system, probably because of the hypertension) or supplements of relaxants but it was marginally reduced (by 10 mmHg) when omnopon was given (Fig. 12:4).

Intrathoracic pressure

This remained unaltered throughout the period of ICP increases and its tracing was that of a fully relaxed and well-ventilated subject.

Systemic arterial pressure

This was measured directly in five cases; one showed a decrease (Fig. 12:5) and the others a statistically insignificant increase during suction, intramuscular injection and insertion of a N/G tube, all other stimuli being ineffective. These alterations did not last as long as either the stimulus or the intracranial hypertension.

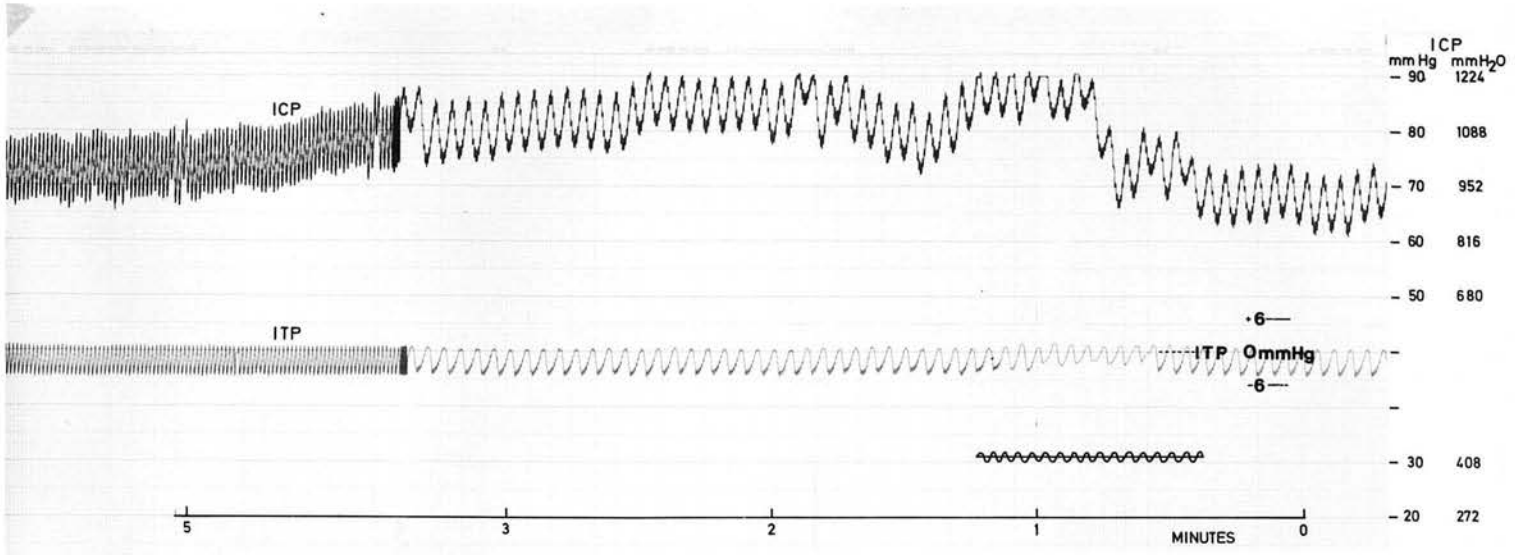


Fig. 12:3

Recording of the ICP and ITP. Shining of a light into the pupils produced a significant increase in ICP which took some time to return to its previous level after withdrawal of the stimulus.

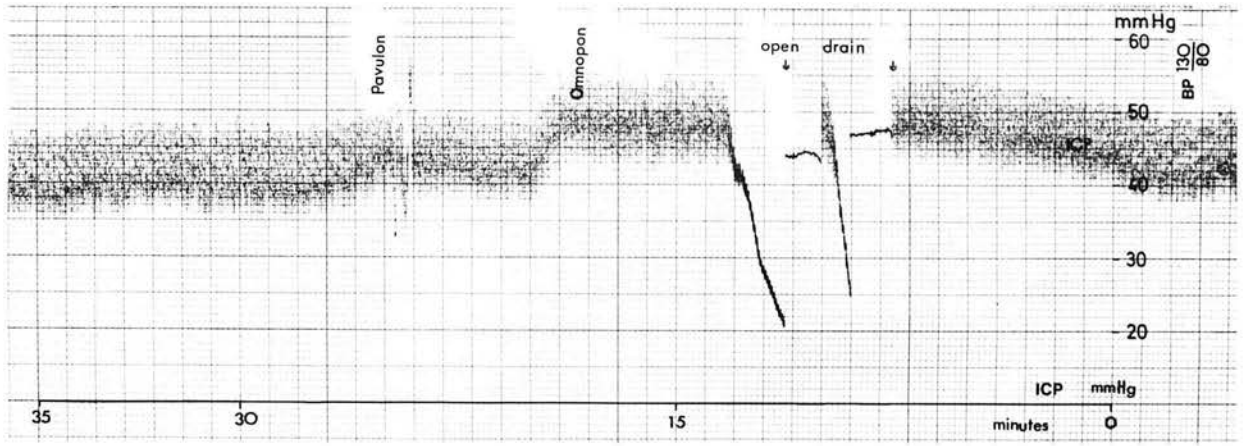


Fig. 12:4

Intracranial hypertension unsuccessfully treated by CSF drainage and administration of supplementary doses of relaxants. Administration of analgesics, however, reduced it by almost 20%.

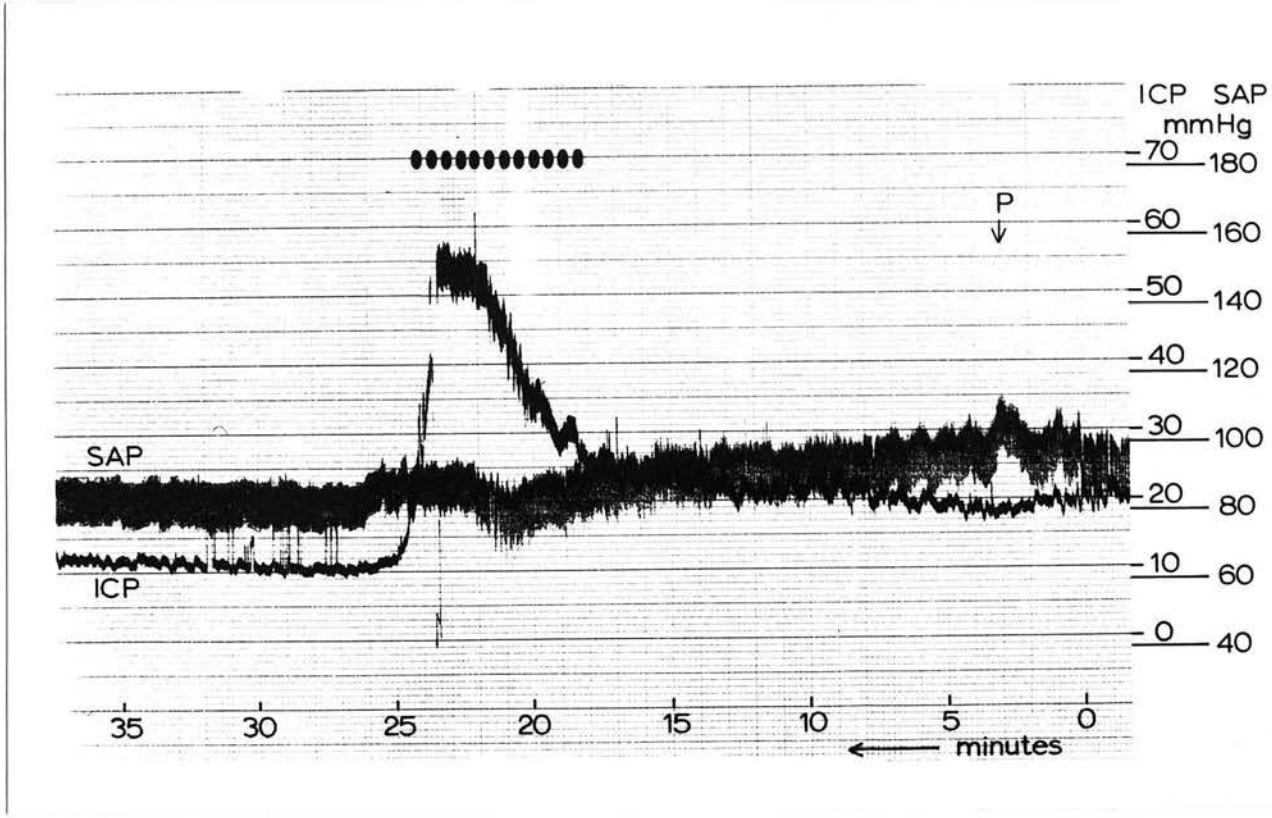


Fig. 12:5

Simultaneous recordings of the ICP and SAP. Endotracheal suction produced a rise in ICP which subsided at the end of stimulation whereas the SAP was reduced.
(P : administration of Pancuronium).

DISCUSSION

CONTROLS

It has been claimed that the increase seen in the CSFP during straining is a dislocation phenomenon due to an increase in the craniospinal venous blood volume. The magnitude of the intracranial hypertension primarily depends on the craniospinal elastance, which we know to be reduced in hydrocephalics and increased in cases with a space-occupying lesion.

It was not surprising, therefore, that greater increases in ICP were seen in normal cases and tumours than in the pure hydrocephalics.

In a recent study of four healthy volunteers Hedlund et al. (1962) showed that muscular exercise had little or no effect on either cerebral blood flow or circulation time, even though marked increases in SAP, pulse rate and cardiac output were observed. They concluded that exercise left the cerebral blood volume unchanged.

Their results seem to be confirmed by the fact that the few of our controls who were monitored during exercise showed no change in their ICP.

HEAD INJURIES

Group I

Endotracheal suction is a most potent stimulus of reflex vagal inhibition or stimulation of the cardiovascular system. In the incompletely anaesthetised and paralysed patient it may cause straining and an increase in both the ITP and IAP.

Of the seventeen (out of 33) cases in which the SAP was continuously recorded, fourteen showed a consistent elevation

in both the ICP and ITP on stimulation. The straining which results as the relaxants wear off is believed to be the cause of the minor elevations in ICP; this view is reinforced by the fact that the appearance of these ICP rises was fully prevented by the administration of supplementary doses of muscle relaxants. Despite this, the reflex cardiovascular responses to suction stimulation persisted.

Group II

In this Group the reaction was of a different order of magnitude and a major problem was posed by the fact that the stimulus of suction produced very significant and dangerous intracranial hypertension. In contrast to Group I, the ITP remained unaltered. Furthermore, stimuli which, in "controls" and Group I, were insufficient to change the resting level of the ICP were now very effective.

Shining a light into the eyes has been reported to produce a local increase in the cerebral blood flow in the occipital lobes (Harper 1972). The elevated metabolic rate of a working brain is believed to produce an increase in CBF at a strictly regional level in order to cope with the demand; a reaction similar to that seen in skeletal muscle where local contractions and local metabolic stimulation result in hyperaemia.

Measurement of the CBF in the frontal and occipital lobes in cats whose brain stem had been transected at the inter-collicular level showed a much greater (x 2) increase in the occipital than in the frontal lobes; this rise was associated with an arousal reaction, as judged from the desynchronisation of EEG activity (Skolasinska et al. 1977).

Gregory et al. (1977) have shown that during somatosensory peripheral stimulation in rabbits the CBF was significantly increased only in the appropriate cortical projection area whereas a non-significant increase occurred in the motor and occipital cortex of both hemispheres. The increased CBF even under normoxic conditions was parallelled by an increase in the total metabolism and production of lactic acid indicating that lactacidosis may be involved in harmonising blood flow with metabolic demand.

Ingvar and Soderberg (1968), who found an increased CBF in animals subjected to brain-stem stimulation, postulated that this was a result of vasodilatation consequent upon an increased metabolic rate and metabolite accumulation.

It is known that in the anaesthetised animal exteroceptive or special sense stimuli (such as pain, pressure, light, sound etc.) feed into the reticular activating system and produce an arousal response on the EEG.

All of this evidence suggests that the arousal reaction increases metabolism and CBF in local areas of specific function and an increase, no change or even a decrease in CBF in non-related functional areas, so that the total CBF is little affected. A small increase is unlikely to affect the cerebral blood volume, because of the activation of the appropriate vasomotor reaction. Impairment of this autoregulatory property of the vascular bed results in widespread vasodilatation, a significant increase in both CBF and volume and therefore of the ICP.

The "controls" used in this study, who, apart from their main chronic complaint were normal, were assumed to have normal

vasomotor reactions. There is no report of a patient with "pure" chronic hydrocephalus having impaired cerebral vasomotor tone. The potentially lethal increases in ICP seen in Group II are explicable only if autoregulation were lost.

The great increase seen in ICP during fits is attributed to global paralysis of vasomotor homeostasis and not to the great increase in CBF alone; only thus could the blood volume and ICP be so dramatically raised (Plum and Wasterlain 1970).

The reactive capacity of the cerebrovascular bed may be tested by inducing systemic hypertension or hypotension and then measuring the ICP. Neither procedure is clinically acceptable because of the danger of producing or aggravating intracranial hypertension. Langfitt et al. (1968) produced vasodilatation and severe brain swelling in animals with impaired autoregulation by artificially raising the SAP; a progressive rise in the resting ICP soon reached the level of the mean blood pressure. The rapidity of onset and the prompt reversibility of the ICP rises are against them being due to cerebral oedema. This view is reinforced by the following observations:

a) Systemic hypertension, which could have caused cerebral hypervolemia by increasing perfusion, was minimal and inconstant (indeed in some cases hypotension was seen).

b) SAP rises were seen ONLY during suction, intramuscular injection and insertion of a N/G tube.

Primary vasodilatation is, therefore, necessary in order to explain the rapid development and reversal of the ICP rises.

The pattern of recovery from intracranial hypertension after photic stimulation differed from that seen after the other NCS.

Two different mechanisms may, therefore, be operative in the genesis of intracranial hypertension.

Evidence is accumulating that the sympathetic (noradrenergic) system plays a part in the control of cerebrovascular reactions but the extent of this is as yet unclear. Despite the tremendous amount of work done on cerebrovascular homeostasis the identity and function of the mechanisms concerned in both health and disease remain obscure.

What is important clinically, however, is that the occurrence of intracranial hypertension during minor nursing procedures means that vasomotor tone is at least impaired and may well be lost. Intracranial hypertension may cause and accentuate hypoxic cerebral damage; the observation that repetition of the same stimulus results in progressively greater rises in ICP is a warning that, despite the otherwise satisfactory state of the patient on IPPV his condition is critically balanced.

The partial effectiveness of omnopon in reducing the ICP in one case underlines the need to completely deafferentate the patient by the administration of strong analgesics and sedatives whilst avoiding their dangerous hypotensive effects. This may be difficult especially if painful injuries such as fractures and burns co-exist with the head injury. The re-arrangement and perhaps the restriction of nursing care stimuli to only the most vital may be indicated, as the etiological treatment of impaired vasomotor homeostasis is presently impossible. The outcome of severe injuries of this type may well hinge on such minutiae.

CHAPTER 13

PROGNOSTIC VALUE OF CONTINUOUS MONITORING OF THE INTRACRANIAL PRESSURE

INTRODUCTION

Continuous monitoring of the intracranial pressure may be of value in the prognosis of severe brain damage. High pressures have been recorded in those cases in which the ICP has been measured and the close relationship between the level of intracranial hypertension and clinical deterioration or neurological death (Lundberg and Troupp 1965, Vapalhati and Troupp 1971) is generally appreciated. Patients with very severe head injuries may, however, have a normal ICP (Jennett and Johnston 1972). In other words, while the absolute level of ICP may be indicative of severe brain damage its value as a prognostic criterion is limited.

Our experience suggests that fluctuations in the level of the ICP and the amplitude and frequency response of the cerebral pulse may be reliable indicators of changes in cerebrovascular haemodynamics; in particular, the morphology of those tracings may provide incontrovertible evidence of arrest of cerebral circulation and brain death (Tsementzis 1978).

The accepted medical definition of brain death applies to patients with arrested respiration due to irreversible brain damage but with intact cardiac function, the latter being preserved only by the use of mechanical ventilation. The generally accepted clinical criteria of brain death are as follows (Mohandas and Chou 1971):

Over a period of at least 12 hours there should be no spontaneous respiration for periods of 4 minutes at a time, and absence of brain stem reflexes. Provided that hypothermia, metabolic disturbances and depressant drugs, including alcohol, have been excluded then brain death may be diagnosed.

Several laboratory tests have been used, more to reinforce the clinical criteria of brain death than to supplant them; a summary of those most commonly used is presented in Table 13:1. The use of the EEG has been stressed by some investigators, but cases are on record who had shown isoelectric (flat) EEG tracings yet had made a very good recovery (Levin and Kinell 1966). Quite apart from this, a 24 hour EEG service is not available in most hospitals. Angiographic and isotope investigations present problems as they require removal of the patient from the intensive care unit and cannot readily be repeated.

PATIENTS AND METHODS

Twenty-six cases with severe brain damage due to either a closed head injury or cerebrovascular surgery were studied. Seven of them, five males and two females, aged 12 to 48 years, died; they developed changes of their ventricular fluid pressure waveform which showed characteristic differences from those seen in the nineteen cases who survived their primary injury. The findings in these two groups have been compared with particular attention to the non-survivors. The neurological state before ventilation, the duration of artificial respiration, the duration of recording and fluctuations of the mean VFP and the necropsy findings in the latter group are summarised in Table 13:2.

The method used for the measurement of ICP has been described (Chapter 3).

No.	Investigation	Results
1	Electroencephalography (EEG)	Isoelectric tracing
2	Echoencephalography	Isoelectric tracing
3	Arteriovenous oxygen difference	Absence of gradient
4	Bilateral carotid and vertebral angiogram	Non-filling of the intracranial vessels
5	Isotope measurements:	
	a) Isotope scintiphotography	Cold area
	b) Beta or gamma-emitting isotopes	Cold area
	c) Cerebral blood flow	Very low flow
	d) Rihsa (spinal subarachnoid space)	Absence of CSF flow
6	Neuropathological findings	Autolytic changes (Respirator brain)

Table 13:1

Laboratory tests used for the diagnosis of "brain death"

TABLE 13:2a

NO.	AGE	SEX	LESION	CLINICAL CONDITION AFTER THE INJURY AND BEFORE ARTIFICIAL VENTILATION	DAYS ON RESPIRATOR	ICP mmHg	AUTOPSY FINDINGS
1	33	M	CEREBROVASCULAR SURGERY (RUPTURED ANEURYSM)	POSTOPERATIVELY RESPONDING TO SIMPLE COMMANDS AND MOVING ALL FOUR LIMBS. REFLEXES PRESENT, WITH BRISK REACTION OF PUPILS TO LIGHT. RESPIRATION AND CIRCULATION WITHIN NORMAL LIMITS.	6	50 - 80	AUTOPSY NOT PERMITTED
2	13	F	HEAD INJURY	UNCONSCIOUS. RESPONDING TO PAINFUL STIMULI IN A DECEREBRATE FASHION, WITH EXTENSOR SPASMS IN ALL FOUR LIMBS. PUPILS NOT REACTING TO LIGHT.	4	30 - 110	VENTILATOR BRAIN
3	21	M	HEAD INJURY	UNCONSCIOUS. UPPER LIMB EXTENSOR RIGIDITY. LT PUPIL REACTING TO LIGHT SLUGGISHLY.	5	70 - 100	VENTILATOR CHANGES
4	26	M	HEAD INJURY	UNCONSCIOUS. RESPONDING TO PAINFUL STIMULI WITH EXTENSOR SPASMS IN ALL LIMBS. RT PUPIL REACTING TO LIGHT. LABOURED RESPIRATION. ON THE 6TH DAY OF ASSISTED VENTILATION DRUGS WERE REVERSED AND PATIENT WAS ABLE TO MAINTAIN SPONTANEOUS RESPIRATION. BLOOD GASES WITHIN NORMAL LIMITS. BECAUSE OF FACIAL TWITCHING, WHICH WAS OBSERVED WHEN THE PATIENT WAS READY FOR DISCHARGE FROM THE INTENSIVE CARE UNIT, THE PATIENT WAS REVENTILATED FOR ANOTHER TWO DAYS.	8	50 - 85	EARLY VENTILATOR CHANGES

TABLE 13:2b

NO.	AGE	SEX	LESION	CLINICAL CONDITION AFTER THE INJURY AND BEFORE ARTIFICIAL VENTILATION	DAYS ON RESPIRATOR	ICP mmHg	AUTOPSY FINDINGS
5	27	M	HEAD INJURY	UNCONSCIOUS. LT PUPIL REACTING SLUGGISHLY. SLIGHT INCREASE IN MUSCLE TONE IN THE UPPER EXTREMITIES AFTER STIMULATION. ADEQUATE RESPIRATION.	3	50 - 80	AUTOPSY NOT PERMITTED
6	48	F	CEREBROVASCULAR SURGERY (RUPTURED ANEURYSM)	POSTOPERATIVELY CONFUSED, PUPILS REACTING TO LIGHT. NO MOVEMENTS ON THE RIGHT SIDE OBSERVED. SPONTANEOUS RESPIRATION.	6	70 - 80	VENTILATOR BRAIN
7	12	F	HEAD INJURY	DECEREBRATE EXTENSOR MOVEMENTS IN ALL FOUR LIMBS. BOTH PUPILS REACTING SLUGGISHLY. ON THE 3RD DAY SHE WAS ALLOWED TO BREATHE SPONTANEOUSLY. ACCIDENTAL BLOCKAGE OF VENTRICULAR DRAINAGE WITH CONCOMITANT RAISED ICP AND LABOURED RESPIRATION. REVENTILATED.	6	70 - 100	VENTILATOR CHANGES

RESULTS

SURVIVOR GROUP (19 cases)

In nine cases we observed plateau waves which attained a maximum value of 90 mmHg. The amplitude and frequency of the cerebral pulse were both increased during the development of easch such wave. At the end of each, the VFP wave form regained its pre-plateau appearance as regards its absolute value, amplitude and frequency (Fig. 13:1).

The tachycardia and systemic arterial hypertension which occurred also subsided to normal levels at the end of each plateau wave.

Withdrawal of a few millilitres of CSF is known to reduce the VFP more effectively than any dehydrating agent or drug. In addition to the recording system, therefore, a drainage system was set up so that when the VFP was dangerously increased, ventricular CSF could drain intermittently into a flask sited 15 cm approximately above the patient's frontal subarachnoid space. Towards the end of each plateau wave a few drops of CSF drained into the flask, whereas prior to the development of an "A" or plateau wave (sudden increases in pressure ranging between 50 to 100 mmHg lasting 5 to 20 minutes and followed by a rapid fall to the previous resting pressure or below) CSF did not drain.

NON-SURVIVOR GROUP (7 cases)

During continuous recording of the VFP all of these patients showed a moderate to high resting pressure and several A waves, the plateau level of which varied from 80 to 110 mmHg (cf. the plateau level of the survivors). In each of these cases, after

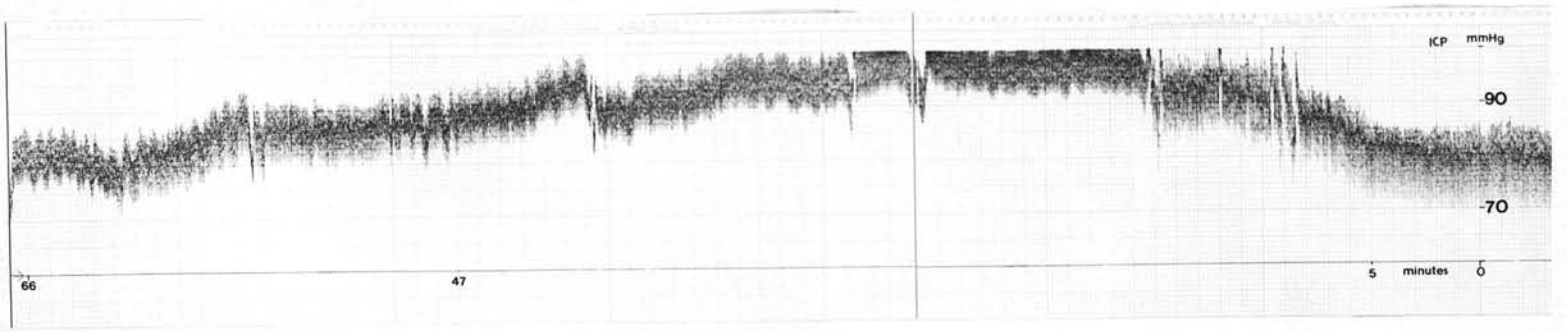


Fig. 13:1

Development and recovery of a plateau wave. The amplitude and frequency of the cerebral pulse are both increased during its development whereas at tis end (recovery) the cerebral waveform regained its preplateau appearance.

a run of A waves, the VFP fell to a level below the previous elevated interplateau levels and the frequency and amplitude of its oscillations were slightly reduced (Fig. 13:2). This fall progressed over a period of 1 to 6 hours and then gradually the pressure rose to an even higher interplateau level than previously and was maintained (Fig. 13:3 and 13:4); NO MORE A WAVES OCCURRED and the patient was clinically dead. The amplitude and frequency of the cerebral pulse showed a progressive reduction and never recovered their preplateau appearance. Later recording showed that the VFP resting level may be maintained thus (up to 2 days in one case with a cerebro-vascular accident) or fall to very low or even negative values. Two main patterns of VFP tracing were distinguished:

a) Cerebral pulsations disappear and the flat VFP tracing drops to very low or negative value; weak pulsations temporarily return after the injection of a few mls of water into the ventricle (Fig. 13:5).

b) The ventricular pulsations are locked in phase with the respiratory excursions; when the ventilator is switched off the previously masked shallow Traube-Hering-Mayer waves are observed at a subnormal frequency (Fig. 13:6).

In one patient who was kept on mechanical ventilation for two days after he developed the above changes, the VFP was not altered by either bilateral jugular vein compression or flexing the neck through 30^{o}. The injection of a minimal amount of saline into the ventricle rapidly and greatly increased the VFP without altering the frequency and amplitude of the cerebral pulse, in complete contrast with the VFP recordings of the survivor group (Fig. 13:4).

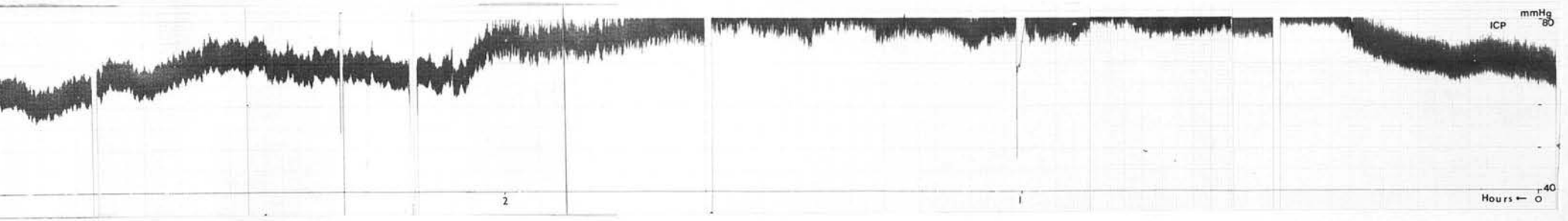


Fig. 13:2

A terminal plateau wave: at its end the VFP falls to a level below the previous elevated interplateau levels and the frequency and amplitude of its oscillations were slightly reduced.

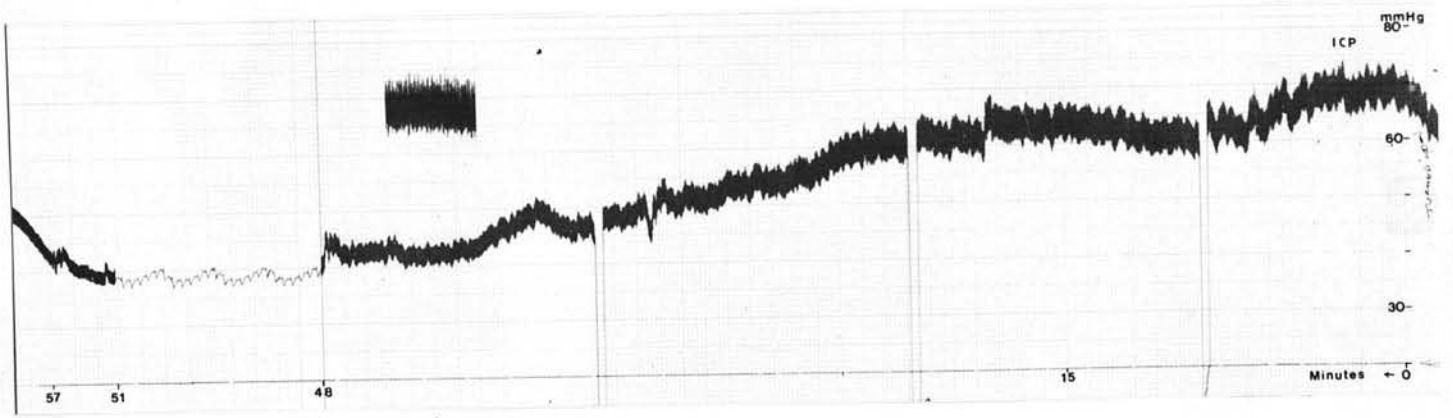


Fig. 13:3

VFP waveform following a terminal plateau wave. Arrows represent times during which the ventricular tube was open to free drainage. Above the tracing a preplateau sample of the VFP waveform.

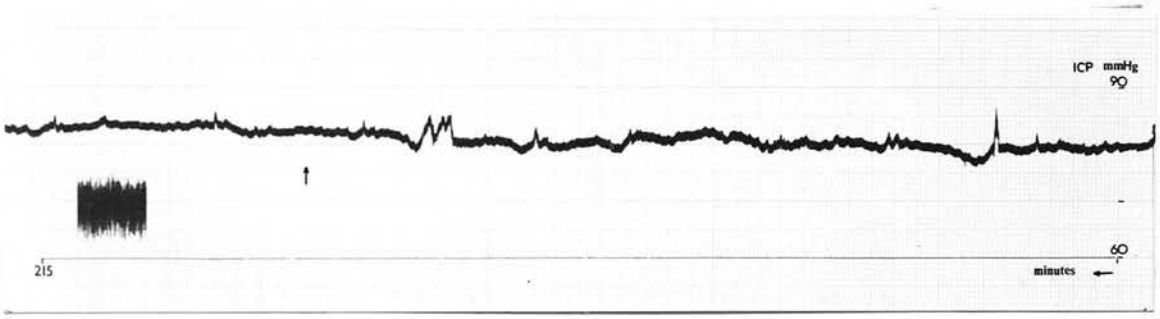


Fig. 13:4

VFP waveform following a terminal plateau wave. Arrow below trace shows time of compression of the external jugular veins. A preplateau sample of the VFP waveform below tracing on the left. (We had to alter the zero level to -20 mmHg on the paper chart in order to increase the upper limit of the recording from 80 to 100 mmHg).

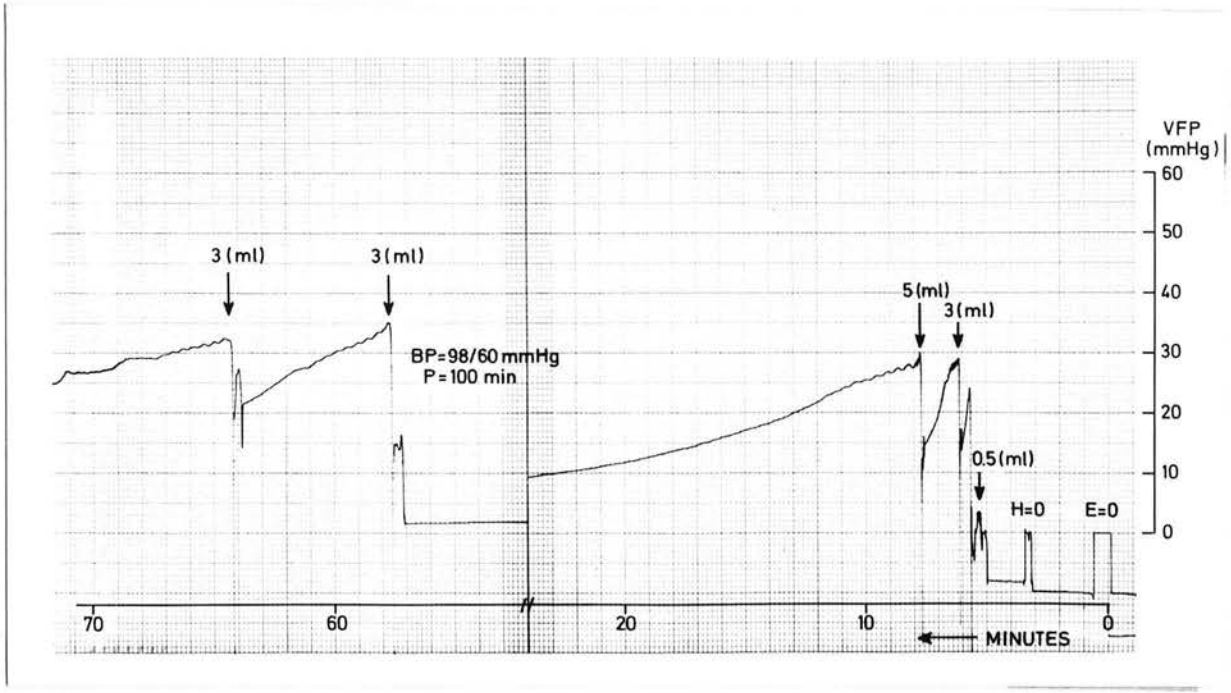


Fig. 13:5

VFP waveform following cerebrovascular arrest and brain death. Cerebral pulsations disappear and the flat VFP tracing drops to very low or even negative values; weak pulsations temporarily return after the injection of a few mls of water into the ventricle.

(E: Electronic zero, H : Hydraulic zero)

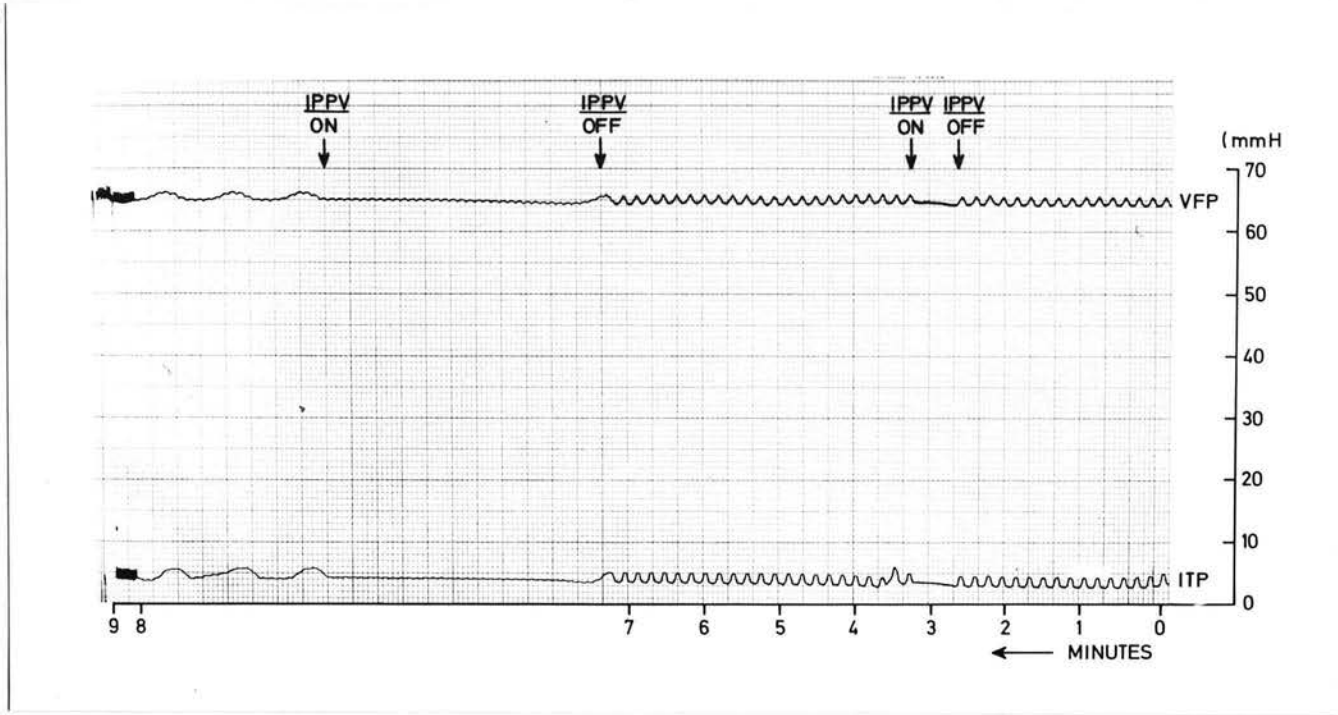


Fig. 13:6

VFP waveform following cerebrovascular arrest and brain death. The ventricular pulsations are locked in phase with the respiratory excursions; when the ventilator is switched off the previously masked shallow Traube-Hering-Mayer waves are observed at a subnormal frequency.

The cerebral perfusion pressure was estimated before, during and after the development of the terminal plateau wave by subtracting the ICP from the mean systemic arterial pressure (MSAP). As can be seen in Fig. 13:7 during the development of the plateau level the increased ICP is compensated for by an increase in both the systolic and diastolic blood pressure (the "Cushing response"). At the end of the plateau level, the MSAP is equal to or at most, only slightly greater than the ICP; cerebral perfusion is thus gravely impaired.

Towards the end of the final plateau wave we could not detect the diastolic pressure by sphygmomanometer, whereas the systolic was easily registered. A low diastolic pressure re-appeared later as the VFP subsided (Fig. 13:7). Later on both systolic and diastolic pressures become significantly low (60-80/40-50 mmHg syst/diast).

In a few patients a small amount of CSF (4-10 drops) drained into the flask immediately after each of the earlier plateau waves, but the later plateaus did not alter the VFP. Finally, the characteristic terminal plateau wave appeared and the patient died.

All five patients who underwent necropsy showed early to advanced "ventilator brain" changes (Walker et al. 1975).

DISCUSSION

The CSF pulsations are synchronous with the arterial pulse and are modified by respiration. Most workers accept that the pulsation is arterial in origin and this is thought by some to be transmitted from the basal and spinal arteries (Antoni 1946, Dunbar et al. 1966) and by others from the ventricular choroid


mmHg
100
0
CXR
V
ICP
50
0
160/98
5 Hours
10mm
170/110
calibration
200/120
148
165/0
168
150/50
150
145/50
163

Fig. 13:7

plexuses (Bering 1955). The amplitude and the frequency of the cerebral pulse may be altered by variations in the ICP (Ryder et al. 1952).

Cerebral pulsations are normally damped by the operation of those mechanisms which tend to prevent the ICP from rising; namely, CSF displacement, reduction or cessation of CSF production or reduction of intracranial blood volume as a result of change in cerebral vasomotor tone. Progressive elevation of the ICP results in sequential exhaustion of these compensatory mechanisms. When damping of the CSF pulsation has thus been abolished, its amplitude increases and the waveform comes to resemble that of the arterial pulse.

This sequence of events is commonly seen during the development of plateau waves. These are thought to result from rapid, reversible increases in the cerebral blood volume, but intermittent blockage of the CSF pathways or alterations in water exchange into the brain tissue have also been incriminated (Lundberg 1960). Our patients, all of whom had prolonged intracranial hypertension, most probably had lost some of their buffering capacity. It is known that, as intracranial hypertension develops, the CSF volume is the first to be lost, initially by displacement of fluid into the spinal subarachnoid space and secondly by diminished production directly due to the increased ICP. Sudden blockage of the CSF pathways produces a relatively small and gradual elevation of the VFP. In order to account for cyclic alterations in brain volume by means of water exchange one would have to postulate a rapidly reversible mechanism whose existence is, in general, denied.

The development of A waves, therefore, would appear to be

due to reversible changes in cerebral blood volume which are mediated by the vasomotor tone, an argument which is supported by the progressive loss of ventricular CSF and the major haemodynamic changes which occur during and after the last A complex. Compensatory mechanisms are, to some extent, preserved during all except the terminal complex. Once the VFP has exceeded some critical level, elevation of the MSAP can no longer maintain adequate perfusion.

We are unable to explain the disappearance of the radial diastolic pressure towards the end of the ultimate plateau complex or its subsequent re-appearance. Direct measurement of the SAP by catheter may elucidate the problem.

The phenomenon of reactive hyperaemia following a period of intracranial hypertension has been recognised since the experimental work of Forbes and Nason (1935). It may, we think, be the explanation of the CSF drainage following a plateau wave: in the recovery phase of an A wave hyperaemia increases the intracranial volume and although, for a time, this can be compensated for by the displacement of CSF, exhaustion of this buffer sooner or later occurs and then the only possible compensation for further increases in ICP is reduction of the cerebral blood volume. This volume can accommodate to intracranial hypertension to only a limited extent and for a limited period.

As the occurrence of CSF drainage during or after an A wave implies a certain integrity of the compensatory mechanism for intracranial hypertension its restriction to the survivor group is not unexpected.

The presence of autolytic changes in the brain at necropsy

suggests that brain death occurred before clinical death. It is not possible to time precisely the onset of these changes; it is thus not possible to correlate the onset of autolysis with the VFP recordings of this study. Case 4, which had an eight day course of VFP monitoring, was shown to be alive by reversing the relaxants and sedatives during the sixth day of ventilation. He was re-ventilated for another two days during which he showed the changes as described above in the VFP recording. Early "ventilator brain" changes were noted at necropsy.

Neurosurgeons often disagree about how long one should persist with mechanical ventilation of cases with severe brain damage. In Edinburgh the minimum duration is 48-72 hours, which is increased in young patients however severe their brain injury may be. The more severe the brain injury the more likely the patient is to succumb soon after injury; it is suggested that as soon as the characteristic VFP tracing has developed the patient should have his drugs reversed, be examined thoroughly and have the clinical criteria of brain death rigorously applied. This would relieve the strain on medical and nursing staff, would release facilities which might be better used and would abbreviate the suffering of the relatives. It might also help speed up kidney donation.

CHAPTER 14

PROGNOSTIC VALUE OF THE AMINE METABOLITE LEVEL IN CEREBROSPINAL FLUID

INTRODUCTION

Patients with severe head injury frequently show clinical evidence of brain stem damage. In experimental animals (Dahlström and Fuxe 1964) the cell bodies of ascending dopaminergic (DA), noradrenergic (NA) and 5-hydroxy-tryptaminergic (5-HT) neurons lie within the brain stem. Lesions of certain of the dopaminergic and noradrenergic cell bodies reduce wakefulness, whilst lésions of the 5-hydroxytryptaminergic cell bodies tend to increase it (Jouvet 1972). The loss of consciousness which accompanies brain stem injury in man might, therefore, be related to damage to one or all of these aminergic systems. We have investigated this possibility by measuring the concentrations of the metabolites of DA, NA and 5-HT (respectively homovanillic acid (HVA), 3-methoxy, 4-hydroxyphenylglycol (MHPG) and 5-hydroxyindolylacetic acid (5-HIAA)) in serial samples of ventricular CSF taken from patients in coma following an acute head injury. Patients with brain tumours or cerebro-vascular accidents in progressive coma which was not accompanied by signs of brain stem injury served as controls.

PATIENTS AND METHODS

PATIENTS

Two groups of comatose patients were studied. Group 1 comprised 9 patients (8 males and 1 female) in coma due to an acute head injury which had usually been sustained in a traffic accident. Group 2 was composed of 6 patients (4 males and 2 females) and comprised the control group.

Patients were selected for this study by the absence of any CSF drainage on opening the drainage tap of the ventricular catheter. In Group 1, the catheter was implanted within 12 hours of the accident and in Group 2 once the coma had become continuous. With the exception of one tumour patient, all received various combinations of the following drugs: penicillin, pancuronium bromide, phenytoin, phenoperidine, omnopon and 2 patients were given metaclopropamide and chlorpromazine respectively. Some patients were ventilated.

CSF SAMPLES

Samples of ventricular CSF were withdrawn at various times throughout the period, not longer than 7 days, that the catheter was left in situ. The first sample was taken within 12 hours of its insertion. Subsequent samples, maximum number 7, were removed at intervals of not less than 4 hours. CSF (0.5 - 3.0 ml) was withdrawn using a syringe inserted into the drainage tube outlet. The CSF was immediately centrifuged and the clear supernanant stored at -20°C until analysed. Coloured samples were discarded.

BIOCHEMICAL ESTIMATIONS

HVA and 5-HIAA were measured fluorimetrically in 0.4-1.0 ml CSF (Davidson et al. 1977). Total and free MHPG were assayed in two separate portions of CSF, of 0.5-1.0 ml. Total MHPG was assayed by gas-liquid chromatography after incubation with the sulphatase preparation "Helicase" to hydrolyse MHPG sulphate (Davidson et al. 1977). Free MHPG was assayed in exactly the same way as total MHPG except that Helicase had not been added.

Protein was measured by the method of Lowry et al. (1951).

RESULTS

All statistical comparisons were made using Student's t-test and a value of $P < 0.05$ was taken to indicate a significant difference.

The results from the head injury patients are given in Table 14:1 (patients 1 - 9) and from the control group of patients in Table 14:2 (patients 10 - 15). The level of CSF protein was high in patients 1, 3, 7 and 15, who had intracerebral haematomas and in patient 13 who had hydrocephalus. The percent free MHPG in eight patients with acute or chronic injuries ranged from 42% to 100% with a mean of $75 \pm 24\%$. There was no significant difference between the mean metabolite concentrations in samples taken on Day 0 and either age or VFP.

Throughout the sampling period the VFP remained fairly constant.

Repeat samples of ventricular VFP were obtained from 8 of the 9 head injury patients (Table 14:1). In patients who recovered consciousness and were discharged, the concentrations of the amine metabolites, with one exception, either remained unchanged or fell slightly with duration of coma. The exception was patient 2, in whom there was a steady increase in HVA concentration; this patient had an upper brain stem lesion but none the less made an excellent recovery. In the 3 patients who died, as coma proceeded the concentrations of the acid metabolites tended to fall and of the glycol metabolite (MHPG) to rise. Over the last 3 days of sampling, CSF was drained intermittently from patient 9 by opening the drainage tap for

Concentrations of HVA, 5-HIAA and MHPG(ng/ml) in serial samples of ventricular CSF from patients who were comatose following a head injury.

	Patient No	Age	Days after insertion of catheter	VFP mmHg	HVA	5-HIAA	MHPG Total	MHPG Free	Protein mg/ml
Recovered	1	48	0	8-9	207	91	13	-	1.29
			3		186	70	-	-	-
	2	17	0	12-15	330	95	17	12	0.73
			2		707	47	13	-	0.54
			3		1324	71	14	-	0.41
	3	45	0	12-15	406	108	48	17	0.75
			8		392		14	6	0.55
	4	18	0	15	446	141	17	12	0.24
			2		456	164	22	13	0.42
			3		332	100	20	-	0.41
	5	7	0	15	130	77	17	13	0.90
	6	18	0	30-35	157	-	14	-	0.26
			3		174	57	-	-	0.20
Died	7	33	0	<20	255	133	-	-	-
			4		440*	172	29	24	1.54
	8	27	0	30-45	174	81	6	4	1.81
			3		<40	<40	-	-	0.21
			5		81	<30	40	44	0.26
	9	27	0	50-60	225	393	15	-	0.58
			1		359	85	10	-	-
			1.5		241	95	12	-	0.26
			2		302	79	9	-	0.26
	intermittent drainage		(3		286	79	7	-	-
			(5		260	79	19	-	0.14
			(6		171	63	-	-	-

'Recovered':Regained consciousness and discharged
'intermittent drainage': CSF drained by opening ventricular drainage tap for a few minutes every 2-3 hours.
'-' :Indicates no estimate
'VFP' : Range of pressure recorded over duration of VFP monitoring
* Patient received chlorpromazine within 24 hours of sampling.

Table 14:1

	Patient No.	Age (yr)	Days after insertion of catheter	VFP mm Hg	HVA	5-HIAA	MHPG Total	MHPG Free	Protein mg/ml
Recovered	10	30	2	8-13	-	116	8	11	0.28
	11	46	0	8-14	250	65	15	-	-
			2		610	153	17	-	0.34
			3		941	93	9	-	0.34
	12	40	2	10-15	221	58	16	-	-
	13	50	0	15-20	483	247	31	13	-
			1		483	289	29	16	2.15
Died	14	6	1	7-9	688*	135	-	-	-
	15	16	0	12-15	133	51	26	11	1.80

Table 14:2

Concentration of HVA, 5-HIAA and MHPG (ng/ml) in serial samples of ventricular CSF from patients who were comatose following a tumour of a cerebrovascular accident.

"Recovered" = regained consciousness and discharged

"-" = indicates no estimate

VFP = range of pressure recorded over duration of VFP monitoring

* = patient received metaclopropamide within 24h of sampling of CSF

a few minutes every 2-3 hours in an effort to reduce the very high VFP. This procedure did not appear to alter the metabolite levels.

In Table 14:2, patients 11, 13 and 14 had tumours and patients 10,12 and 15 had cerebrovascular accidents. The concentration of HVA increased progressively over the sampling period in patient 11. This patient, who recovered, had a frontal astrocytoma which possibly obstructed the foramen of Munro. Patient 13 had enlarged ventricles probably due to a tumour which blocked the aqueduct.

The mean metabolite concentrations in the last CSF sample from patients who recovered and patients who died, regardless of the cause of the coma, are given in Table 14:3. Excluded from these values are the HVA levels in patients 7 and 14 who received chlorpromazine and metaclopropamide respectively. There was no significant difference between the concentrations of HVA and 5-HIAA in the patients who recovered and in the patients who died. The concentration of total MHPG was significantly higher ($P < 0.02$) in patients who died.

DISCUSSION

The concentrations of HVA, 5-HIAA and total MHPG in ventricular CSF were similar to values reported in patients with similar pathology (West et al. 1972, Wilk 1976). Our observation that about 75% of MHPG in ventricular CSF is unconjugated is in agreement with the work of Chase et al. (1973). In four patients (3,4, 13 and 14) the concentration of HVA in the first CSF sample was greater than 400 ng/ml, i.e. outside the range of 130-330 ng/ml found in the other eleven patients.

Patients (n)	mean ± S.D. (n)		
	ng/ml		
	HVA	5-HIAA	Total MHPG
Recovered (10)	465 ± 383 (9)	103 ± 68 (9)	16 ± 6 (8)
Died (5)	158 ± 75*(3)	87 ± 61 (5)	28 ± 8 (4)

Table 14:3

Concentrations of HVA, 5-HIAA and MHPG in ventricular CSF, with respect to outcome, in patients who had been comatose for 0.5 - 6 days.

'Recovered' = regained consciousness and discharged.

*excluded are 2 patients with high HVA values who were given chlorpromazine or metaclopropamide within 24 hours of sampling the CSF (see text).

The high HVA in patient 14 was probably due to treatment with metaclopropamide, which is known to increase the concentration of HVA in mouse brain (Peringer et al. 1978). Patients 4 and 13 were known to have ventricular dilatation, attributable in patient 13 to a tumour blocking outflow from the third ventricle. Such a block could be expected to produce a rise in the concentration of HVA in ventricular CSF by preventing access of the ventricular CSF to the HVA re-absorption site in the region of the fourth ventricle (Guldberg et al. 1966). West et al. (1972) found increased levels of the acid metabolites in samples of ventricular CSF from patients with posterior fossa tumours who had obstructed CSF outflow pathways. The elevated HVA in patient 7 was probably related to the administation of chlorpromazine 25 mm intra muscularly within 24 hours of removing the sample of CSF (Fÿro et al. 1974).

The similar metabolite concentrations found in the control patients do not support the hypothesis that damage to aminergic cell bodies is a feature of coma resulting from acute head injury. Valid comparison of the effects of progression of coma on the metabolite levels in the acute and chronic group cannot be made because serial samples were obtained from only 2 chronic patients. Interesting trends were, however, seen if the patients were considered with respect to outcome rather than cause of coma. Of the 7 patients who recovered and from whom serial samples were obtained, in 5 there was no marked or consistent change in CSF metabolite levels as coma progressed. In two patients (2 and 11), there was a progressive rise in HVA. The clinical picture of patient 2 suggested he had a rostral brain stem injury, which could have involved the substantia nigra.

Destruction of the dopamine-containing cells of this region in rats produces a progressive fall in the dopamine content of the terminals in the caudate nucleus between 30 and 48 hours after making the lesion (Ungerstedt 1971). Since released dopamine is rapidly metabolised to HVA and the levels of HVA in ventricular CSF parallel the levels in the caudate nucleus (Guldberg and Yates 1969), the progressive rise in HVA in ventricular CSF from patient 2 could reflect trauma-induced release of dopamine from the nigro-striatal system. If this damage did in fact occur, it did not appear to have any clinical significance, since the patient made a good recovery. The foregoing explanation cannot, however, be applied to patient 11, who had a frontal astrocytoma and no clinical signs of brain stem injury. Of the 3 patients who died and from whom repeated samples of CSF were obtained, there was a tendency for the concentrations of the acid metabolites to decrease and the concentration of total MHPG to rise, as coma progressed. The significantly higher total MHPG found at day 0 or after 1 - 6 days coma in the five patients who died was not accompanied by increases in the levels of the acid metabolites, suggesting that the increased MHPG concentration was not related to a reduced formation of CSF. Free MHPG, which accounted for 75% of the total MHPG in ventricular CSF could, therefore, be due to an ante-mortem reduction in the cerebral circulation. A steady increase in ventricular MHPG levels in coma might, therefore serve as an indication of brain death.

PART FIVE

CONCLUSIONS

1. The relationships between intensity and duration of radiofrequency current, the size of the lesion and the impedance before and after destruction were explored and the data thus acquired were used as a guide to the production of small, reproducible, non-haemorrhagic lesions in cats.

Despite the wide anatomical scatter of lesions it was evident that a smaller current made a small lesion slowly while a larger current made a larger lesion more quickly. The lowest current resulted in a small, ill-defined oedematous area without necrosis. Well-demarcated, reproducible lesions of adequate volume resulted from the use of a current of 90-110V.

2. The continuous recording of the ICP in experimental decerebrate rigidity demanded the integrity of the cranium and the avoidance of cardiorespiratory disturbances, haemorrhage or oedema, all of which could readily confuse the situation.

In an attempt to identify and delineate the mesencephalic reticulum the electrical activity from cortex, subcortex, tectum and tegmentum was monitored. The tegmentum could be identified by this means only after correlation of the known co-ordinates of the electrode tip with the pattern of activity from the adjacent and target areas. Electrical stimulation of the tegmentum elicited "tegmental reactions" in the majority of animals.

Using these data we made unilateral, midline or bilateral and midline mesencephalic tegmental lesions. Unilateral lesions produced mainly ipsilateral rigidity whereas central and bilateral lesions produced bilateral decerebrate rigidity.

A central lesion alone did not produce adequate rigidity, and had to be combined with bilateral lesions to be most effective. The degree of rigidity attained, however, differed from one animal to the other, despite the fact that the lesions were placed at the same co-ordinates in each. Cardiorespiratory complications occurred in all but six animals; these were considered to be ideal preparations because of this and the fact that they developed maximal rigidity. Individual variations in the size of the brain or minor differences in the extent of the lesions are the probable causes of such differences.

3. Experiments were performed on 26 cats in order to determine the mechanical effect of acute decerebrate rigidity on the ICP and the mechanisms concerned.

It has been shown that:

Even extreme rigidity of the peripheral musculature alone has no effect on the ICP whether or not the truncal muscles are activated.

Simultaneous elevation of the intra-thoracic and intra-abdominal pressures is the factor primarily operative in raising and maintaining the elevated ICP.

When cerebrovascular homeostasis is already defective a subsidiary but not unimportant role is played by the elevation of the systemic arterial pressure.

Under conditions of normal brain elastance, mild and short-lasting spasms have no effect on the ICP. When brain elastance has been artificially increased similar spasms produce a marked increase in ICP.

4. Two methods were used to measure muscle tone in cases with decerebrate rigidity.

In the first method forces of square waveform were applied and the calculated compliance of the joint was used as an index of rigidity. Oscillatory transients were seen at the same frequency as the physiological tremor. The range of normal variation in compliance was large and the values measured in the patients fluctuated so much as to limit the value of this index.

In the second method, using forces of sinusoidal waveform the resonant frequency of the joint was measured and used as an index of rigidity. This index proved reliable and reproducible.

5. Decerebrate rigidity, as a mechanical factor in raising and maintaining the raised ICP, and brain elastance, as a possible modulator of this effect, were measured in thirteen head-injured patients. These three parameters were correlated with a view to clarifying some of the problems posed by these difficult cases.

It appeared that well-developed decerebrate rigidity increased the ICP. This relationship was direct: the greater the rigidity and/or cerebral elastance the greater the rise in ICP during decerebrate spasms and vice versa. The two factors mainly responsible were muscle hypertonicity and increased cerebral elastance.

The intracranial hypertension was caused by the rise in the ITP and the consequent increase in the craniospinal venous blood volume; the ICP and ITP ran parallel as regards their amplitude and waveform but the SAP appeared to play no direct part

in the rise in ICP. Systemic hypertension may play an indirect contributory role because of the increase in brain elastance which it causes.

Spontaneous waning of the rigidity or its abolition by muscle relaxants returned the ICP to its previous resting level. Pancuronium produced deeper and more lasting relaxation than either Valium or Largactil.

As long as the elastance remained high, the onset of rigidity could result in disproportionate and dangerous increases in ICP. Although it may not always be possible to reduce the abnormally high elastance, the rigidity can certainly be abolished and thereby prevent lethal increases in ICP.

6. Three patients with a severe head injury developed minor facial twitching while their intracranial, intrathoracic and systemic arterial pressures were being monitored and they were on mechanical ventilation. In one the twitching spread to one thumb and the index finger. These twitches co-incided with great and damaging increases in the ICP, while the ITP and SAP were virtually unchanged. Small doses of Valium or Epanutin were effective in two but in the third the twitching was uncontrollable and he died.

The rises in ICP were attributed to cerebrospinal vaso-dilatation which was presumed to be due to the accumulation of cerebral metabolites, since other causative factors such as systemic hypertension and hypoxia were under control.

Cerebral elastance modulated the rise in ICP. When the former is reduced as in our one hydrocephalic case, little

or no increase in ICP might occur even in the fitting, spontaneously ventilated subject.

7. The effect on the ICP of routine nursing procedures such as the observation and charting of "vital signs" (blood pressure, pulse and respiratory rates, the reaction of the pupils to light), endotracheal suction and chest physiotherapy, injection of drugs and oral hygiene was studied in severe head injuries treated by paralysis and mechanical ventilation.

In 14 cases (out of 39) small rises in ICP were observed during suction, insertion of a N/G tube or intra-muscular injection; this was associated with a correspondingly small rise in ITP and a fluctuating SAP. Since these rises could be successfully treated with additional doses of relaxants, the intracranial hypertension could be attributed to the rise in ITP and IAP.

In six patients disproportionate and, on occasion, lethal intracranial hypertension was triggered by any stimulus except sound and it did not respond to the administration of more relaxants, although in one case to which Omnopon was given this reduced it slightly. Intracranial hypertension was attributed to an increased CBF, which, in the presence of impaired vasomotor homeostasis causes an increase in both the intracranial blood volume and pressure. De-afferentation by the use of analgesics and limitation of the "nursing care stimuli" is recommended in order to avoid this disaster.

8. Fluctuations in the absolute value of the ventricular fluid pressure (VFP) with changes in the amplitude and frequency of the oscillations of the ventricular fluid waveform, changes

in the ventricular CSF volume and in the diastolic blood pressure were observed in seven patients who developed "brain death" following either a head injury or a cerebrovascular accident. These were compared with the findings in nineteen patients who survived similar brain damage.

The findings in the two groups differed significantly:

A series of characteristic changes in the absolute value of the VFP as well as in the amplitude and rate of the cerebral pulse could provide incontrovertible evidence of the integrity of the cerebral circulation.

The presence of ventricular CSF in cases with intracranial hypertension was a favourable prognostic sign; its absence was indicative of progressive and potentially lethal intracranial hypertension.

Short lasting "disappearance" of the diastolic pressure towards the end of the ultimate plateau wave was an additional sign of a poor prognosis.

9. The concentration of homovanillic acid (HVA), 3-methoxy, 4-hydroxyphenylglycol (MHPG) and 5-hydroxyindolylacetic acid (5-HIAA) were measured in the ventricular CSF from fifteen patients who were comatose as a result of an acute head injury, a tumour or cerebrovascular accident. The metabolite levels were not related to the ventricular fluid pressure. In the eight patients who recovered and from whom serial samples of CSF were obtained, the metabolite levels did not change as coma progressed (except for two patients in whom HVA increased). The concentration of MHPG, but not of HVA or 5-HIAA, was greater ($P < 0.02$) in the five patients who

died without regaining consciousness, than in the ten patients who recovered. A progressive increase in ventricular MHPG levels in coma might therefore serve as an indicator of a non-reversible brain dysfunction. This is to be investigated in animals.

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APPENDIX I

PREPARATION OF MICROELECTRODES FOR DEPTH RECORDING OF BRAIN ACTIVITY

1) Electrodes are constructed from tungsten wire 0.5 mm diameter

2) Straightening the wire: A length of wire is suspended from a clamp with a 7lb weight attached to the end, heated to red heat with a bunsen burner and allowed to cool. This is done three times and the wire cleaned with emery paper and wire wool.

3) Cutting the wire: The wire is cut in lengths of approximately 15 cm on a carborundum wheel and the cut ends cleaned with emery paper.

4) Sharpening the tip: This is done electrolytically using a carbon indifferent electrode in a saturated solution of sodium nitrate. The tip of the needle is lowered vertically into the bath and current passed:

8 - 10 V for 4 - 5 minutes

4 - 5 V for 1 - 2 minutes

2 V to finish off.

The tip is examined under a microscope and further fashioning of the tip done at 20 volts for a few seconds. The electrode is then washed in boiling distilled water or toluene.

5) Insulation: The electrode is dipped into a jar containing:

Araldite resin 25% CIBA (or any nontoxic insulating resin)

Araldite hardener 25%

Toluene 50%

The excess is allowed to run off and the electrode suspended vertically, tip down, in a hot air oven at 150^{o}C for 30 minutes. This process is repeated three times.

6) Impedance testing: Usually a minute area of the tip remains uninsulated. The electrode impedance is tested and should be

1.5 ohm or greater. If the tip has become insulated and the impedance is therefore infinite, a small area of the tip is cleared by passing it into a bubble of saline/detergent mixture in a wire loop and passing a current of 50V between electrode and bubble. This may require to be done several times to bring the impedance to the required level.

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Torque resonance relationship in the wrist: sex difference

BY M. LAKIE and S. A. TSEMENTZIS*. *Departments of Surgical Neurology** *and Physiology, University of Edinburgh*

A printed motor concentric with the wrist joint has been used to apply sinusoidally changing forces to the hand. Movement occurs in the horizontal plane (Walsh, 1972). The displacement of the hand and its velocity of movement were recorded.

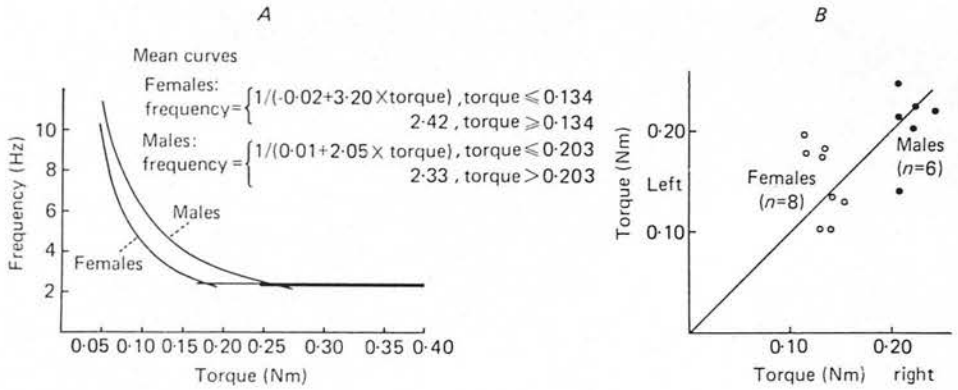

Fig. 1. *A*, rise in resonant frequency as torque is reduced below threshold level. *B*, torque threshold levels showing differences between men and women but no consistent difference between the two hands.

The wrist resonance of fourteen normal subjects was studied. Above a certain torque threshold this resonant frequency was constant and not significantly different ($r = 36$, $P < 0{\cdot}1$) between men (mean 2·33 Hz) and women (mean 2·42 Hz); below it was variable, rising as the torque was reduced. The threshold torque level was significantly lower (1% level using a Wilcoxon Rank Sum Test) in the women (0·13 Nm) than in the men (0·20 Nm) (Fig. 1*A*). Handedness of subjects did not alter these results (Fig. 1*B*). In a few cases the frequency at high torques ($\sim$ 0·45 Nm) showed a deviation from the constant value at somewhat lower level.

At low frequencies the system behaves in a linear manner with moderate torques and becomes non-linear when the torque is reduced below a threshold level. The threshold level is different in men and women. This may be a reflexion of a difference in the joint itself or the associated tendons or muscles.

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ACTA
NEUROCHIRURGICA

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Significance of the Ventricular Fluid Pressure Wave Form in the Diagnosis of Cerebral Circulatory Arrest and Brain Death

By

S. A. Tsementzis

With 7 Figures

Summary

The fluctuations in the absolute value of the ventricular fluid pressure (VFP) with simultaneous changes in the amplitude and frequency of the oscillations of the ventricular fluid wave form are described in seven patients who developed brain death following either a head injury or a cerebrovascular accident, and are compared with those observed in nineteen patients who survived similar brain pathology. The findings in the two groups were significantly different. It is suggested that VFP monitoring does provide reliable evidence of brain death even while the patient is on artificial respiration.

Key words: Intracranial pressure recording—Ventricular fluid pressure wave form—brain death—diagnosis.

Introduction

The accepted medical definition of brain death applies to patients with arrested respiration due to irreversible brain damage but with intact cardiac function, the latter being preserved only by the use of mechanical ventilation. The clinical criteria for establishing brain death have been formulated and generally accepted as follows (Mohandas *et al.* 1971). Over a period of at least 12 hours there should be no spontaneous respiration for periods of 4 minutes at a time, and absence of brain stem reflexes. Provided that hypothermia, metabolic disturbances, and depressant drugs, including alcohol, have been excluded then brain death may be pronounced. Several laboratory tests have been

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used, more to reinforce the clinical criteria of brain death than to supplant them; a summary of those most commonly used is presented in Table 1. The use of the EEG has been stressed by investigators, but there are examples of cases with isoelectric (flat) EEG tracings with very good recovery (Levin *et al.* 1966). Also a 24 hours EEG service is not

Table 1

No.	Investigation	Results
1	Electroencephalography (EEG)	Isoelectric tracing
2	Echoencephalography	Isoelectric tracing
3	Arteriovenous Oxygen differences	Absence of gradient
4	Bilateral carotid and vertebral angiogram	Non-filling of the intracranial vessels
5	Isotope measurements:	
	a) Isotope scintiphotography	Cold area
	b) Beta or gamma-emitting isotopes	Cold area
	c) Cerebral blood flow	Very low flow
	d) Rihsa (spinal subarachnoid space)	Absence of CSF flow
6	Neuropathological findings	Autolytic changes (Respirator brain)

available to most Hospitals. Angiographic and isotope investigations present problems in use as they require removal of the patient from the intensive care unit and are of limited value for making repeated measurements.

Intracranial pressure monitoring may be of value in the prognosis of brain damage. High pressures have been found in the few cases of brain death in which the ICP has been measured (Quaknine *et al.* 1973). However, there are a few examples in the literature of patients with severe head injuries who have survived in spite of high ICP. In other words the absolute level of ICP may be indicative of severe brain injury but cannot alone be used to establish the diagnosis of brain death. Our experience suggests that the wave pattern of the recording may correlate with changes in intracranial cerebrovascular dynamics and could be used as a reliable criterion of arrested cerebral circulation. This could be of great value in those patients with brain injuries in whom although there are signs of severe damage, there may still be a good chance of survival. At present these patients are put on long term assisted respiration either because controlled ventilation is used for their better management, or because they cannot maintain adequate spontaneous ventilation. Accurate clinical examination is impossible as long as the patient remains paralysed, and since there are thus no clinical signs of brain

death other laboratory tests are not applicable. It is suggested that monitoring of the ventricular fluid pressure wave form could provide reliable evidence of arrested cerebral circulation and therefore of brain death.

Material and Methods

Five males and two females, aged 12 to 48 years, sustained severe brain damage, five from closed head injury and two following cerebrovascular surgery. Their neurological conditions before being put on ventilation, duration of ventilation, the times of monitoring, and fluctuations of the main ventricular fluid pressure (VFP), and the necropsy findings are summarized in Table 2. The VFP was measured through a rigid transparent polyethylene ventricular catheter with a Bell & Howell physiological pressure transducer (type 4-422-0001/2) and recorded at constant amplification by a two-channel felt pen recorder (type 2800, Bryans Southern Instruments Ltd.) for a period of three to eight days. The hydraulic zero and the liquid continuity of the fluid in the tubing system to the transducer's pressure chamber were regularly checked. Postmortem examination was done in five cases.

A further seventeen cases of brain injuries who survived have been studied during the last 13 months. Recordings of their VFPs were used for comparison with those of the above seven patients.

Results

During the course of the ventricular fluid pressure recording our seven patients developed moderate to high resting pressure and several A-waves, the plateau levels of which were between 80–110 mmHg. Usually, and as we observed in the recordings of the survival group, following an A-wave the wave form returned to its pre-plateau appearance with regard to amplitude, frequency, and usually the pressure level (Fig. 1). However, in our cases following some A-waves the VFP fell below the abnormal resting level; the oscillations were less discrete and the amplitude showed a slow but definite decrease (Fig. 2). In Figure 3 we can see the continuous decline of the VFP curve until it reaches a low level and after a period, which ranges from one to six hours, the VFP starts rising again to a level above the abnormal pre-plateau resting value. It then maintains this level (except in case No. 2, where the VFP soon fell below the resting pressure and remained there without any change in the following three hours of monitoring), and *no more A waves occur* (Fig. 4). Figs. 2, 3, and 4 are taken from the same patient. Towards the end of the last A wave we were unable to detect the diastolic pressure with the sphygmomanometer, whereas the systolic pressure was easily registered. A low diastolic pressure was detected only when the VFP started to fall (Fig. 6). Fig. 5 shows a recording made during the second day after the last A wave. Compression of the

Table 2

No.	Age, Sex	Cause of injury	Clinical condition after the injury and before artificial ventilation	Days on respirator	ICP monitoring mmHg	ICP monitoring days	Autopsy findings
1	33, M	Cerebrovascular surgery (ruptured aneurysm)	Postoperatively responding to simple commands and moving all four limbs. Reflexes present, with brisk reaction of pupils to light. Respiration and circulation within normal limits	6	50—80	6	PM not permitted
2	13, F	Head injury	Unconscious. Responding to painful stimuli in a decerebrate fashion, with extensor spasms in all four limbs. Pupils not reacting to light	4	30—110	4	Ventilator brain
3	21, M	Head injury	Unconscious. Upper limb extensor rigidity. Lt pupil reacting to light sluggishly	5	70—100	5	Ventilatory changes
4	26, M	Head injury	Unconscious. Responding to painful stimuli with extensor spasms in all limbs. Rt pupil reacting to light. Laboured respiration. On the 6th day of assisted ventilation drugs were reversed and patient was able to maintain spontaneous respiration. Blood gases within normal limits. Because of facial twitching, which was observed when the patient was ready for discharge from the intensive care unit, the patient was reventilated for another two days	8	50—85	8	Early ventilatory changes

5	27, M	Head injury	Unconscious. Lt pupil reacting sluggishly. Slight increase of muscle tone in the upper extremities after stimulation. Adequate respiration	3	50—80	3	PM not permitted
6	48, F	Cerebrovascular surgery (ruptured aneurysm)	Postoperatively confused, pupils reacting to light. No movements on the right side observed. Spontaneous respiration	6	70—80	6	Respirator brain
7	12, F	Head injury	Decerebrate extensor movements in all four limbs. Both pupils reacting sluggishly. Ventilated. On the 3rd day she was allowed to breathe spontaneously. Accidental blockage of ventricular drainage with concomitant raised ICP and laboured respiration. Reventilated. Never recovered	6	70—100	6	Ventilatory changes

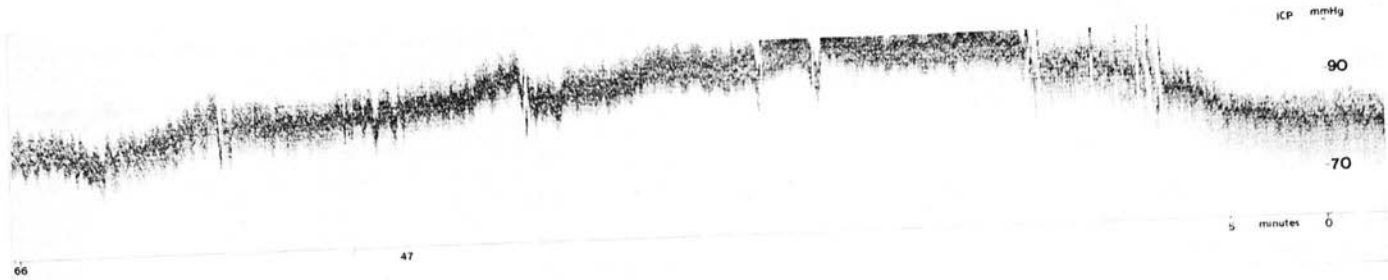

Fig. 1

Fig. 2

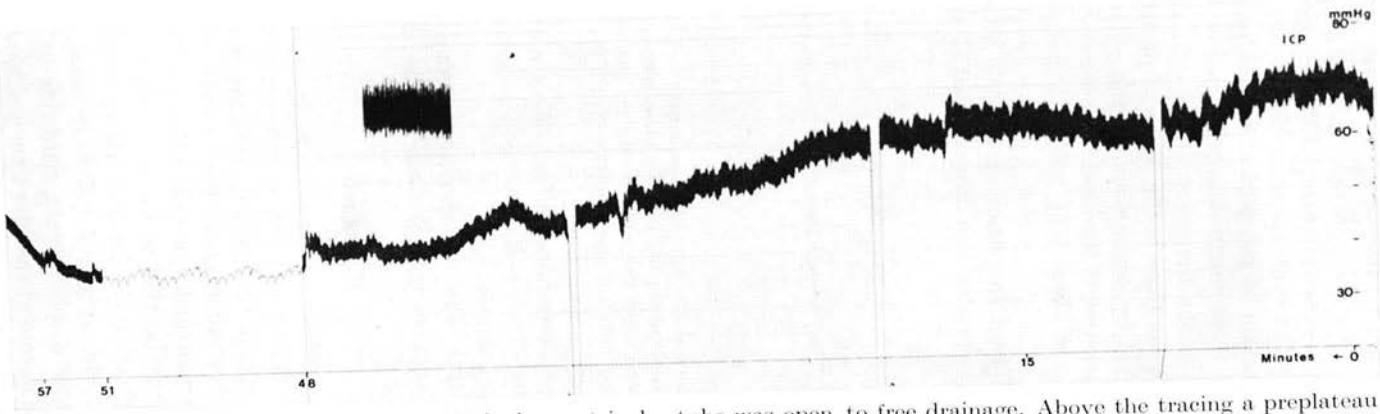

Fig. 3. Arrows represent times during which the ventricular tube was open to free drainage. Above the tracing a preplateau sample of the VFP wave form

external jugular veins does not alter the VFP. The injection of a minimal amount of saline into the ventricle immediately raised the VFP enormously, a clear indication of the critical volume/pressure relationship within the cranium in these circumstances. This procedure did not alter either the amplitude or the frequency of the oscillations, in complete contrast to the VFP recordings in the group of patients who survived. The VFP is not altered by compression of the external jugular veins or by changes in the position of the head from the resting to the upright position (an alteration of about 30°), provided that the hydraulic zero remains unchanged.

B waves of a constant frequency of $1\frac{1}{2}$ per minute are observed in Fig. 5. When the respirator was disconnected B waves disappeared,

Fig. 4. Arrow below trace shows time of compression of the external jugular veins. A pre-plateau sample of the VFP wave form below tracing on the left. (We had to alter the zero level to — 20 mmHg on the paper chart in order to increase the upper limit of the recording from 80 to 100 mmHg)

and the patient made no respiratory effort. We are also able to see the fine and shallow Hering–Traube–Mayer waves at a constant subnormal frequency of 13–14 per minute.

All the five patients who underwent necropsy showed early to advanced ventilator brain changes (Walker, E. *et al.*, 1975).

Discussion

Cerebrospinal fluid pulsations are thought by most investigators to originate from the arterial pulse and to contain a respiratory component. The main site of transfer of the arterial pulsation is regarded by some as being the basal and spinal arteries (Antoni 1946, Dunbar *et al.* 1966) and by others as the ventricular choroid plexuses (Bering 1955). The amplitude of the ventricular CSF wave form may be altered by variations in intracranial pressure (Ryder *et al.* 1952). CSF pulsation in thy presence of normal or slightly raised ICP is reduced by compensatory mechanisms such as CSF displacements, reduction or cessation of CSF production, alteration in cerebrovascular tone and blood volume, and by dural distention. Progressive elevation of the ICP results in sequential

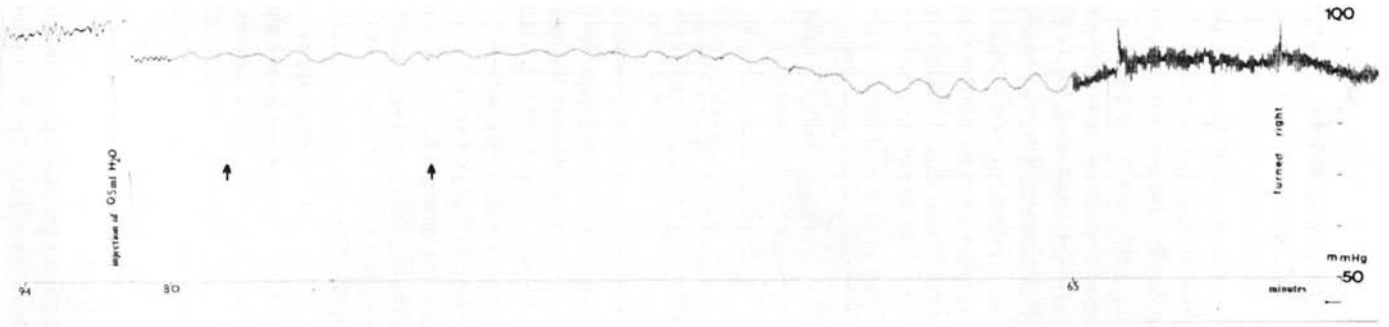

Fig. 5. Arrows below VFP tracing show a momentary compression of the external jugular veins. (The speed of the paper was increased from 5 mm/min to 0.5 mm/sec in order to clarify all the waves in the tracing)

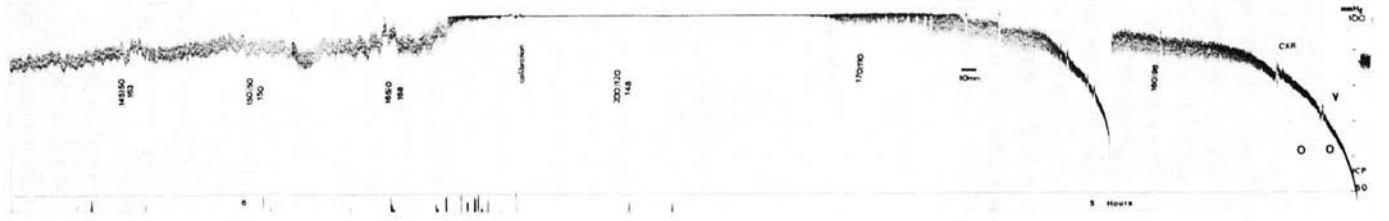

Fig. 6

exhaustion of these compensatory mechanisms, thus abolishing their damping effects on CSF pulsations. The amplitude increases and the wave form resemble more the arterial pulse.

Lundberg suggested that the plateau or A waves might be produced by rapid and reversible changes in the cerebral blood volume or by intermittent blockage of the CSF pathways, but he did not exclude the possibility that they might be due to water exchange into the brain tissue. Our patients with prolonged intracranial hypertension must have lost their buffering mechanisms. It has been reported that the CSF volume is the first to be lost, initially by displacement into the spinal subarachnoid space and later by diminished production, since this is pressure dependent (Shapiro, H. 1974). Sudden blockage of the CSF pathways raises the VFP gradually. The sudden and large changes in

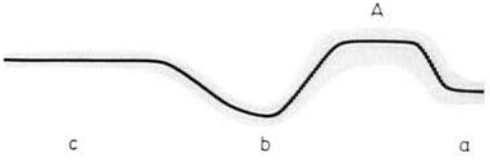

Fig. 7. *a* pre-plateau recording. *A* plateau-like wave. Main fluctuations of the VFP curve with regard the mean VFP and its amplitude

the VFP during an A wave could not be explained on the ground of increased vascular permeability and subsequent fluid exchange with the brain substance. The development of A waves in our cases, is thought to be due to changes in the cerebrovascular blood volume. This is reinforced by the changes in the wave form of the VFP, which occur following a plateau-like wave. With these changes CSF pulsation is diminished, and it is postulated that this reflects such a severe slowing of the cerebral circulation that brain death is inevitable. These changes in the VFP are summarized in Fig. 7.

What is the reason for the decrease in the VFP below the abnormal resting pressure level? Langfitt, T. W., *et al.* in 1969 have shown a diffuse collapse of the cerebral vessels, including the sinuses and the large arteries, when intracranial pressure equalled the mean arterial pressure (MAP). It is suggested that, during the increase in the VFP of an A wave, the pressure may exceed the MAP and by compression of the vessels blood would be displaced into extracranial channels. Since the volume/pressure relationship is so critical, a small amount of displaced blood could produce a significant fall in the VFP.

The subsequent rise of the VFP, which occurs over the following one to six hours, is, we suggest, due to fluid exchange within the brain tissue. Increase of the tissue osmotic pressure could conceivably occur

as a result of wide spread leakage of particles from damaged cells of all types (Gordon 1976). Fluid would migrate from the intravascular to the extravascular space until the hydrostatic equals the osmotic pressure when the flow would stop. The rigid low amplitude VFP tracing, which is observed in Fig. 4 and 7 (*c*), may be explained by the established equilibrium between the hydrostatic and osmotic pressures.

We are not able to explain the disappearance of the diastolic radial pressure when measured by a sphygmomanometer towards the end of the last A wave, or its reappearance soon after the A wave is over. Direct measurement of the arterial pressure may be of value in interpreting these events.

In general, it would be particularly interesting to relate the changes in the VFP wave form to cerebral blood flow and perfusion pressure.

The occurance of B waves appears to be due to ventilation and is of no value in the diagnosis of brain death.

The shallowness and slowness of Traube-Hering-Mayer waves offer further evidence of the failure of the cerebral circulation.

The presence of advanced autolytic changes in the brain at necropsy suggests that brain death occured long before its clinical diagnosis. Neuropathologists are unable to time precisely the onset of those autolytic changes; it is thus not possible to correlate the onset of autolysis with our VFP recordings. Case 4, which had an eight day course of VFP monitoring, was shown to be alive by reversing the relaxants and sedatives during the sixth day of ventilation. He was reventilated for another two days in which he presented the above-mentioned changes in the VFP recording. Early ventilatory changes were noted at necropsy.

Neurosurgeons often disagree about how long one should persist with mechanical ventilation of cases with severe brain damage. In Edinburgh the minimum duration is 48–72 hours, which is increased in young patients who show evidence of very severe brain injury; but the more severe the brain injury the more likely the patient is to succumb soon after the injury. As soon as the changes in the VFP described above are observed, we suggest that patients on the respirator should have their drugs reversed and be given a thorough neurological examination, in which the clinical criteria of brain death should be applied. This would lessen the strain on medical and nursing staff, would release facilities which might be better used, would reduce the suffering of the relatives, and would also speed up kidney donation.

Acknowledgement

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The Effect of Decerebrate Rigidity on the Intracranial Pressure

An Experimental Study

By

S. A. Tsementzis, F. J. Gillingham, E. R. Hitchcock, and A. Gordon*

With 17 Figures

Summary

The mechanical effect of acute decerebrate rigidity upon the ICP and the mechanisms underlying the relationship between them have been investigated with experiments performed on 26 cats. It has been shown that:

a) Extreme rigidity of the peripheral musculature with or without partial activation of the trunkal muscles produces no change in ICP,

b) the simultaneous elevation of the intra-thoracic and intra-abdominal pressures is the factor primarily operative in raising and maintaining the elevated ICP,

c) when cerebrovascular homeostasis is already defective a subsidiary but not unimportant role is played by the elevation of the systemic arterial pressure,

d) under conditions of normal brain elastance mild and short-lasting spasms produce no effect on the ICP. In an animal, however, in which the brain elastance had been increased by inflating a small air-filled balloon, similar spasms produced a marked increase in ICP.

Key words: Intracranial pressure; decerebrate rigidity; intrathoracic and intraabdominal pressure; systemic arterial pressure and cerebrovascular tone; brain elastance.

Introduction

Patients often exhibit decerebrate rigidity following a severe head injury, either as a result of primary impact lesions within the brain stem or secondary stem lesions resulting from raised intracranial pressure and transtentorial herniation. Clinically the syndrome is manifested by extreme spasms of the skeletal muscles of the limbs and those of the thorax and abdomen associated with major haemodynamic and respiratory changes.

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Decerebrate rigidity is considered to be a "release effect" of the brain stem efferent systems consequent upon withdrawal of the normal descending impulses inhibitory to the myotatic reflex. The maintenance of the rigidity requires the integrity of reflex centers located within the higher brain stem in the area between the caudal thalamus and rostral end of the pons (Sherrington 1897/98, Thiele 1905, Brown 1914, Bazet and Penfield 1922, Ranson and Hinsey 1924).

Detailed studies (Rhines and Magoun 1946, Magoun and Rhines 1947, Bach and Magoun 1947, Lindsley *et al.* 1949, Schreiner *et al.* 1949, Morruzi 1950, Starzl *et al.* 1951 a, b, French and Magoun 1952, Sprague and Chambers 1953) have established that tonic postural mechanisms are regulated by the functionally defined facilitatory and inhibitory components of the reticular formation. The facilitatory system, under the influence of ascending sensory and labyrinth tonic excitatory impulses, drives the spinal motor neurons to high level activity via the reticulospinal, vestibulospinal, and possibly the tectospinal pathways. The facilitatory system is controlled by cortical, thalamic, and cerebellar inhibitory impulses. In the absence of inhibitory control a constant barrage of excitatory impulses is delivered to the skeletal muscles, the result being decerebrate rigidity. This concept of the genesis of the syndrome is considered to be equally applicable to man and the experimental animal.

Cases with true decerebrate rigidity with verified brain stem lesions have been reported in which the hypertonicity was mainly of the flexor (Walshe 1921/22, 1923) or extensor muscles (Davis 1925, Nielsen 1941); to the former (flexor rigidity) the term "decorticate" has been applied, and the latter (extensor rigidity) has been described as "decerebrate". These two distinct patterns are believed to relate to the completeness and location of the lesion and, presumably, they relate to the organization of the postural mechanisms within the reticular formation.

Quinke (1891), during a lumbar puncture in a hydrocephalic patient, first observed an increase in the cerebrospinal fluid pressure (CSFP) during coughing, straining, or abdominal compression; he measured this by means of an open-ended water manometer. This observation was later confirmed by others who attributed it to an increase in the intracranial venous blood volume due to slowing of the cerebral venous return by the rise in the intrathoracic pressure (Becht 1920, Mayerson and Loman 1932, Bedford 1935). Rises in CSFP during straining, coughing and jugular compression are commonly observed.

The CSFP was first continuously recorded graphically with an optical manometer by Hamilton *et al.* (1936). They recorded increases as high as 60 mm Hg in the CSFP during coughing and straining in normal subjects. The clinical significance of this effect was first appreciated by Hunter (1959, 1960). Discussing the value of controlled ventilation in neurosurgical practice, he emphasized the need for muscle relaxants as a means of preventing increases in the CSFP due to straining during intubation. He explained that during straining the increase in the intra-abdominal pressure drove blood forcibly up the vena cava and this led to venous conjestion of the head and neck, and subsequently to a rise in the intracranial pressure.

It is not known if, in fact, limb muscle spasms alone have any effect on the CSFP and, if so, how.

Hamilton *et al.* (1943) have shown that in the normal human increases in the CSFP were associated with rises in the arterial pressure produced by the propagation of the increased intrathoracic pressure. Löfgren in 1973 found that a rise in the arterial pressure up to 200 mm Hg in normal dogs produced a five-fold increase in the intracranial pressure/volume relationship. This means that a rapid intracranial volumetric increase would be less readily compensated when the arterial pressure is also elevated and, therefore, a higher increase in CSFP would be produced than that under normal arterial pressure.

Severe spasms of the skeletal muscles, as in decerebrate rigidity, may well produce changes in the intra-thoracic and intra-abdominal pressure and secondary alterations in the central venous and arterial pressures. Depending on the nature and location of the injury within the brain stem primary arterial pressor responses may be elicited (Eliason *et al.* 1954, Lindgren *et al.* 1956) which, in the presence of defective cerebrovascular autoregulation due to trauma, would alter the level of the intracranial blood volume and that of the ICP in an uncontrolled fashion.

The effect of decerebrate rigidity on the ICP, however, does not appear to have been investigated so far either clinically or experimentally. Jennett and Plum (1972), discussing the syndrome of "persistent vegetative state" after brain damage, and also Jennett and Johnston (1972), summarizing the uses of ICP monitoring in clinical management, referred to a head-injured patient with extensor decerebrate rigidity whose ICP was normal. Out of 29 patients who showed signs of early decerebration. Mello *et al.* (1976) reported 12 without intracranial hypertension. They studied the brain stem vessels for histological changes in order to determine whether vascular or neuronal lesions were the cause of decerebration. The other

17 patients were found to have moderate to greatly increased ICP. They did not disclose, however, what pathology was responsible for the rise in the ICP. They did not monitor any of the cardiovascular or respiratory parameters, nor measure the degree of rigidity, all or any of which factors might have offered some explanation of this effect.

These few previous reports discounting the possible influence of muscle spasm on the ICP have tended to be more of the nature of casual observations, rather than of detailed studies. It thus seems reasonable to argue that severe decerebrate spasms might, by increasing the craniospinal venous blood volume, play a mechanical role in raising and maintaining the elevation of ICP. The magnitude and rapidity of this effect would obviously be of interest. Craniospinal venous engorgement may be due to either raised intra-thoracic (ITP) or intra-abdominal pressure (IAP) or both, or to widespread compression of the intramuscular veins of the limbs and the displacement of their contents into the major capacitance veins. Systemic arterial pressure (SAP) changes might also play a role in raising the ICP. It could be of great practical importance to know the relative significance of these factors in the elevation of ICP, which, by aggravating transtentorial herniation, may accentuate a brain stem lesion and convert a reversible physiological lesion into a permanent anatomical one.

Answers to these questions could materially affect the management of severe head injuries in which decerebrate rigidity may develop, in particular, in children and young adults whose brain stems appears to be relatively resistant (Powiertowski 1970). To date mechanical ventilation has been employed primarily to correct the systemic arterial hypoxia caused by increased respiratory effort and muscle hypertonicity, thereby preventing the secondary development of brain swelling (Brown 1970, Bracket 1970). The only head injuries which benefit from it are those suffering from systemic arterial hypoxia (Brown 1970, 1978). This concept, supported as it is by the well-established value of adequate respiration in the management and prognosis of head injuries, has dominated the present management policy in Edinburgh.

While we do not underestimate by any means the value of adequate ventilation of the head injured, we suggest that decerebrate rigidity itself may have a direct mechanical effect in raising and maintaining the raised ICP. It is known that above 450 mm H_2O an increase in ICP reduces the cerebral blood flow (CBF) (Zwetnow 1970) by mechanical vasocompression, and this leads (just as does systemic hypoxia) to local cerebral hypoxia (Brock 1970, Siesjo *et al.*

1970), which results in brain tissue acidosis and swelling (Langfitt *et al.* 1966, Jennett and Johnstone 1970).

If rigidity per se has no effect on the intracranial pressure then muscle paralysis and supportive ventilation of these patients is of limited value; but, if, on the other hand, decerebrate rigidity does increase the ICP, paralysis of striated muscles and ventilation not only correct blood gases but also should directly reduce the ICP.

Elucidation of the effect of rigidity per se on the ICP demanded, that as far as possible, other factors, such as haemorrhage, swelling, acute hydrocephalus, and hypoxia, which are often associated with brain stem injuries and might account for changes in intracranial dynamics, should be eliminated. An experimental study of the effects of decerebrate rigidity produced in cats by focal mesencephalic lesions, therefore, was undertaken in parallel with a clinical study of this problem.

Material and Methods

Twenty-six healthy cats weighing between 2.5 and 3.5 kg were used.

Anaesthesia was induced with Halothane (Halothane-May & BaKer Ltd.), nitrous oxide, and oxygen. An endotracheal tube (Y-Portex) was inserted, and light anaesthesia maintained with Halothane 0.5 to 1.0%, nitrous oxide 70%, and oxygen 29.5–29.0%.

Measurements:

The intracranial pressure (ICP) was measured by means of a Millar Micro-tip catheter pressure transducer (Millar Instruments, INC, No. 7 F, PC-470) in the right lateral ventricle (Fig. 1). Acurate recording, however, did not depend on precise ventricular implantation, because the transducer gave a perfectly adequate recording when implanted in the brain parenchyma of cats (Clark *et al.* 1975) and humans (Jeffreys 1977).

Central venous pressure (CVP), systemic arterial pressure (SAP). The venae cavae were cannulated either through the external jugular or left femoral vein in order to measure the CVP, and the systemic arterial pressure was measured through a cannula introduced into the thoracic aorta via the left femoral artery; in each case a 60 cm, OD 1.65 mm (12 G) cannula (Portex) was introduced.

Intra-thoracic (ITP) and intra-abdominal pressure (IAP). These were measured by small oesophageal catheters (Morgan Ltd.) introduced into the lower end of the oesophagus and the stomach.

Respiration. In a few animals the chest was encircled by a mercury-filled rubber tube so that the respiratory excursions could be displayed on a calibrated chart (stethogram). In the majority of the animals respiration was assessed from the ITP tracing.

The vascular cannulae and the oesophageal catheter(s) were connected to Bell & Howell physiological pressure transducers (type: 4-422). Together with the Millar transducer these were connected to a M 19 heat-pen recorder (Devices) for the continuous recording of the ICP, CVP, SAP, ITP, or IAP.

Muscle tone was assessed from the electrical activity of the upper and lower limb muscles with bipolar needles, data being displayed on a multichannel EEG recorder (Officine Galileo, Mod. E 8 a).

Continuous recordings were made of the *electrocardiogram* (ECG—lead II, intramuscular needles).

The animal's *rectal temperature* was kept constant at 38–38.5 °C by means of a thermostatically controlled electric blanket.

Systemic arterial pCO_2, pO_2, Hydrogen ion activity, and standard bicarbonates were determined every 20 minutes throughout the experiment.

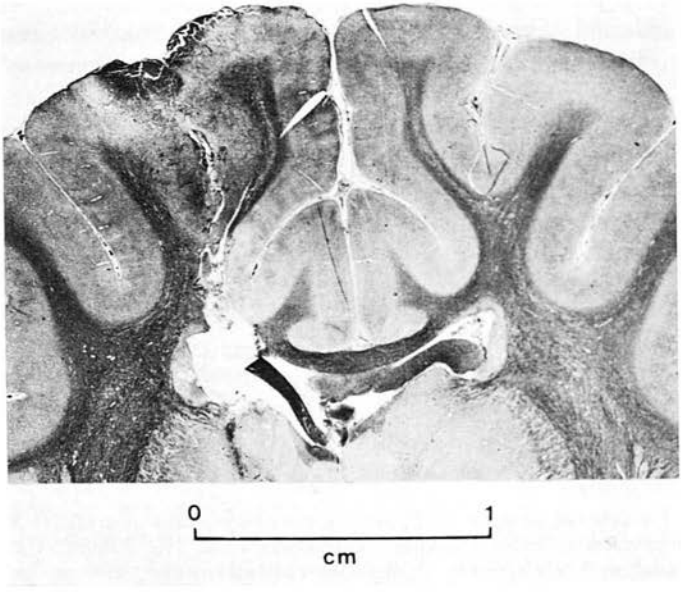


Fig. 1. Section of a cat's brain through the ventricular system; track of insertion of the Millar Micro-tip transducer into the lateral ventricle. (Loyez stained. Magnification ×4)

Preliminary Study in Normal Non-Decerebrate Animals

Appreciating the probable complexity of the factors involved in alteration in ICP during decerebrate spasms, we undertook a preliminary pilot study of some of these on six animals (Table 1).

These animals were set up as described, differing from the animals with decerebrate rigidity only in so far as no stereotactic procedures were performed.

The external and internal jugular veins were temporarily occluded in two animals. The internal jugular vein of a cat receives blood from the venous sinuses of the brain (inferior cerebral), from an occipital vein, from muscular branches, and from pharynx and palate (Crouch and Lackey 1969).

The SAP was increased by the use of Angiotensin (Vasopressin-CIBA, 0.01 μg/ml and 0.1 μg/ml).

The CVP was raised by the quick injection of boli of 30 ml of saline into the venae cavae.

Paediatric sphygmomanometer cuffs were used to increase the intra-thoracic and intra-abdominal pressures.

Main Study in Animals With Decerebrate Rigidity

Twenty animals were attached to a Narishige stereotactic frame (Mod. SN-2). A dental burr was used to make the skull holes, which were sealed with dental cement (Directon Sealant) after the completion of the lesions. The stereotactic coordinates used were those of Snider and Niemer (1969). The mesencephalic reticular formation was preliminary identified by combined visual and audio depth recording from a 5–10 μ tip-protrusion tungsten microelectrode. This localization was confirmed by stimulation with a silver electrode. Radiofrequency lesions were made with a Grass lesion maker (Mod. LM-3) with a gold-plated tip electrode. (A detailed account of the method of production of decerebrate rigidity will be published separately).

Table 1

No.	Procedure	Times per animal	No. of animals
1.	Obliteration of both jugular veins bilaterally	1	2
2.	Elevation of the central venous pressure (CVP)	4	6
3.	Elevation of the intra-thoracic pressure (ITP)	4	6
4.	Elevation of the intra-abdominal pressure (IAP)	4	6
5.	Simultaneous elevation of the ITP and IAP	4	6
6.	Elevation of the systemic arterial pressure (SAP)	2	6
7.	Simultaneous elevation of the SAP, ITP, and IAP	2	6

The anaesthetic was discontinued just before the lesions were made, and the observations were terminated as soon as decerebrate rigidity had developed and its effects recorded.

Results

Normal, Non-Decerebrate Animals

Obliteration of the internal and external jugular veins

Obliteration of the internal jugular veins alone or in conjunction with the external jugular veins produced a small, sudden rise in the ICP of 6–8 mm Hg above the normal level. The elevated ICP returned to its previous normal level within a matter of seconds (Fig. 2).

Increase of the central venous pressure

The quick injection of boli of 30 ml of saline into the vevae cavae produced an immediate, small (< 10 mm Hg) and transient increase in ICP, which in fact returned to normal by the end of the injection.

Increase of the intra-thoracic pressure

A pressure of 60 mm Hg was applied around the thorax via a sphygmomanometer cuff, and this raised the ICP up to 12 mm Hg

above the normal value. This increase in ICP was maintained as long as the ITP was kept elevated. Further elevation of the external pressure to 100 mm Hg produced no additional increase in ICP. This procedure, however, also produced a profound decrease in the mean systemic arterial pressure (MSAP), and both the amplitude and frequency of the arterial pulse were greatly reduced, while the CVP was significantly increased (Fig. 3). These changes were sufficiently severe to endanger the animal, and the cuff was deflated immediately.

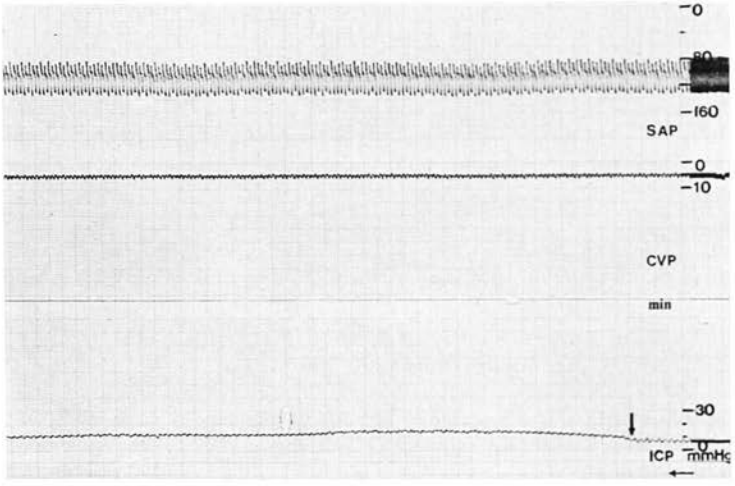


Fig. 2. Effect of occlusion of the internal and external jugular veins bilaterally (arrow) on the ICP, SAP, and CVP

Increase of the intra-abdominal pressure

A similar external application of 60 mm Hg (and up to 100 mm Hg) pressure round the abdomen increased the ICP to about 17 mm Hg above the normal level; the amplitude of its fluctuations was also increased. In contrast to the effect of the elevation of the ITP, the MSAP slightly increased, while the amplitude of the arterial pulse was increased and the rate was decreased (Fig. 3).

Simultaneous increase in the ITP and IAP

A simultaneous rise in the ITP and IAP produced a very marked rise in ICP of about 40–45 mm Hg. Simultaneously a profound elevation in CVP was recorded; the MSAP was largely unaffected and the amplitude of the arterial pulse was reduced. The rise in ICP was maintained so long as the ITP and IAP were kept elevated (Fig. 4).

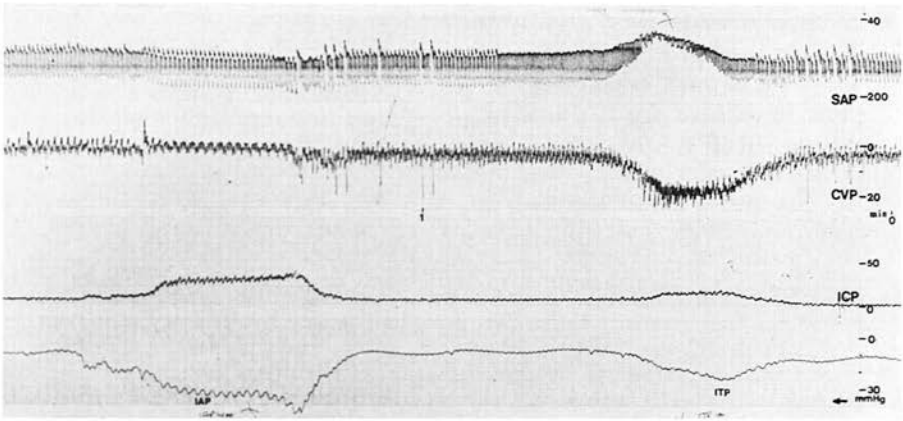


Fig. 3. Effect of the directly raised ITP and IAP separately upon the ICP, CVP, and SAP. The lower trace is that of the IAP

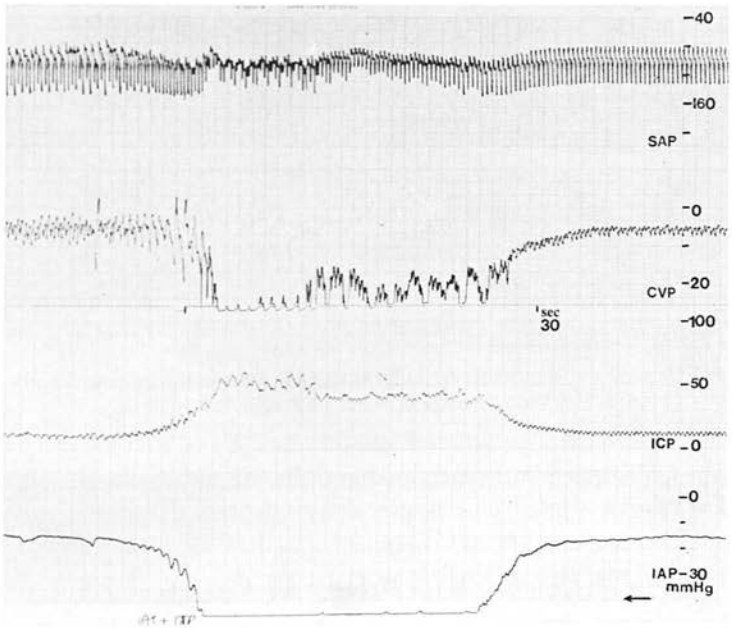


Fig. 4. Effect of the simultaneous increase in ITP and IAP upon the ICP, CVP, and SAP

Simultaneous increase of the ITP, IAP, and SAP

The SAP was elevated by intravenous injection of Vassopressin. This produced a very small increase in ICP. When the systolic arterial pressure had risen to 200 mm Hg or more the thoracic and

abdominal cuffs were rapidly inflated to a pressure of 60 mm Hg. This resulted in a very large increase in ICP to about 50–53 mm Hg above its normal value. Release of the thoracic and abdominal compression reduced the ICP instantly at a level just slightly higher than the normal (Fig. 5).

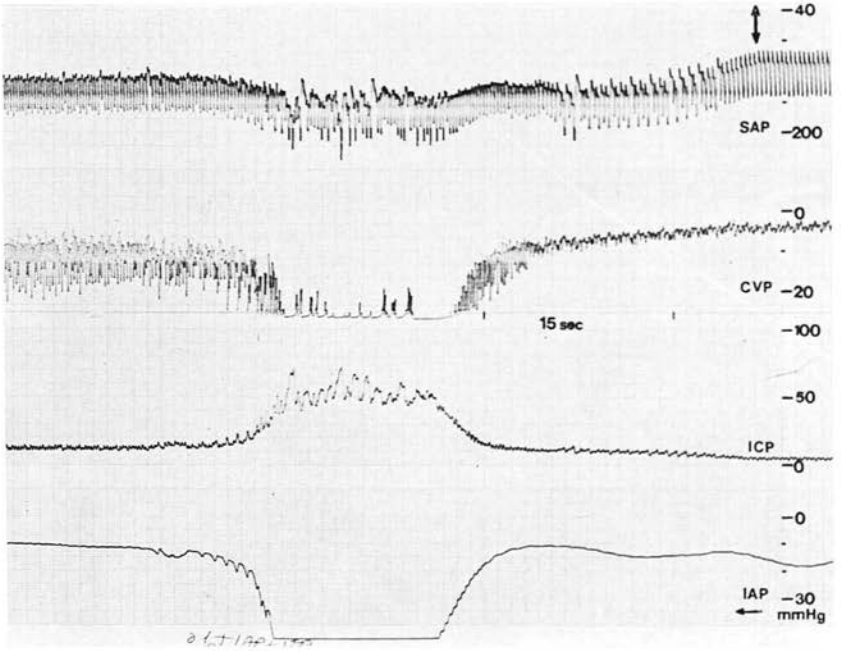


Fig. 5. Effect of the simultaneous increase in SAP (arrow shows time of injection of Vasopressin), ITP and IAP upon the ICP

The CVP was greatly increased and the MSAP was increased.

The above described changes are presented diagramatically in Fig. 6 (1–4).

Animals With Decerebrate Rigidity

Decerebrate rigidity was produced in twenty cats (Fig. 7). The arrangement of the animals with regard the development of decerebrate rigidity is presented in Table 2.

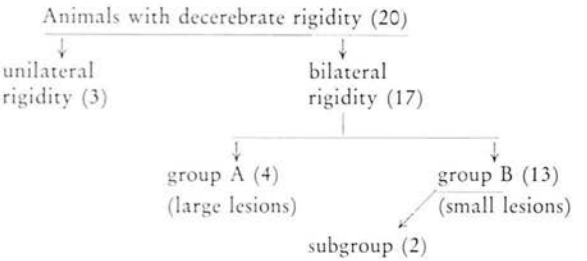
Unilateral rigidity (three animals)

Unilateral lesions produced mainly ipsilateral decerebrate rigidity in all three.

A continuous tonic muscle contraction (> 50 microvolts) produced no effect on the ICP in two of them; similarly the ITP, CVP, and SAP remained unaffected.

In one animal after a left-sided lesion an extreme extensor and flexor spasm (> 150 microvolts, Fig. 8) produced transient, small, short-lasting phasic changes in ICP, these changes consisted of a minimal increase in the amplitude and minor decrease in the rate of the cerebral pulse. The changes in ICP, ITP, and SAP monitored before, during, and after the development of the decerebrate spasm are presented in Fig. 9.

Table 2

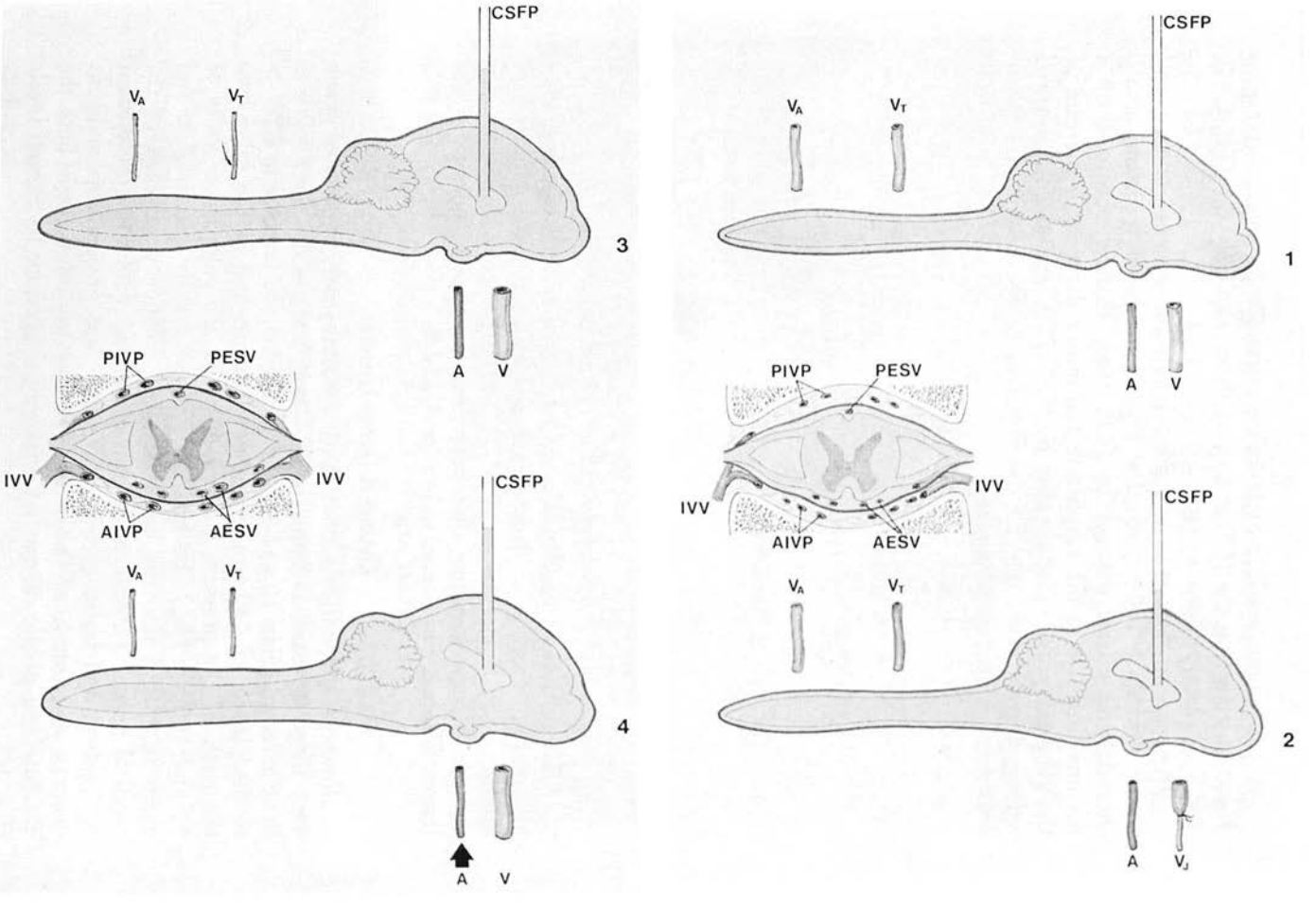


Bilateral rigidity (17 animals)

Bilateral lesions produced a varied degree of decerebrate rigidity bilaterally. During a decerebrate spasm two main patterns of alterations in ICP, CVP, SAP, ITP, and IAP were identified and it was revealed at autopsy that they correlated with the size of the lesion. These are presented as groups A and B.

Group A (large lesions)

Four of the animals developed simultaneously with the spasm very large increases in both the ICP and SAP, while the CVP was little affected (Figs. 10 and 11). In particular, the increase in ICP reached levels of 140 mm Hg in two animals and in the other two the peak of the pressure wave well above the calibration scales of 50 and 100 mm Hg. The increase affected mainly the absolute and mean ICP, and also the amplitude and frequency response of the cerebral pulse. This elevation was associated with the development of rigidity, and lasted as long as rigidity was present. Spontaneous decrease or cessation of the spasms for short periods brought both the absolute and phasic changes of intracranial pressure to normal levels (Fig. 10).


CSFP
V_A
V_T
A
V
3
PIVP
PESV
IVV
IVV
AIVP
AESV
4
1
2
V_J

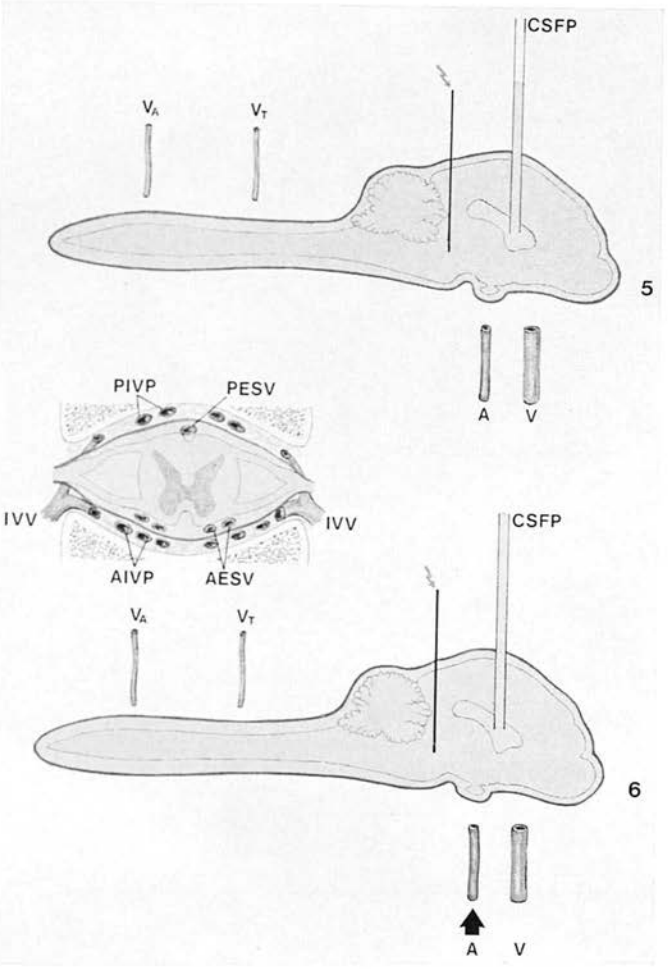


Fig. 6 (1–6). Schematic representation of the alterations in ICP and its mechanisms in both decerebrate and non-decerebrate animals. 1 normal, 2 ligation of both jugular veins bilaterally, 3 simultaneous elevation in ITP and IAP, 4 simultaneous elevation in SAP (↑), ITP, and IAP, 5 changes in ICP during decerebrate rigidity without increase in SAP, and 6 changes in ICP during dec. rigidity and raised SAP (↑) under conditions of a defective cerebral homeostasis. *A* = systemic arterial pressure, *V* = central venous pressure, V_J = jugular veins, V_T = intrathoracic veins, V_A = intra-abdominal veins, *CSFP* = cerebrospinal fluid pressure, *IVV* = intervertebral veins, *AIVP* = anterior internal vertebral plexus, *AESV* = anterior external spinal plexus, *PIVP* = posterior internal vertebral plexus, *PESV* = posterior external spinal veins

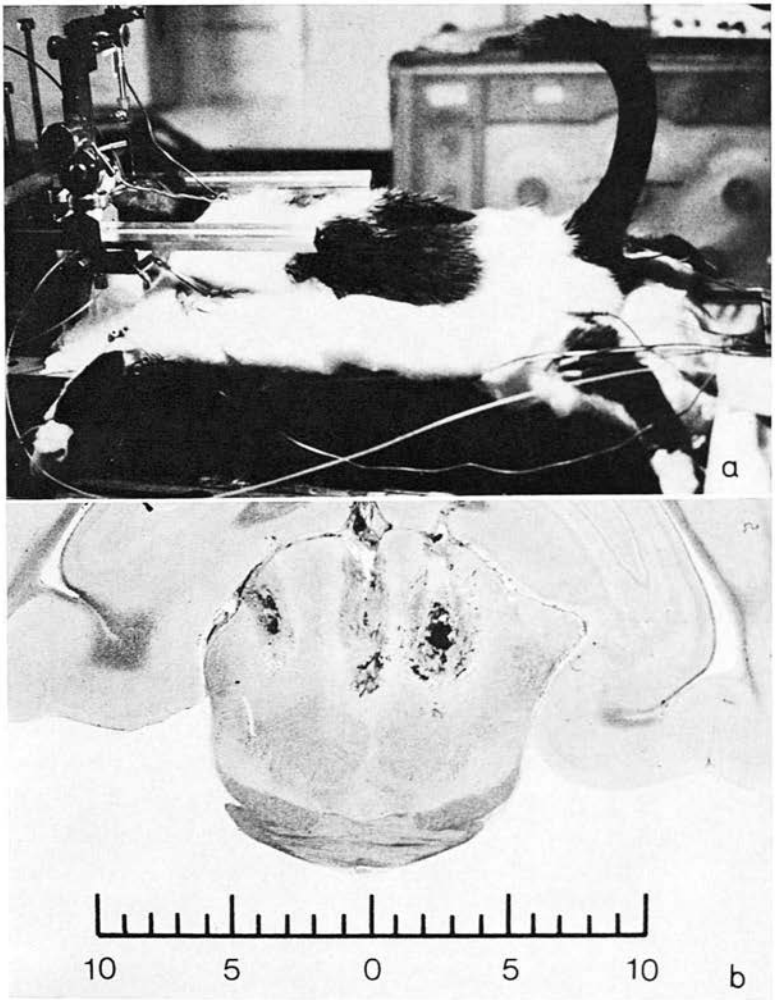


Fig. 7. a) One of the animals with a typical decerebrate posture. The fore limbs are adducted, fully extended and pronated, this being obviously seen in the paws. The hind limbs are outstretched, and piloerection of the dorsum hair and erection of the tail is seen. b) A midbrain section just before the intracollicular plane, in which we made most of our lesions in order to produce decerebrate rigidity. (Loyez stained. Magnification ×4)

Introduction of the coagulation electrode into the target area produced no effect on either the ICP, SAP, or CVP. During coagulation, however, a marked increase in ICP alone without any effect on the SAP, CVP, and respiration was observed (Figs. 10 and 11).

Fig. 8. Unilateral decerebrate rigidity. EMG from extensor (top trace) and flexor (bottom trace) of the fore limb of a cat. Unilateral rigidity with predominantly extensor features was produced by one laterally placed small (2×2 mm) mesencephalic lesion. The tonic contraction of high amplitude and frequency was turned into a periodic, short-lasting tremor, which tailed off into a continuous tonic and small amplitude muscle discharge

This rise in ICP returned to its previous normal level when the radiofrequency current was switched off.

The SAP was markedly elevated during decerebrate spasms. Both systolic and diastolic pressures were affected, the former slightly more than the latter. The MSAP was greatly increased (to 90–95 mm Hg) as calculated by the formula of Yang *et al.* 1972)

$$\text{MSAP: } \frac{\text{systolic pressure} + (\text{diastolic} \times 2)}{3}$$

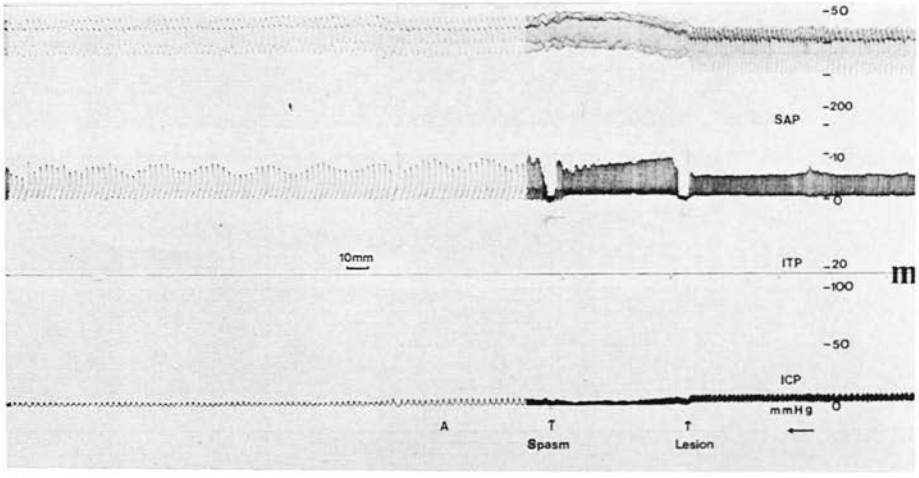


Fig. 9. Changes in ICP, ITP, and SAP in a cat before, during, and after the development of unilateral severe decerebrate rigidity. The ICP was raised, but only by 2–3 mm Hg, above the normal level. Small phasic changes are seen which comprise an increase in the amplitude and slowing of the frequency of the cerebral pulse. The animal virtually stopped breathing in expiration and there was also a small rise in the mean ITP. Despite the initial small fall in SAP following the lesion, which was followed by a reduction of the amplitude of the cerebral pulse, the SAP remained within normal limits and did not alter during the spasm. Soon the ITP recovered its previous level by the lessening of the spasm. Similarly the ICP returned to normal level only when rigidity was decreased (Fig. 8, at *A*). The remaining rigidity did not affect the ICP, ITP thereafter (time in minutes: m)

Bradycardia occured in all animals, and arrythmias were recorded in two of them. The elevation in SAP correlated with the development, continuation, and severity of the decerebrate spasms.

A small increase in CVP (to + 11 mm Hg) was recorded during decerebrate rigidity. This increase affected the mean value, while the amplitude of the venous pulse was reduced.

The ITP in the one animal in which it was recorded was found to be elevated by approximately 50 mm Hg.

Alveolar hyperventilation (increase in amplitude and rate of respiration) was present in all animals with decerebrate rigidity. In this particular group, immediately after the development of the initial spasm the respiratory rate was reduced by approximately 40% for 10–15 minutes during which time, however, hyperventilation always accompanied the intermittent decerebrate spasms.

Fluctuations in the mean arterial blood values of pCO_2, pO_2, hydrogen ion activity, and standard bicarbonate before, during, and after the development of decerebrate rigidity are presented in Table 3.

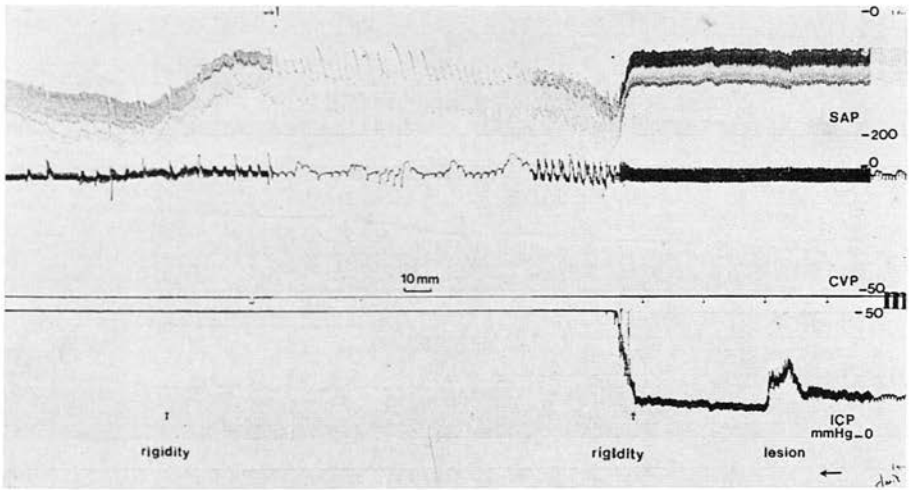


Fig. 10. Fluctuations in ICP, CVP, and SAP before, during, and after the development of bilateral severe decerebrate rigidity in cats. A substantial increase in ICP during coagulation is observed without concomitant alterations in SAP and CVP. Soon (within two minutes) after the completion of the lesions bilaterally an intense and prolonged decerebrate spasm occurred, which produced an abrupt and marked rise in ICP (plateau waves). This increase, the peak of which well exceeded the top calibration scale (50 mm Hg), lasted throughout the decerebrate spasm. A concomitant marked increase in SAP, systolic as well as diastolic, took place. Bradycardia and extrasystoles also appeared. By comparison with the rise in ICP and SAP there was only a small increase in CVP

Decerebrate rigidity developed immediately (within 1–2 minutes) after the completion of the lesions, the animals developing extreme and violent spasms. The fore limbs were adducted, fully extended and pronated, this being most easily seen in the pays (Fig. 7). The hind limbs were thrust backwards and outstretched, while the claws were protruded. The rigidity was pronounced in the proximal joints, particularly of the fore limbs, and, although it affected both extensor and flexor muscles the former were mainly affected. The abdominal

muscles were tense and the thorax was fixed. Piloerection, predominantly of the dorsal hair and erection of the tail, was also observed. In the EMG high frequency spike potentials were recorded of up to 200 microvolts during maximal contraction.

Group B (small lesions)

Thirteen animals in which decerebrate rigidity was produced showed a range of changes in ICP, from *none*, through *moderate*, to

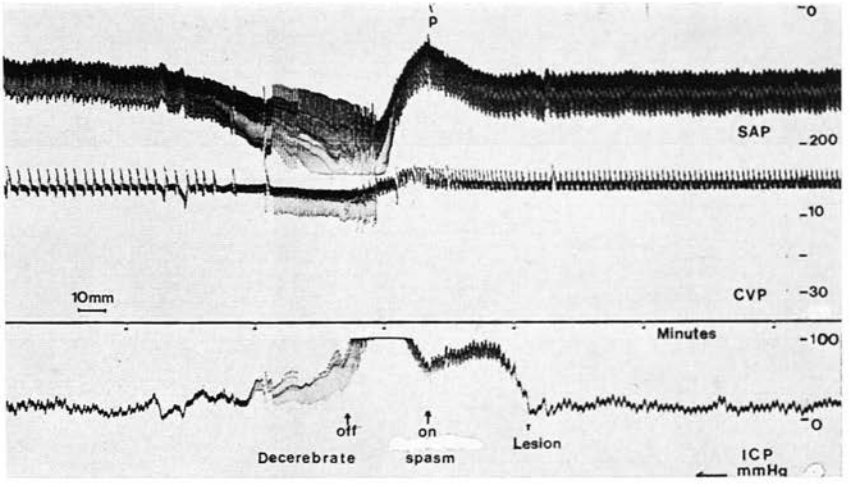


Fig. 11. Fluctuations in ICP, CVP, and SAP before, during, and after the development of decerebrate rigidity. A substantial increase in ICP without alteration in SAP and CVP occurred during coagulation and under normal blood gases. Approximately 30 seconds elapsed between the completion of the bilateral lesions and the development of bilateral severe decerebrate rigidity which produced a marked increase in ICP to well above the cal. scale (0–100 mm Hg). The amplitude and frequency of the cerebral pulse was increased, as it is seen at the declining part of the ICP tracing. A striking increase in SAP was recorded during the spasm, affecting both the systolic and the diastolic pressure. The CVP was slightly elevated during the spasm. Tachypnoea was the feature during the spasm, while at the end of it a reduction in the respiratory rate by approx. in 40% this occurred temporarily for about 10 minutes. All changes returned to their previous appearances and characteristics by the end of the spasm

a *large* increase (Figs. 12 and 13). Simultaneously, a direct proportional increase in the ITP, IAP, and CVP was recorded. The SAP remained mostly unaffected.

In particular, we recorded short-lasting oscillations of the cerebral pulse of low, medium, and high amplitude, and of increased rate during decerebrate spasms. These changes were closely associated

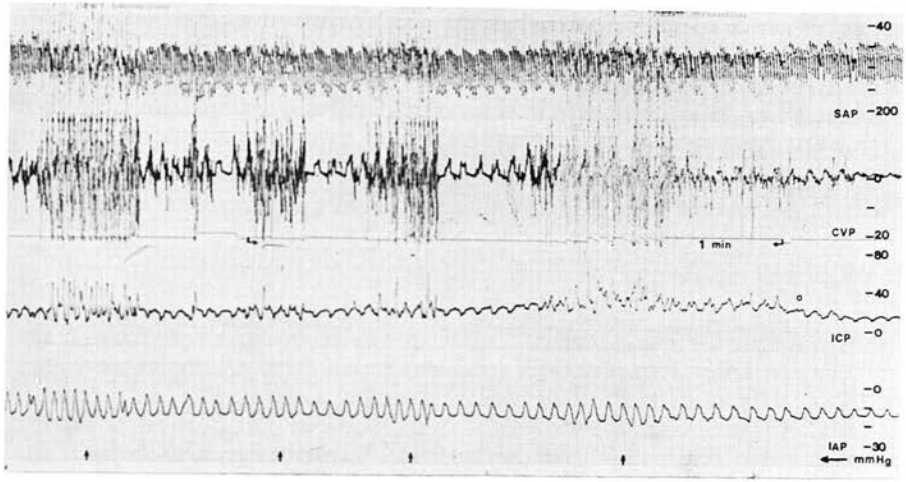


Fig. 12. Recording of ICP, CVP, SAP, and IAP of a cat during decerebrate rigidity. Spontaneous increase in rigidity (arrows) produced a marked increase in CVP and ICP and small increase in IAP, phile the SAP remained virtually unchanged

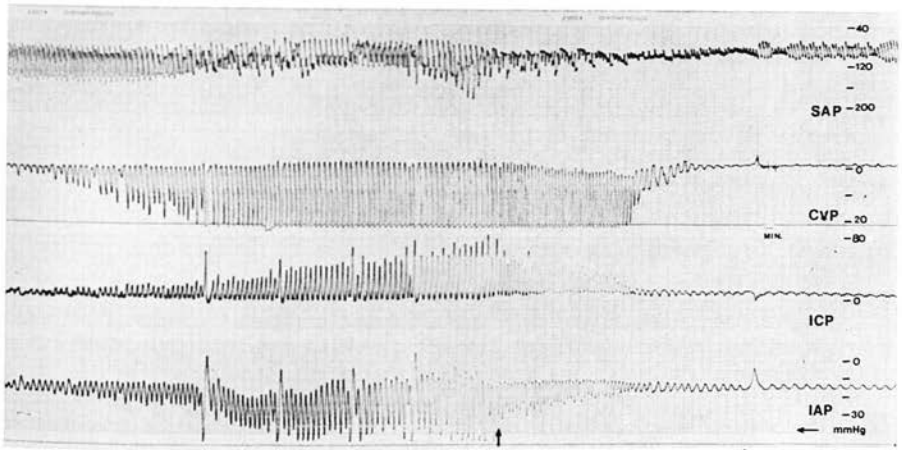


Fig. 13. Continuous recording of SAP, CVP, ICP, and IAP during decerebrate rigidity in a cat. An extreme decerebrate spasm increased in ICP, IAP and most substantially the CVP, while the arterial pulse was greatly reduced. An indication of raised ITP alone, as it is discussed in the text. A spontaneous further intensification of the rigidity (arrow) produced a further increase in IAP and ICP, and increased the SAP in its absolute level and amplitude of the arterial pulse when compared with the previous recording or after the reduction of the rigidity. Reduction of the intensity of rigidity reduced the rise in IAP, ICP, CVP, and SAP to the previous level immediately

with similar phasic changes in the ITP, IAP, and CVP. In other words, the cerebral, venous, and respiratory pulses were all of the same configuration. It was impossible to determine which of the above pressure parameters was altered first, even in high speed recording, because of the close parallelism of the alterations in their values.

The SAP did not alter. On a few occasions, however, sporadic, short-lived widening of the pulse pressure was recorded (Fig. 12); these phasic changes were closely associated with similar but much

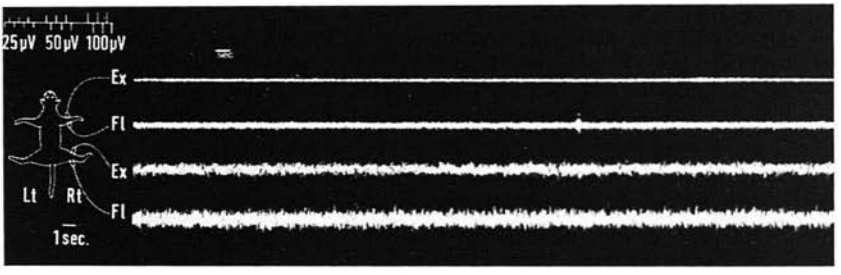


Fig. 14. Decerebrate rigidity in a cat. EMG of extensors (*Ex*) and flexors (*Fl*) of the fore and hind limbs. Continuous tonic contraction of all four limbs has developed following bilateral mesencephalic lesions. Rigidity was mainly of the hind limbs and it was of the flexor more than the extensor muscles. Clinically the animal was "quiet", and showed the typical posture of decerebrate rigidity

more prominent alterations of the venous pulse, which in fact preceded them. Slight elevation of the SAP was recorded only after extreme decerebrate rigidity and especially when the IAP was markedly raised as a result of the spasm (Fig. 13).

In a subgroup of two animals of group B with decerebrate rigidity (Table 2) no change in ICP was observed; similarly there was no change in ITP, CVP, or SAP during the rigidity. It was also surprising but very interesting that there were no cardiovascular or respiratory complications when these were monitored by means of SAP, CVP, and ITP measurements. Clinically the animals were "quiet" with continuous severe decerebrate rigidity. The fore limbs were fully extended forwards in pronation, the hind limbs were outstretched backwards, and the tail was erected. In the EMG a continuous tonic muscle discharge (high frequency action potentials of 25–170 microvolts) was recorded in all four limbs. The rigidity mainly affected the hind limbs and it was much more prominent in the flexors than the extensors (Fig. 14).

Hexamethonium bromide (10 mg/kg was administered IV to one animal of group B with decerebrate rigidity which had shown a

moderate increase in ICP during spasms associated with rise in CVP, ITP, and a slight increase in SAP. The SAP soon fell to 70/40 mm Hg, a level within the autoregulatory ability of the cerebrovascular tone to maintain adequate cerebral perfusion (Harper 1966). Decerebrate rigidity of the same magnitude as before the administration of the hypotensive drug produced almost the same moderate rise in ICP; the CVP and ITP were affected similarly. The SAP remained unchanged.

The amplitude of the cerebral pulse, however, was comperatively reduced.

Towards the end of the recordings the brain was exposed but it did not bulge into the bony defect; subsequently with the lessened effect of the Hexamethonium the SAP started to rise and the cerebral cortex soon herniated through the skull window.

Fluctuations in the mean arterial pCO_2, pO_2, H^+ and standard $-HCO_3$ of group B before, during, and after the development of decerebrate rigidity are presented in Table 3.

One objective of the experiments was to identify the sites within the midbrain where the smallest lesions would produce maximal decerebrate rigidity. It was hoped thus to eliminate the cardiovascular and the transient respiratory complications which appeared after extensive lesions within the mesencephalon in group A, thereby abolishing their effect on the raised ICP and allowing study of the effect only of the muscular contractions on the ICP. These small and discrete lesions produced a variable amount of rigidity, which could be graded as *severe*, *moderate*, or *mild*.

The anatomical distribution of the rigidity also varied. Extensor and flexor, but most profoundly extensor rigidity developed in the majority of the animals (Fig. 15). In a few of them, however, there was extensor rigidity of fore and hind limbs with silent flexors (Fig. 16) or mainly flexor and less extensor rigidity affecting mostly the hind limbs (Fig. 14). The first type of rigidity was more effective in raising the ICP than the others; the third in particular produced no change in ICP, which is discussed below.

Autopsy revealed no intracranial or subarachnoid haemorrhagic lesions.

In one animal with established decerebrate rigidity, which was present as a continuous muscle discharge with sudden spontaneous intensifications in rigidity, the ICP was artificially raised by implanting a latex balloon epidurally in the cranium; the balloon was slowly inflated by introducing a small quantitity of air, so that a rise in the ICP of about 38–40 mm Hg was not associated with changes in SAP or CVP. An attempt was thus made to reproduce

Table 3. *Arterial Blood Values (Mean ± SD) for Hydrogen Ion Activity (H^+), Carbon Dioxide Tension (pCO_2), Oxygen Tension (pO_2) and Standard Bicarbonate in Cats Before (approx. 20 minutes), During (0) and After (+ 20–30 minutes and + 60–80 minutes approx.) the Development of Acute Decerebrate Rigidity Produced by Focal Mesencephalic Stereotactic Lesions.* (Group A: animals with large lesions; group B: animals with small lesions)

Group (No. of cats)	Hydrogen ion activity (nmol/l)				Carbon dioxide tension (KPa)				Oxygen tension (KPa)				Standard bicarbonate (mM/l)			
	— 20	0	+ 20 >	+ 60 >	— 20	0	+ 20 >	+ 60 >	— 20	0	+ 20 >	+ 60 >	— 20	0	+ 20 >	+ 60 >
A	33.65	33.70	34.05	35.55	3.88	3.88	3.86	3.82	12.50	12.70	12.17	11.72	21.12	21.12	20.42	19.25
(4)	± 0.88	0.82	0.75	0.80	0.20	0.17	0.15	0.12	0.86	0.77	0.77	0.53	0.92	0.98	1.05	0.63
B	36.50	36.53	36.67	37.24	3.96	3.94	4.01	3.87	12.46	12.50	12.13	11.86	20.99	20.85	20.45	19.50
(11)	± 0.90	0.94	0.83	0.93	0.20	0.17	0.14	0.12	0.66	0.70	0.72	0.57	1.00	0.91	1.06	0.92
	t 0.71	0.68	0.80	1.71	0.81	0.60	1.83	0.61	0.09	0.17	0.09	0.42	0.22	0.49	0.45	0.49

t = Student's paired t-test (comparison of the same time-samples between groups A and B).

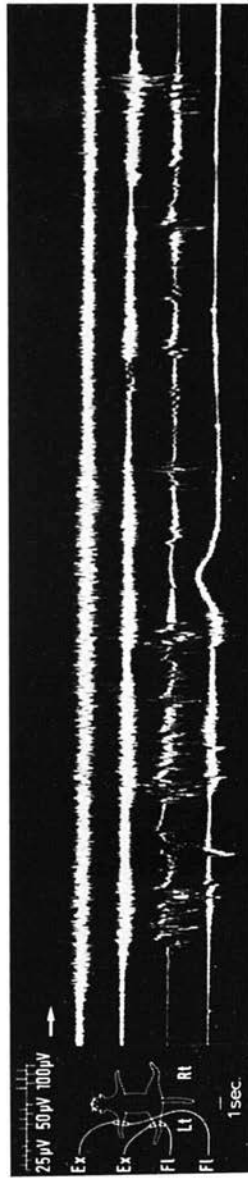


Fig. 15. Decerebrate rigidity in cat. EMG of the extensors (*Ex*) and flexors (*Fl*) of the fore and hind limbs of a cat. Decerebrate rigidity of extensor type. The extensors of both limbs are most affected. Spontaneous progression movements seen in both flexors enchanced the extensor discharge which took a fusiform appearance (stretch reflex). Clinically the animal showed a vigorous onset of spasms, with rigidity of all four limbs especially of the proximal joints, pilo-erection and erection of the tail

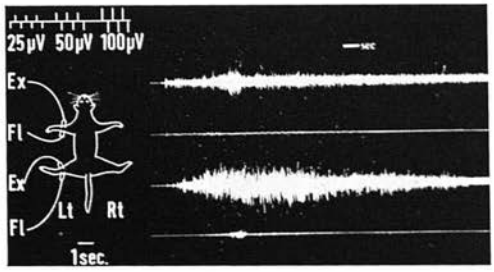


Fig. 16. Decerebrate rigidity in a cat. EMG of the extensors (*Ex*) and flexors (*Fl*) of the fore and hind limbs. Extensor decerebrate rigidity with "silent" or little activation of the flexor muscles following bilateral mesencephalic lesions

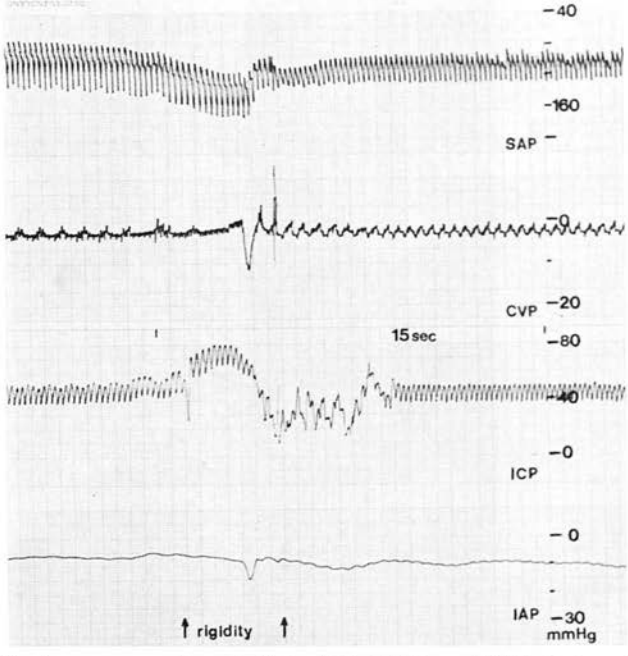


Fig. 17. Continuous recording of IAP, ICP, CVP, and SAP during decerebrate rigidity. Increase in brain elastance and ICP by inflating slowly an air-filled balloon epidurally without increase in SAP, CVP, or IAP. A mild, short-lasting spasm produced a very substantial increase in ICP while similar spasms produced no change in ICP under conditions of normal brain elastance and ICP. The SAP, CVP, and IAP were also increased

the conditions in which decerebrate rigidity is associated with or is due to haemorrhage, swelling, or concomitant acute hydrocephalus, and study the effect of rigidity upon the ICP. It is known that in

those circumstances the buffering mechanisms against the raised ICP are exhausted (Langfitt *et al.* 1966, Miller and Caribi 1972, Miller 1973, Löfgren 1973) and the brain elastance is greatly increased. As anticipated, short-lasting spasms produced a very large increase in ICP of about 35–40 mm Hg, whereas under conditions of normal intracranial elastance similar spasms produced no effect of the ICP (Fig. 17).

The above described fluctuations in ICP during decerebrate spasms in both groups A and B are presented diagramatically in Fig. 6 (5–6).

Discussion

It has been shown in these experiments that only bilateral and severe decerebrate rigidity substantially increased the ICP; this increase appeared in two distinct patterns.

In group A decerebrate animals with large lesions and decerebrate rigidity large typical intracranial plateau waves were recorded (Lundberg 1960). The only concomitant event of significance was an elevation of SAP; the CVP was insignificantly increased.

In group B animals with decerebrate rigidity and small lesions, however, intracranial plateau waves never developed and the elevation of the ICP varied directly with the increase in ITP, IAP, and CVP, and with the degree of rigidity. A close parallelism between the cerebral, venous, and respiratory pulses in time and magnitude was evident. The rise of SAP was insignificant. In other words, changes in the ICP reflected events in the venous circulation.

The explanation of two such different patterns of ICP alterations must be sought in differences in the intensity and distribution of the decerebrate rigidity and in the cardiovascular events.

Sherrington (1898), Thiele (1905), Bazet and Penfield (1925), and Ranson (1927) in the classical mesencephalic transections of cats and other animals observed great variations in the intensity and distribution of rigidity between extensor and flexor muscles as well as between fore and hind limbs despite the employment of a standard technique. The degree of rigidity was also determined not only by variations in the physiological state of the animal but also by the physical factors under which the experiments were performed and the precise details of the technique employed. Creed *et al.* in 1932 stated: "The degree of the rigidity varies from experiment to experiment probably owing to small differences in the level or details of the trauma".

The situation is further complicated in our experiments by the fact that our small and descrete lesions may have incompletely

damaged some target areas. Fulton (1947) has stressed the importance of the completeness of the lesion for the full development of decerebrate rigidity.

Monitoring of the EMG activity has been used extensively for the clinical (Hoeffer and Putman 1940, Levine *et al.* 1964, Leavitt and Beasley 1964, Levine *et al.* 1969, Jones *et al.* 1970, Feldman and Sahrmann 1971) and almost exclusively for the experimental assessment of muscle tone (Lindsley *et al.* 1949, Schreiner *et al.* 1949, Sprague *et al.* 1948, Feldman 1971). It is known that under normal physiological conditions the EMG assessment of rigidity (based on the measurement of the amplitude of muscle action potentials, and the frequency analysis of the spikes) correlates well with clinical estimation of muscle tone (Watts 1924, Seyffarth 1941, Loofbourrow 1948). Sprague *et al.* (1948) reported that a maximally contracting normal muscle discharged at up to 50 microvolts. When their one decerebrate patient was "at rest", Hoeffer and Putman (1940) recorded a constant activity of low (20–40 microvolts) voltage from all muscles; this activity was enhanced by passive movements. Lindsley *et al.* (1949), in their EMG study of spasticity following lesions of the supressor areas within the brain stem of cats, recorded a stretch-evoked discharge which had an amplitude of almost 200 microvolts. Similar findings were reported by Sprague *et al.* (1948) in the most severe grade of decerebrate rigidity.

The findings of these experiments are in agreement with these above. The constant tonic discharge which was recorded had an amplitude of 25–50 microvolts, and was of low frequency. During maximal contraction or spontaneous paroxysmal intensification of rigidity, action potentials of increased amplitude (to 170–200 microvolts) and frequency were recorded.

The severe rigidity in the two EMG's of Figs. 14 and 15 (representative of the subgroup of the two animals with normal ICP and group B with raised ICP respectively) showed no significant quantitative differences in either the amplitude of the action potentials or the frequency of the spikes. Clinically these animals showed no gross differences in the stiffness of their legs. This was taken to indicate the good correlation between the mechanical and the electrical events in the contracting muscles. Whereas in the first animal the thoracic and abdominal muscles were inactive, in the second they were vigorously contracted. EMGs were not recorded from these muscles, and it is impossible to assess their tone clinically, as in the limbs, but the ITP and IAP were increased only in the second animal. The fact that both of these pressure parameters remained unchanged in the first animal was indicative of the non-activation or of limited ac-

tivation of the respiratory extensor and powerful abdominal flexor muscles. The CVP, SAP, and ICP were unchanged in the latter case.

It thus appears that:

a) Decerebrate rigidity does not always affect the ITP and IAP (and subsequently the CVP and SAP) even if the limb rigidity is extreme and

b) the ICP is raised only if ITP and IAP are increased by the rigidity. Evidently, therefore, decerebrate rigidity will increase the ICP only if it causes elevation of the truncal cavity pressures (ITP and IAP).

These would explain the finding of a normal ICP in the presence of severe extensor decerebrate rigidity by Jennett and Plum (1972) and by Jennett and Johnston (1972).

The hypothesis that a widespread compression of the intramuscular veins of the limbs by spasm and the displacement of blood into the central veins and a subsequent rise in CVP would produce a rise in the ICP is not supported by these observations. Although the increased venous return from the limbs plays no direct role in the elevation of ICP during decerebrate spasms it may be, however, that in cases with synchronously raised ITP and IAP it exacerbates the effect of these on the ICP by increasing the volume of the central venous pool; this blood, as is argued later, is displaced into the veins of the spinal canal and cranial cavity. Conceivably the greater the volume within the capacitance veins the more is available for displacement into the craniospinal system and, therefore, the more the ICP would be raised.

Before we discuss the effect of the various factors responsible for the elevation and maintenance of the raised ICP which may act either alone or in combination during acute decerebrate rigidity it is necessary to discuss the causes of raised ICP. Theoretically any increase in the volume of cerebrospinal fluid, brain tissue or craniospinal blood could be responsible.

The rate of CSF production in the rabbit has been estimated to be 0.8 ml/hour (Welch 1963). Lundberg (1960) reported that in one patient with an obstructed aqueduct a rise in the ICP from 10 mm Hg up to 20–30 mm Hg took nearly three hours to develop. In our cases, while the increased production and reduced or absent absorption of the CSF may have played a small additive role, the rapid dynamic changes in the ICP which were observed cannot reasonably be explained as due to alterations in CSF production or absorption.

Changes in the brain tissue volume due to of water exchange are unlikely to play any major role in a sudden increase in ICP; and if

this were indeed the case one would expect a progressive elevation in ICP uninfluenced by the onset or cessation of the decerebrate spasms.

The phasic changes in the ICP were associated with similar changes in the systemic arterial and venous pressures during decerebrate rigidity. The only likely explanation, therefore, is that these changes were due to alterations in the craniospinal blood volume.

An increase in the cerebrospinal blood volume can be produced by:

a) an increase in the systemic arterial pressure,
b) decrease in cerebrovascular resistance (CVR),
c) an increase in the craniospinal venous blood volume.

Roy and Sherrington (1890) first stressed the importance of the SAP and humoral factors (such as CO_2, O_2) in the control of cerebral vascular tone and consequently the ICP. Hypertension alone induced by vasopressin (Sokoloff 1959) or by L-noradrenaline (Moyer and Morris 1954) produced no change in the cerebral blood flow and volume in man. The cerebral blood flow (CBF) and volume of normal subjects with elevated SAP and cardiac output due to muscular excercise remained unaffected (Kleinerman and Sancetta 1955, Hedlund *et al.* 1961). Similarly in the present "non-decerebrate" experiments a significant rise in the SAP, and therefore of the perfusion pressure, produced only a minor elevation in the resting level of the ICP. The CBF rate and volume, therefore, are not passive functions of the SAP as was postulated at the begining of the century (Hill 1896, Bayliss and Hill 1895/96); they are maintained within normal limits even though the SAP and perfusion pressure are changed well beyond their physiological range. This is believed to be accomplished, at least under physiological conditions, by adjustments of the cerebrovascular resistance, but the mechanism is far from clear.

Cerebrovascular resistance (ratio of cerebral perfusion pressure to CBF) is the resultant of various factors, namely the blood viscosity, extravascular (tissue) pressure, and vascular calibre as determined by the activity of vasoactive agents and neural reflex arcs. A decrease, as in anaemia (Robin and Gardener 1953), or an increase, as in polycythaemia (Nelson and Fazekas 1956), of the blood viscocity, produced a decrease or increase in CBF respectively. The extravascular pressure, namely the ICP, may be raised up to 450–500 mm H_2O without significant alteration of the CBF (Wolff 1948, Zwetnow 1958); a continuous increase of ICP to the level of the MSAP, however, leads to cessation of the cerebral circulation (Pribram 1960, Langfitt *et al.* 1969). It has been repeatedly demonstrated in both man and animal by a variety of techniques that CO_2 (Reivich 1964, Harper and Glass 1965, James *et al.* 1969), O_2 (Schmidt *et al.* 1945,

Lambertsen *et al.* 1953, McDowall 1966), and pH of CSF (Siesjo *et al.* 1968, Kjallqwist *et al.* 1969) all have a profound effect on the cerebral vasomotor tone. In fact, CO_2 is the most potent vasodilator substance known and because it is also the end product of brain metabolism some investigators have been led to the conclusion that it is the main regulator of the cerebral vascular tone (Lassen 1959, Sokoloff 1959, Michenfelder *et al.* 1969); they attributed no significant vasomotor function to the extensive perivascular autonomic nerve net in the dural, pial and intracerebral vasculature of man and animal. Support for their opinion was derived from the experimental work by Dumke and Schmidt 1943, Harmel *et al.* 1949 and Shenkin *et al.* 1951. Dumke and Schmidt showed that section of the cervical sympathetic nerves had no effect on the CBF. Their observations that administration of low oxygen or high carbon dioxyde concentrations separately produced no change in the respiration and an insignificant rise in the CBF suggest that injury to the sinus nerve had complicated their operation of sympathectomy and thus altered the true response of vessels to both neural and chemical factors. Harmel *et al.* (1949) and Shenkin *et al.* (1951) observed no changes in CBF after bilateral block of the stellate ganglion. Fluorescent histochemical studies showed that removal of the superior cervical ganglion abolished the fluorescence of the perivascular adrenergic nerves, while removal of the stellate ganglion reduced but did not abolish it.

Chorobski and Penfield (1932), Penfield (1932), and McNaughton (1938) have ascribed vasoconstrictor and dilator function to the cerebrovascular sympathetic nerves. More recent evidence also favours the existence of a genuine neural control mechanism of the cerebral vascular tree. Bridges *et al.* (1958) showed a decrease in cerebral blood volume after stimulation of the superior cervical ganglion whereas procaine blockade increased it. Administration of high CO_2 or low O_2 consequently had the same effect as procaine blockade. Stimulation or blockade of the stellate ganglion produced similar but weaker reactions. James *et al.* (1969) and Purves and James (1969), after section of the cervical sympathetic nerves, showed a 14% increase in CBF over control values; the blood gases and SAP were rigorously controlled. When the operation was performed under conditions of high pCO_2 or low pO_2 the rise in CBF was much more marked and it was no longer independent of SAP changes. This would suggest that neural vasomotor activity interacts with the other regulatory factors; the precise nature of this interaction is still obscure.

During the making of a coagulation lesion in all four animals of group A we observed a substantial increase in ICP which lasted for

the duration of the radiofrequency current. During this period there was alteration neither of the arterial pressure, elevation of which could account for the rise in ICP, nor of the respiration. The arterial blood gases were normal and the EMG showed the electrical activity of a relaxed subject. This increase in ICP would thus appear to be due to a primary temporary vasodilatation, an observation which offers supportive evidence of a primary neurogenic control of the cerebrovascular homeostasis. The mechanism of this vasodilatation is not clear. Speculatively, it may be due either directly to activation of the parasympathetic vasodilator center or indirectly to inhibition of a sympathetic vasoconstrictor reflex arc.

In the same four animals the elevation in SAP which developed immediately with the decerebrate rigidity was the dominant feature together with the observed increase in ICP. This systemic arterial hypertension may be due to a central effect of the midbrain lesion mediated by sympathetic overactivity. The major vasomotor centers are located within the medulla but there is also a separate corticospinal pathway by which vasomotor tone is regulated; vasomotor neurons have been demonstrated within the mesencephalic tectum and tegmentum, activation of which can elicit both pressor and depressor responses (Eliason *et al.* 1954, Lindgren 1955, Lindgren *et al.* 1956). The rise in SAP, however, did not develop immediately after the completion of the lesion, except in one animal, but simultaneously with the development of decerebrate rigidity. This would suggest that the rise in SAP was secondary to muscular hyperactivity and would explain why SAP returned to a normal level at the end of the spasms.

We have previously discussed why a rise in the SAP alone does not raise the CBF and ICP. It could be argued that a simultaneous increase in SAP, ITP, IAP, and CVP might produce such an elevation; that this is not the case was demonstrated in the "non-decerebrate" animals, in whom artificial elevation of all these parameters to a level similar to that observed during rigidity produced less increase and a different contour of the ICP wave tracing.

Primary cerebral vasodilatation was considered to be responsible for the rapid and generalized brain swelling which resulted from lesions in the midbrain (Le Beau and Bonvallet 1938) and in the floor of the fourth ventricle (Obrador and Pi-Sunër 1943).

While acute swelling could explain the rapid and large augmentation in the ICP of these animals this should have been maintained independently of the muscle spasms. The observed increase was limited to the duration of the spasms and the concomitant arterial hypertension.

Located within the mesencephalic tegmentum are not only pathways controlling the vasomotor tone but also the reticular formation, lesions of which produce decerebrate rigidity (Denny-Brown 1962, Gilman 1965, Mettler 1978). The lesions in the present experiments located in these areas produced decerebrate rigidity and imbalance of the cerebral vasomotor tone. The resultant vasoconstrictor paresis allowed the substantial increase in SAP to drive arterial blood freely through the cerebral vessels thus increasing the cerebrovascular volume and consequently the ICP. The associated minor increase in CVP and therefore of the craniospinal venous volume would play a secondary role in the elevation of ICP. Conversely, the increase in the craniospinal venous blood volume, which results from the rise in systemic venous pressure becomes of major importance in the augmentation of the ICP in animals of group B, while the role of the SAP and of the vasoconstrictor tone of the cerebral precapillaries is a minor additive one. None of the animals with decerebrate rigidity in group B ever developed intracranial plateau waves as did those in group A and the maximum value of their ICP was much less. A more striking feature, however, was the development of very substantial phasic changes rather than the absolute level.

Cerebrospinal fluid pulsations are considered to reflect changes in the arterial and venous circulation, the latter being transmitted by respiratory movements. Most investigators believe that they originate from the arterial pulsation and are modified by respiration (Antoni 1946, Bering 1955, Dunbar *et al.* 1966). Recently, however, it was demonstrated that CSF pulsations follow the contour of venous rather than the arterial pulsation and it was suggested, therefore, that the brain pulsations may also follow the venous rather than the arterial pattern (Hamit *et al.* 1965). It was further postulated that the static CSF pressure is maintained by the arterial pressure while the phasic changes are effected mainly through the venous channels.

The marked phasic changes in the cerebral pulse oscillations which were observed in group B were synchronous with those of the respiratory and venous ones. Simultaneously the CVP and ITP or IAP were greatly elevated while the SAP remained virtually unaltered. The height of the cerebral pulse varied in parallel with that of the venous pulse and respiratory excursions. This strongly suggests that cerebral pulsations and pressure reflect transmission of venous pressure and pulsations rather than arterial ones.

The relationship between the systemic venous pressure changes and those of the CSFP is well established and it is known that the latter is modified to some extent by changes in the venous pressure

(Becht 1920, Weed and Flexner 1933, Bedford 1935, Ryder *et al.* 1952). The cranial venous blood can be "backed up" by raising the pressure in the superior vena cava, and this increases the ICP. This elevation, however, is temporary as has been shown in these experiments involving occlusion of the jugular veins. Similarly Myerson and Loman (1932) and Bedford (1935) produced a transient increase in ICP by ligation of both internal jugular veins, the normal level being speedily restored. This restoration was attributed to an "escape mechanism" namely the collateral drainage of the cerebral venous sinuses into the spinal epi- and subdural veins.

Brescht (1829) and Batson (1940, 1942, 1944) have illustrated the communication of the internal spinal veins with the venae cavae through the azygos and hemiazygos veins and petrosal sinuses; they pointed out that, as this venous system is valveless, blood can flow freely in either direction. An increase, therefore, in ITP and IAP (as during severe decerebrate rigidity), by preventing cerebral venous blood into the latter, increases the craniospinal volume and results in a significant rise in the ICP. We point out that a maximal increase only occurs if both ITP and IAP are elevated.

Various investigators have stressed the importance of either the increase in ITP due to coughing or in the IAP due to abdominal compression in the genesis of raised ICP. Nobody, however, has measured either the ITP or IAP and correlated their increases directly with CSFP changes. Except for Hamilton *et al.* (1936). They studied the effect of increased ITP on the SAP and on the CSFP in normal and tuberculous subjects with artificial pneumothorax. There was a rise of about 50 mm Hg during straining or coughing. This rise increased the CSFP and the SAP; they paid much attention to the role which the raised ITP played in elevating the SAP, and postulated that the augmentation in SAP was due to the raised CVP, although they did not measure it.

Our findings are at variance with these.

a) A high increase in ITP produced less rise in ICP. It was also shown that IAP was slightly the more potent factor in raising and maintaining the elevated ICP. When these factors were combined the effect was not linear but exponential. In the latter case the level of rise in ICP was found similar to that of the above workers.

b) An "isolated" increase of any magnitude in either the ITP or IAP cannot be produced because of the mobility and elasticity of the diaphragm which is bound to transmit applied pressures from one cavity to the other. An isolated increase in ITP produced a very profound reduction in SAP which was sustained as long as the ITP

was kept elevated. Increase of the IAP alone or in combination with the ITP produced a small increase in SAP. The SAP went up only when the IAP was elevated, despite the fact that the CVP was increased by both procedures.

Straining or coughing, therefore, raised not only the ITP but also the IAP; this would explain the findings of a high elevation in CSFP and of the SAP by the above workers.

From the experiment with the artificially raised ICP it is evident that in clinical decerebrate rigidity the intracranial elastance is an additional factor which determines the level of rise in conjunction with all the other factors discussed (the degree of rigidity, the level of elevation of ITP and IAP, and systemic hypertension if there is impaired control of cerebrovascular tone. This is clinically investigated.

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