Some blood pressure studies in normal horses and in horses affected with chronic obstructive pulmonary disease.

by

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This thesis has been composed by me and describes my own work. It has not been submitted in any form to any other University.

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CONTENTS

SECTION I.

Page

Page

SECTION II.

MEASUREMENTS OF RIGHT HEART BLOOD PRESSURES IN HORSES

Page

Page

PILOT EXPERIMENT NO. 2.

Page

Page

SUMMARY

The literature indicated that the main obstacle to indirect peripheral blood pressure measurements (sphygmomanometry) in horses, is the lack of a large superficial artery capable of being temporarily occluded. Consequently, the standard human sphygmomanometric techniques employing palpatory and auscultatory methods are unsatisfactory in horses. Some other sphygmomanometric techniques including the xylol bead modified palpatory, the photoelectric and the modified auscultatory methods were assessed by trials on horses. The latter method was shown to be the only potentially useful technique.

Blood pressure measurements using this technique showed that the blood pressure of resting horses shows continuous short term cyclic variations, an observation which was supported by direct peripheral blood pressure measurements. Peripheral blood pressure was shown to significantly increase in horses during excitement and also following submaximal exercise. During longer term studies, many technical difficulties were encountered with the modified auscultatory technique and it was concluded that it would be unlikely to become acceptable for general clinical use.

The literature concerning right heart blood pressure measurements in horses indicated that very little information was available concerning the right heart blood pressure alterations that occur in chronic pulmonary disease. Angiographic studies indicated that the use of a single hydrostatic

baseline for all right heart blood pressure measurements, as is currently used by all authors, causes an underestimation of right ventricular pressure. A separate hydrostatic baseline was therefore established for right ventricular blood pressure measurements.

It was shown that horses clinically affected with chronic obstructive pulmonary disease (COPD), had pulmonary and systolic right ventricular hypertension and that this hypertension became reversed during remission stages of the disease. Further studies showed that a close relationship existed between carotid arterial hypoxaemia and pulmonary hypertension in COPD affected horses.

This relationship between arterial hypoxaemia and pulmonary hypertension in COPD was substantiated by inducing partial remission of pulmonary hypertension in clinically affected horses, by oxygen administration. In contrast, pulmonary hypertension was induced by rendering normal horses temporarily hypoxaemic, by administration of nitrogen enriched air.

Marked pulmonary hypertension was also induced during experimental hypercapnia or acidosis production. Bicarbonate, atropine or furosemide administered intravenously had no significant short term effects on pulmonary arterial pressure.

No clinical or cardiac catheterisation evidence of right heart failure was observed in any COPD affected horses. These observations were substantiated by the relative in-

frequency of right ventricular hypertrophy that was observed on post mortem examinations of horses affected with chronic pulmonary disease.

ABBREVIATIONS

PBP	peripheral blood pressure
CPK	createnine phosphokinase
GOT	glutamine oxaloacetic transaminase
RA	right atrium
RAP	right atrial pressure
RV	right ventricle
RVP	right ventricular pressure
PA	pulmonary artery
PAP	pulmonary arterial pressure
PAW	pulmonary arterial wedge
LV	left ventricle
P_aO_2	arterial oxygen partial pressure
P_aCO_2	" carbon dioxide " "
Ppl	intrapleural pressure
MAX Δ Ppl	maximum intrapleural pressure change
MAX Ppl Exp.	maximum intrapleural pressure during expiration
MIN Ppl Insp.	minimum intrapleural pressure during inspiration
Std. Bic.	standard bicarbonate
B.E.	base excess
H.W.	heart weight
B.W.	body weight
COPD	chronic obstructive pulmonary disease (horses)
COLD	chronic obstructive lung disease (humans)

SECTION I

PERIPHERAL BLOOD PRESSURE MEASUREMENTS.

INDIRECT MEASUREMENT OF PERIPHERAL BLOOD PRESSURE

GENERAL INTRODUCTION

Indirect measurement of peripheral blood pressure (PBP) or sphygmomanometry has been a standard part of clinical examination in man since the development of the auscultatory sphygmomanometric technique by Korotkoff (1905). It is used to assess many disease states and its widespread use has allowed the recognition of new diseases that are directly related to abnormalities of PBP levels. It is very likely that sphygmomanometry would be of great value in veterinary practice if a suitable technique was available. Although equine sphygmomanometry has not been extensively used to date it has proved useful to monitor laminitis, (Garner et al., 1975) anaesthesia, Garner (1975 pers. coms.) and surgical shock, Gay et al., (1977A).

The limited use of equine sphygmomanometry has not been due to lack of interest, as the literature shows that numerous attempts have been made to measure this parameter using a wide and often ingenious variety of techniques, equipment and sphygmomanometric sites. Indeed it appears that much greater efforts have been made to develop a suitable equine sphygmomanometric technique than were made in human medicine before the reliable auscultatory method was discovered. In fact the very first PBP measurement (Hales 1733), PBP recordings (Ludwig 1847) and intracardiac blood pressure measurements (Chaveau and Marey 1861) were performed on horses.

The search for a practical equine sphygmomanometric

technique still continues and in the last decade reports of some potentially useful techniques have been published.
In this work the available sphygmomanometric methods and their applications to equine work to date will be reviewed and the more promising of these techniques will be assessed by trials. Providing one or more of these techniques proves to be reliable in the horse, PBP studies in horses using one of the techniques will be undertaken.

CHAPTER I.

REVIEW OF THE LITERATURE.

1. DEVELOPMENT OF TECHNIQUES FOR THE MEASUREMENT OF PERIPHERAL BLOOD PRESSURE (PBP).

Although the measurement of peripheral blood pressure (PBP) in human clinical medicine only rose to importance in the late nineteenth century, for a long time prior to this physicians had unknowingly utilised PBP observations. Thousands of years B.C. the Egyptians recognised the importance of pulse palpation in human medicine and were well practiced at it (Sigerist 1951). A Chinese physician, Choven Yoo Y, in the year 200 BC is said to have related PBP changes to a specific disease, noting "A hard pulse difficult to compress with kidney disease" (Volhard 1949). The Greeks associated heart beats with the pulsations in a ligated blood vessel but did not realise that the heart caused these pulsations. Surprisingly the Greeks and Romans, despite their extensive water distribution systems had no concept of pressure (Geddes 1970).

Nearly 1500 years later the next recorded development in circulatory knowledge came from William Harvey of London who in 1628 stated "The blood by the pulsations of the ventricles is forcibly ejected to all parts of the body, therein steals into the veins and porosities of the flesh", but he did not explain exactly the forces involved (Harvey, 1628).

The first person actually to measure the pressure imparted to the blood by the heart, was the Rev. Stephen Hales, an English clergyman, in 1731. He directly cannulated the femoral artery of a cast unanaesthetised mare with a brass pipe which was connected to a vertical glass tube 9 feet 3 inches high.

He observed the blood slowly climb stepwise up this glass tube and noted pulsations of 2-4 inches in the blood column, synchronous with the horse's heart beat. These small pulsations were the pulse pressure which was much damped due to his crude PBP measuring system (Hales 1733). Hales also measured the height of the blood column from the estimated level of the left ventricle, thus standardising the measurement procedure by using a proper hydrostatic baseline. Unfortunately many of his successors even in this century failed to use a satisfactory hydrostatic baseline. Hales recorded a mean PBP in this horse equivalent to 180 mm Hg. This mean equine BP level is above currently accepted normal levels and is probably due to the painful measurement procedure, which elevated the horse's heart rate from 36 per minute before the experiment to 55-100 per minute during the experiment.

For approximately the next 120 years all the major developments in PBP measurement concerned direct methods, i.e. where the PBP was measured by directly opening into the artery. Poiseuille (1828) made the first technical improvement by using a U tube manometer containing mercury to directly measure PBP in a dog. The mercury U tube had the advantage over a blood filled tube of reducing the height of the column by approximately 13 fold. Poiseuille is also credited with being the first person to use an anticoagulant to prevent blood clotting in a vascular catheterisation system, using a "sub-carbonate of soda solution" in the tube connecting the arterial cannula to the mercury manometer. Poiseuille also introduced the currently used units of measuring PBP i.e.

mm Hg.

From this time onwards the Hg manometer became very popular for a wide variety of static pressure measurements and is still widely used because of its advantages which include, self calibration, ease of construction and because its internal diameter makes no difference to its accuracy (Geddes 1970). Liquid manometers have a low natural frequency because of their inertia and cannot respond uniformly to all pressure input frequencies, which in the case of PBP pulse waves can be several hundred cycles/second. They are therefore unsuitable for measuring systolic and diastolic PBP values, as they tend to damp out the rapid pressure fluctuations (Masters 1952, Shirer 1962). However this disadvantage of the Hg manometer can be utilised to record mean PBP by damping the system further through adding a constriction to the system.

Magendie (1850) improved the U tube manometer by introducing into it a wide Hg reservoir as one limb of the U tube and using a thin glass tube arising from the base of this reservoir as the other limb. The top of the wide reservoir was connected to the animal's artery. This system increased the sensitivity of the Hg manometer by increasing the surface area over which the PBP acted, and also by decreasing the inertia of the responding mercury column.

Carl Ludwig developed the first graphical recorder used in any physiological study by putting an ivory float with a pen attached to it in the free limb of a Hg U tube. This

pen recorded the detected pressure values on a smoked drum which was rotated by clockwork. He performed this first graphical recording while measuring a horse's PBP. However, Ludwig realised that his recorded PBP values were not true diastolic or systolic levels due to the limitations of his equipment (Ludwig 1847).

All these were direct methods used on experimental animals and occasionally on humans during limb amputations, but due to their obvious disadvantage of causing suffering to the subject, were seldom used by clinicians.

Because of the disadvantages of direct PBP measuring methods, investigators began to seek ways to measure PBP indirectly i.e. without arterio-puncture. By palpating a superficial artery, the pressure within can be estimated by feeling the force needed to compress it. This digital technique continued as the main clinical PBP measurement method in the nineteenth century until reliable indirect PBP measurement devices became available.

The lack of objectivity of the palpatory method was realised even when it was being commonly used in human medicine (Cushing 1903). Brunton (1909) stated that considerable error in pressure value interpretation could occur even with experienced clinicians. Another disadvantage was that no objective information about the PBP level could be conveyed from one observer to another. Janeway (1901) also drew attention to "Pascal's Law" i.e. that the force necessary to compress an artery is proportional not only to the blood pressure but also to the diameter of the artery. Therefore,

the pressure always feels higher in a larger artery and the variation in size of arteries in different individuals made it possible for only a rough estimation of PBP within it to be made by direct palpation. In addition palpatory assessment can at best give only a systolic value, but diastolic pressure is much closer to mean PBP and is a more valuable clinical measurement than systolic PBP (Geddes 1970). Regretfully this is still the standard method of PBP measurement in veterinary medicine where even larger variations in arterial sizes occur within and between species.

Herrison (1834) is credited with attempting to develop the first instrument to indirectly measure PBP. He used a Hg filled tube which had a membrane at its base which was placed over an artery and the arterial pulse induced oscillations in the Hg column. No oscillatory criteria for pressure measurements were given by Herrison and it is unlikely that this instrument was accurate.

Vierdort (1855), a German physiologist, introduced the basic principle of sphygmomanometry, i.e. the measurement of the counter pressure necessary to obliterate the pulsations of a peripheral artery, as a measure of the PBP level in that artery. He designed a cumbersome mechanical instrument called a "Sphymograph" in which weights were directly added to a pulse recorder which was sited over the radial artery. The weight required to occlude the radial pulse was taken as the systolic pressure level.

Marey (1860) developed a smaller and more accurate sphygmograph which was strapped to the wrist of the subject whose PBP was being measured. For the next 35 years, instruments based upon Vierdort's principle were widely used by physiologists in Europe and America. Many of the devices using this principle were grossly inaccurate, some giving results of 2-10 times the real value and all these sphygmographs were used only briefly in clinical medicine due to their shortcomings (Masters et al. 1952).

Marey (1878), introduced a sphygmomanometer which applied counter pressure to the whole forearm. The arm was immersed in a water-filled container with a window. A reservoir attached to this container could be raised thus increasing the pressure in the container and eventually causing the arm to blanch and this counter-pressure level was taken as the systolic PBP (or systole). Marey also observed that pulse waves were transmitted from the reservoir to the Hg manometer attached to the container and caused oscillations in it. These induced oscillations in the Hg manometer were noticed to change in magnitude as the pressure in the container changed and he claimed that the point at which these oscillations reached maximum coincided with systole. The use of the point of maximum oscillations as the systolic criterion was disputed at that time by Janeway (1901). A major disadvantage with this method was the difficulty in sealing the arm water-tight into the sphygmomanometer (Geddes 1970). Marey is also credited with making the first attempt to indirectly measure diastolic PBP by use of his oscillatory method, but he did not give a clear

oscillometric criterion for the diastolic end point (diastole).

A sphygmomanometer similar to Marey's in which just four fingers were inserted into a water filled container was later designed by Mosso (1895). The above instruments of Marey and his followers were impractical and cumbersome. Their use was shortlived and mainly restricted to laboratories (Geddes et al. 1966).

The first practical sphygmomanometer for use in man was developed by Von Basch (1876), a Viennese physician who is regarded as "The father of clinical sphygmomanometry". He used a water filled capsule called a pelote connected to a Hg U tube manometer which was placed over to occlude a superficial bone backed artery e.g. radial or temporal artery, while the distal pulse in the artery was palpated. The pressure in the pelote was increased until the distal pulse disappeared and this occlusive pressure was taken as being equal to systolic PBP. This method gave satisfactory values and was used widely but the equipment was cumbersome and there was also some difficulty in applying pressure to the artery because of the small size of the pelote (Janeway 1901). Potain improved the Von Basch instrument by using the less cumbersome aneroid manometer to measure the counter pressure (Potain 1902).

A very significant advance in the science of sphygmomanometry was made by Riva Rocci (1896) in Italy and independently a year later in Britain by Hill and Barnard with the introduction of an inflatable circular rubber cuff to compress the limb and consequently the artery from which the PBP was

being measured. The cuff was attached to a manometer and to a hand bulb which was used for cuff inflation. This very simple instrument had the advantage over its many and often complicated predecessors of evenly applying the counter pressure to the artery (Hill and Barnard 1897). These authors also observed that oscillations were induced in the cuff's manometer during cuff deflation and changes in amplitude of these oscillations were used as systolic and diastolic endpoints. However no definitive systolic or diastolic endpoints were established for this oscillatory method of sphygmomanometry. The Riva Rocci cuff quickly became the standard method of applying counterpressure with all methods of sphygmomanometry and has remained so.

An improvement in the oscillatory method of sphygmomanometry was made by Erlanger (1904) who developed an instrument which both amplified and recorded the oscillations which were induced in the aneroid manometer attached to the Riva Rocci cuff during its deflation and so made the changes in amplitude of these oscillations easier to detect. A further improvement was made by Pachon (1909) who developed an instrument with two aneroid gauges attached to the arm cuff. One of these gauges acted as a manometer while the other, a more sensitive one, was used for oscillation detection. Although oscillometric sphygmomanometry was gradually superceded in the 20th century by the auscultatory method, it continued to be used by some anaesthetists in situations where auscultatory method was ineffective e.g. in hypotensive surgical patients

suffering from shock (Barry 1950).

Barry described four phases of oscillation which can be detected during cuff deflation.

1. Supra-systolic oscillations
2. Oscillations of increasing amplitude
3. " " maximum "
4. " " decreasing "

The supra-systolic oscillations are due to pulsations of the artery against the proximal border of the inflated cuff and the use of a double cuff method eliminated these potentially confusing oscillations. The oscillations of increasing amplitude are due to the initial passage of pulse waves under the occlusive cuff as its pressure falls below systole and with the use of a double cuff, this point is unambigous and corresponds with systole (Ellis 1973).

The point of oscillations of maximum amplitude and the oscillations of decreasing amplitude have been considered by different authors as the diastolic end-point (or diastole) (Geddes 1970, Barry 1950). Neither of these end-points has been confirmed by direct PBP measurements, thus no satisfactory criterion for diastole exists with the oscillometric method of sphygmomanometry (Collins and Magora 1963, Geddes 1970).

In the early twentieth century there was an increasing need for a reliable and simple clinical PBP measuring method in human medicine. This need was filled by Korotkoff (1905) a Russian physician who developed the auscultatory method of sphygmomanometry. Korotkoff, while compressing a forearm

with a Riva Rocci cuff, observed that a completely open or completely occluded brachial artery produced no sounds, but that when the cuff pressure was raised above the expected arterial systolic pressure and then decreased slowly, a sequence of sounds was produced from the artery, which could be auscultated by a stethescope over the artery distal to the cuff. Korotkoff described four phases of sound production during cuff deflation.

First phase - Short tones appear (his systolic criterion).

Second phase - Murmurs appear.

Third phase - Sounds appear.

Fourth phase - Sounds disappear (his diastolic criterion).

He stated that his clinical experience had supported the validity of his method. This breakthrough was not widely accepted as few would believe that such a simple method would give reliable values for both systolic and diastolic PBP after the limited success of so many complicated methods. The auscultatory method then lacked a solid theoretical basis and Korotkoff admitted this (Korotkoff 1905). Despite numerous studies by both physicists and biologists into the genesis and nature of Korotkoff sounds, including those by Korns (1926) Chungcharoen (1964), Tavel et al. (1969) and Ur and Gordon (1970), this method still lacks a definite theoretical basis but this makes it no less useful a technique for, like so many biological phenomena which defy accurate description, it exhibits a high degree of repeatability and dependability (Geddes 1970).

The auscultatory method of sphygmomanometry continued to have many critics. The findings of Cook and Taussig (1917) harmed its reputation when they described a phenomenon known as the "Auscultatory Gap". This phenomenon occasionally occurs during cuff deflation, when the Korotkoff sounds completely disappear temporarily in the third phase, but on lowering the cuff pressure further, the normal sequence of sounds of the 3rd phase are again heard. This auscultatory gap could be mistaken for the fourth phase i.e. the normal cessation of sounds and so erroneously high diastolic PBP values could be obtained unless observers were aware of this phenomenon and continued to deflate the cuff and await the return of the normal sequence of sounds.

Warfield (1912) was the first to examine independently the accuracy of the auscultatory method, by simultaneous direct and indirect B.P. measurement on the opposite femoral arteries of a dog. He concluded that the point of muffling of sounds i.e. a new phase he described which occurred between Korotkoff's 3rd and 4th phases was the proper diastolic criterion rather than the cessation of sounds i.e. the 4th phase as was advocated by Korotkoff.

Later many workers including Bonsdorf (1932) and Ragan and Bordley (1941) also verified the accuracy of the auscultatory method when they compared the auscultatory method results favourably with rapidly responding direct PBP measuring methods in human volunteers.

The controversy as to whether the disappearance or the muffling of the Korotkoff sounds coincided with diastole con-

tinued for many years with various groups of workers finding opposing results. An expert committee of the American Heart Association in 1967 stated that muffling of the Korotkoff sounds was the more accurate criterion for diastolic PBP (American Heart Association 1967), thus reversing the findings of an earlier committee (American Heart Association 1951).

A wide range of automatic and semi-automatic indirect PBP measurement devices which utilised Korotkoff sound recordings (i.e. modified auscultatory methods) were developed from 1940 to 1960. These were primarily developed for home monitoring of PBP by hypertensive individuals, who were unable to measure their own PBP by the standard auscultatory method, such as the instrument developed by Gilson et al. (1941). More sophisticated instruments of this type were later developed for continuous indirect PBP monitoring of patients in intensive care units (Currens et al. 1957). These instruments automatically inflated and deflated the occlusive cuff and a microphone distal to or beneath the occlusive cuff recorded the Korotkoff sounds. They were programmed to give a systolic PBP reading at the onset of the Korotkoff sound recording and a diastolic PBP reading at the disappearance, or in some later instruments at the muffling, of the recorded Korotkoff sounds.

The accuracy of most of these PBP recorders was questionable and those few that were critically examined were shown to be inaccurate (Anon 1971). The inaccuracies may have

been due in part to their sound recording and amplifying equipment which was often designed without any regard to the frequency spectrum of the Korotkoff sounds. Geddes et al. (1959) noted that the complexity of equipment required to detect, amplify and record these low intensity sounds predisposed to technical errors.

The placing of the microphone beneath the occlusive cuff as described by Currens et al. (1957) helped to produce better Korotkoff sound recordings with less background interference. The use of a piezocrystal as a microphone within the occlusive cuff itself was shown by Geddes et al. (1959) to be an even more effective method of recording Korotkoff sounds. Most crystals exhibit the piezoelectric effect i.e. develop electrical potential along certain axis in response to mechanical deformation and therefore are classified as piezo-crystals. These piezocrystals have had a two-fold use in sphygmomanometry, being used to detect Korotkoff sounds at a distance from the artery or applied firmly above the artery for pulse detection (Geddes and Baker 1968).

Currens et al. (1957) also used their automatic sphygmomanometric instrument experimentally on dogs and found that it compared favourably with direct methods. They did not state which diastolic criterion they used with the recorded sounds.

A record of Korotkoff sounds from a human given in their paper is clear but their published "typical record" of canine Korotkoff sounds is a very unsatisfactory recording.

Korotkoff sounds had previously been recorded from man

by many earlier workers including Fantus (1917) using a "signal magnet" and by Korns (1926) who made a detailed analysis of Korotkoff sounds in man.

The recording and amplification of Korotkoff sounds does not appear to have been used in man in situations where the standard auscultatory method has failed. This modified auscultatory technique was used for such reasons on horses by authors including Dear (1968) and Ellis (1973), Dear placing the piezocrystal beneath the occlusive cuff, and Ellis placing the piezocrystal within the cuff sleeve.

A further method for detecting pulse return is the measurement of changes in the optical density of tissues distal to the occlusive cuff. One such method utilising a photoconductive cell was described by Robinson and Eastwood (1959) for use in infants and in hypotensive subjects where the auscultatory method was unsatisfactory. Weinman et al. (1960) also described a similar instrument, particularly for use in small experimental animals like the rat. These instruments utilise a small photoconductive cell and a light source which are fitted on the opposite sides of a hairless small extremity e.g. a human nailbed or a laboratory animal's shaved tail or leg. Modern photoconductive cells e.g. cadmium selenide cell are very sensitive to the red part of the light spectrum and so these cells are ideal for studying peripheral circulatory changes (Weinman et al. 1960). The signals from the photo-conductive cell, caused by the passage of light through the tissues, are amplified and recorded

simultaneously with the occlusive cuff pressure.

When the occluding cuff pressure remains above systolic PBP, the optical density of the extremity remains steady, because of the absence of blood flow. On dropping the occlusive pressure to just below systolic PBP level a small amount of blood flow occurs at the peak of systole and this flow causes some small fluctuations in the optical density of the distal tissues. As the cuff pressure decreases further, pulsatile blood flow occurs in the occluded limb for a greater part of the pulse until eventually the cuff pressure reaches diastole, when the blood flow is no longer disrupted for any part of the pulse cycle and so the blood flow and consequently the tissue optical density fluctuations are maximal. The recorded occlusive pressure at which the optical density pulsations begin is taken as the systolic level and where these pulsations first reach maximum levels is taken as the diastolic level of blood pressure.

With this instrument it is also possible to record the shape of the peripheral pulse wave and to quantitatively study blood flow in the peripheral circulation, as the amount of light traversing the finger is inversely proportional to the amount of blood it contains (Weinman et al. 1960). These authors used this method in rats and a cat and concluded that it was a reliable method for measuring PBP in animals.

A method utilising ultrasound to measure PBP was described by Ware (1965) and Ware et al. (1966). This method was designated as ultrasound kinetoarteriography or doppler ultrasonic sphygmomanometry and was designed particularly

for PBP measurement during military air transportation by critically ill patients where a combination of hypotensive shock and high environmental noise made the standard auscultatory method ineffective. The system utilises two piezocrystals within an occlusive cuff, one producing ultrasounds and the second detecting the ultrasounds which are reflected back by the tissues of the limb within the cuff, including the artery. Stationery structures reflect ultrasounds back without altering their frequencies, whereas moving structures cause frequency changes in the reflected sounds by the Doppler effect (Stegall et al. 1968).

When the occlusive cuff pressure is decreased to systolic level blood pressure begins to cause movement of the compressed arterial wall. The beginning of arterial wall movement is taken as the systolic end-point and the cessation of wall movement, i.e. when the vessel is open throughout the pulse cycle, is taken as the diastolic end-point (Stegall et al. 1968). The relatively small motion of an uncompressed arterial wall does not produce a detectable signal with this apparatus (Stegall et al. 1968).

In normotensive subjects this method is slightly more accurate than the auscultatory method but occasionally small low frequency signals can be detected while the cuff pressure is well above systolic levels and these could lead to erroneously high systolic estimations (Stegall et al. 1968). A phenomenom similar to the auscultatory gap has also been

described with this method by McCutcheon and Rushmer (1967). Another disadvantage is the expense and complexity of the equipment. Stegall et al. (1968) concluded that the use of this method in man was justified only where the standard auscultatory method was unsuccessful.

Physicians have long observed that the standard auscultatory and palpatory sphygmomanometric techniques are often ineffective in infants because of the weakness of even the normal neonatal pulse, consequently new techniques including the use of sensitive pulse detectors i.e. modified palpatory methods were developed to overcome this problem. One such instrument utilising an electrical capacitance movement detector was developed by Brecht and Boucke (1952) and this instrument was used for equine sphygmomanometry by Kunzle (1957) and Grauwiler et al. (1958). Another such modified pulse detector utilising a piezocrystal was developed by Geddes and Hoff (1960). This instrument utilised movement of the piezocrystal induced by arterial pulsations.

A simpler modified palpatory method was developed by Ashworth et al. (1959). Their method utilised two cuffs, one which was used for pulse occlusion and the second for pulse detection. This second cuff was attached by narrow bore plastic tubing to a glass capillary tube containing drops of xylol. Arterial pulsations detected by the pulse detection cuff were transmitted to the capillary tube. In this minute air space even very small transmitted pulsation caused air displacement which resulted in rhythmic visible movements of the xylol beads. The beginning of the xylol

bead movements was used as the criterion for systole. As with all palpatory methods, diastolic levels could not be measured by this method.

CONCLUSIONS

Although many of the initial developments in the measurement of peripheral blood pressure by direct methods were made on domestic animals, all indirect measurement techniques were developed primarily for use in man where this comparatively new science of sphygmomanometry is now firmly established as being one of the most important aspects of a clinical examination.

After the initial use of many ineffective and cumbersome techniques, two sphygmomanometric techniques are currently widely used. These are the palpatory method which can only give a systolic value and the more widely used auscultatory technique, which can give in addition the potentially more useful diastolic PBP value.

Since the establishment of the two standard techniques, there has been little need in human medicine to seek new sphygmomanometric methods except for special situations where the standard techniques fail. Minor sphygmomanometric techniques developed for these situations include the xylol pulse indicator developed for paediatric use and the doppler ultrasonic technique developed for patients being transported by air.

2. THE USE OF SPHYGMOMANOMETRY IN THE HORSE

INTRODUCTION

More than 70 authors utilising a wide variety of techniques, equipment and sites have attempted sphygmomanometry in the horse. A list giving some brief details of the more important of these studies is given in Table I:1. This subject has previously been reviewed by Gall (1967) and Ellis (1973).

The aim of this present review is to assess the various sphygmomanometric techniques, equipment and measuring sites which have been previously used in the horse, and to select from the results of those previous studies, some of the more useful techniques and sites for use in the envisaged sphygmomanometric experiments.

As each sphygmomanometric site used in horses to date has been shown to have its own specific difficulties (Ellis, 1973), it was decided to review the literature on equine sphygmomanometric techniques and equipment in sections relating to the sites at which these techniques and equipment have been used.

All current sphygmomanometric techniques utilise the Riva Rocci occlusive cuff, but these cuffs can vary in width, length and shape. The literature on occlusive cuffs is reviewed separately at the end of this section.

EXTERNAL MAXILLARY ARTERY

The external maxillary artery was used by Gotze (1916) as a sphygmomanometric site in the horse. He found this artery impractical for PBP measurement because of head move-

TABLE 1:1

PREVIOUS INDIRECT ARTERIAL BLOOD PRESSURE (PBP) MEASUREMENTS IN HORSES

AUTHOR	METHOD	ARTERY	NO. OF HORSES	MEAN AND/OR RANGE OF PBP IN MM Hg	
				Systolic	Diastolic
SCHMID	Palpatory	Coccygeal	64	113(102-133)	-
GOTZE (1916)	Oscillometry	Metacarpal	89	172(155-196)	123(110-141)
" "	"	Coccygeal	100	111(95-131)	65(49- 78)
" "	Palpatory	External Maxillary	3	125	-
FONTAINE (1919)	Palpatory & Oscillometry	Coccygeal	120	85(70-98)	48(40- 58)
SCHILLING (1919)	Oscillometry	Coccygeal	130	(90-100)	(40- 58)
KIESEL (1927)	Palpatory	External Maxillary	?	?	?
HORNUNG and TORGU T (1930)	Oscillometry	Coccygeal	?	(80-105)	(40- 65)
MGLBJ (1930)	Oscillometry	Coccygeal	50	(80-100)	(40- 60)
COVINGTON and McNUTT (1931)	Palpatory & Oscillometry	Coccygeal	224	94(86-104)	(45- 68)
LAFAYE and HOLSTEIN (1931)	Oscillometry	Median	6	?	?
NEUMANN-KLEINPAUL et al (1932)	Oscillometry	Coccygeal	193	87(59-105)	45(26- 65)
LAFAYE (1932)	Oscillometry	Metacarpal	?	(150-190)	(90-120)
LAFAYE (1933)	Oscillometry	Median & Coccygeal	?	?	?
SCHWARTZ (1933)	Oscillometry	Coccygeal	189	96(59-146)	52(20- 99)
HOFMANN (1934)	Oscillometry	Coccygeal	627	96(68-133)	59(31- 91)
BELLON (1937)	Oscillometry	Coccygeal	?	(130-150)	(70- 90)
SHARABRIN (1938)	Oscillometry	Coccygeal	?	(100-120)	(35- 50)
GEHRING (1939)	Oscillometry	Coccygeal	80	102(78-122)	56(40- 80)

TABLE 1:1

PREVIOUS INDIRECT ARTERIAL BLOOD PRESSURE (PBP) MEASUREMENTS IN HORSES

AUTHOR	METHOD	ARTERY	NO. OF HORSES	MEAN AND/OR RANGE OF PBP IN MM Hg	
				Systolic	Diastolic
SCHMIDT (1946)	Auscultatory	Median	17	129(80-168)	83(40-126)
HILDEBRANDT (1950)	Oscillometry	Coccygeal	20	99	51
OTTE (1951)	Oscillometry	Coccygeal	23	?	?
HIEPE & GURTLER (1955)	Auscultatory	Exteriorized carotid Loop	1	118(110-124)	82 (72- 92)
KUNZLE (1957)	Modified Paplatory	Coccygeal	3	126	-
GRAUWILER et al (1958)	Modified Palpatory	Coccygeal	7	108(80-125)	67 (45- 90)
CHOWDHURY & BANERJEE (1960)	Auscultatory	Median	115	159(144-194)	120 (105-150)
LASKOV et al (1960)	?	Coccygeal	?	?	?
ENGLEHARDT & HAMPEL (1962)	Modified Palpatory	Coccygeal	?	?	-
FRITSCH (1965)	Oscillometry	Coccygeal	?	?	?
BAYER & RHEINLANDER (1967)	Modified Palpatory	Coccygeal	16	?	-
DEAR (1968)	Modified Auscultatory	Coccygeal	1 gen. anaesthesia	193	121
SMITH (1969)	Auscultatory	Ant. tibial	30 gen. anaesthesia	70-180	25-140
STROMBERG (1969)	Doppler	Lat. digital artery	4	144.5	?
GEDDES et al (1970)	Oscillometry	Coccygeal	3 gen. anaesthesia	?	?

TABLE 1:1

PREVIOUS INDIRECT ARTERIAL BLOOD PRESSURE (PBP) MEASUREMENTS IN HORSES

AUTHOR	METHOD	ARTERY	NO. OF HORSES	MEAN AND/OR RANGE OF PBP IN MM Hg	
				Systolic	Diastolic
GLEN (1970)	Xylol pulse indicator	Coccygeal	? (gen. anaes.)	?	?
CARRAUD (1971)	Oscillometry	Coccygeal	77	138.9 + 7.5	73.5 + 8.8
LAPRAS et al (1971)	Oscillometry	Coccygeal	77	140	75
COFFMAN et al (1972)	Doppler	Coccygeal	13	133	68
DESBROSSE (1972)	Modified Auscultatory	Coccygeal	40	130	60
GARNER et al (1972)	Doppler	Coccygeal	10	-	-
GLEN (1972)	Xylol pulse indicator	Coccygeal	20	140 corrected	-
ELLIS (1973)	Modified Auscultatory	Coccygeal	-	-	-
HAHN et al (1973)	Doppler	Coccygeal	6 anaesthetised	-	-
GARNER et al (1975)	Doppler	Coccygeal	11	121	69
JOHNSON et al (1976)	Doppler	Coccygeal	456	+ 111.8 - 13.3	+ 69.7 - 13.8
GEDDES et al (1977)	Oscillometry	Coccygeal	12 anaesthetised	-	-

ment induced by the procedure and also because of the weak pulse in this artery. Keisel (1927) also used this site but did not report any difficulties associated with its use. No further reports are recorded on the use of this artery, probably because of the difficulties reported by Gotze (1916). In addition, the position of this small mobile artery necessitates for its occlusion the use of a pelote (see page II), with its inherent inaccuracies, rather than the more accurate Riva Rocci occlusive cuff.

CAROTID ARTERY

The auscultatory method was satisfactorily used by Hiepe and Gurtler (1955) on carotid arteries which had been surgically exteriorized in skin pouches, a preparation usually described as a "carotid loop". Obviously this method would be impractical for routine measurements but these authors suggested that this technique would be useful for PBP measurements in pharmacological trials. It appears that with considerably less time and effort, carotid puncture and direct measurement would give a more accurate, complete and, in addition, graphical record for such trials.

COMMON DIGITAL ARTERY

Götze (1916), Fontaine (1919) and Hofmann (1934) attempted sphygmomanometry from the common digital artery by palpatory, oscillometric and auscultatory methods. Using rectangular occlusive cuffs placed immediately below the carpus, these authors found this site unsuitable for all three methods due to restlessness involving leg movement, induced

in the horses by the technique. In some animals the presence of bony exostoses and thickened tendons prevented proper arterial occlusion (Gotze, 1916).

MEDIAN AND DEEP MEDIAN METACARPAL ARTERY

Auscultatory Method

Placing the occlusive cuff directly proximal to the carpus, the auscultatory method was found to be successful at this site by Schmidt (1946) and Chowdhury and Banerjee (1960), but not by Ellis (1973). To reduce frictional noises, Schmidt shaved the leg at the auscultation site. Chowdhury and Banerjee flexed the leg if the animal was restless. Schmidt did not perform any verification studies by comparison with direct measurements and also his published PBP values (TableI:I) have an unacceptably wide range, which is probably due to the subjectiveness of the auscultatory method at this site (Grauwiler et al. 1958). Chowdhury and Banerjee attempted verification by comparison of their indirectly obtained results with directly measured PBP values. Unfortunately these authors used a mercury manometer for their direct measurements and this type of manometer cannot give accurate systolic or diastolic pressure values because of its inherent inertia. Their results differ greatly from those of Schmidt (1946), and also have very wide range (see Table I:I).

Ellis (1973) observed that this site was unsatisfactory for sphygmomanometry because cuff inflation was resented by the horses and frequently induced leg movement and occasional snatching of the cuffed foreleg off the ground. This caused interference in the detection of pulse return by

palpatory, auscultatory and modified auscultatory methods. Muscle movements also caused fluctuations in the occlusive cuff pressure. Even in a quiet horse, with the auscultatory site shaved, no detectable Korotkoff sounds were auscultated at this site by Ellis. In conclusion, it appears that the auscultatory method can be successfully used on the median artery in some quiet animals, but its accuracy at this site has not been established.

Palpatory Method

Chowdhury and Banerjee (1960) claimed success with the palpatory method at the median artery, but Ellis (1973) could not palpate any pulse at this site in half the horses she examined. Even in those horses with a palpable pulse she often found difficulties in constantly identifying the pulse because of limb movement.

Modified Auscultatory Method

Ellis (1973) using a piezocrystal microphone beneath the occluding cuff was unsuccessful in measuring PBP in conscious or unaesthetised horses at this site. This was because of limb movement in conscious horses causing extraneous noises and also due to environmental noises and noises induced by the handbulb valve manipulations of the observer. The latter two complications would presumably apply to measurement at any site when using this method.

ANTERIOR TIBIAL ARTERY

Using the auscultatory method, Smith (1969) has indirectly measured PBP in anaesthetised horses from the anterior tibial artery, just above the hock. Comparing his indirectly

obtained values with direct recordings in 10 horses, he found that the systolic values compared favourably, except when the horses were hypotensive, as for example when in shock, when he found the indirect method unreliable. However, his indirectly obtained diastolic values were found to differ in many instances from those obtained directly.

Apart from the inaccuracy and unreliability of the auscultatory method, it is doubtful whether this site could be employed in the conscious animal. Because of the position of the artery deep within muscles, it is very unlikely to be fully occluded by cuff pressure, and in addition cuff inflation would probably induce voluntary limb movement as it does during recordings from the forelimbs, where it makes accurate determinations impossible.

THE MIDDLE COCCYGEAL ARTERY

Most authors who have attempted to measure PBP indirectly in the horse have used the middle coccygeal artery. This small artery is a branch of the left or right sacral artery and runs relatively superficially on the ventral midline aspect of the tail (Sisson & Grossman, 1953).

The Palpatory Method

There is disagreement in the literature about the ease of direct palpation of the coccygeal arterial pulse. Fontaine (1919) and Covington and McNutt (1931) claimed to have used the palpatory method satisfactorily to measure systolic pressure in a large number of horses and these authors recorded no difficulties associated with this method and site. Schmid (1912) also found the palpatory method successful at this

site in most of the horses he examined but he reported difficulty in some animals due to tail movement. Schilling (1919) reported difficulty in palpating the coccygeal pulse, especially in the lower two thirds of the tail and Kiesel (1927) was unable to palpate a pulse in more than half of the horses he examined. Ellis (1973) was able to palpate the coccygeal pulse in only 7 out of 20 anaesthetised horses and in 9 out of 20 conscious horses. The differences in the ease of palpation of the coccygeal pulse recorded by the various authors may be due in part to differences in tactile sensitivity between these workers and also to differences in the strength of the coccygeal pulse between horses. The results indicate, however, that in horses the palpatory sphygmomanometric technique at the coccygeal artery is unreliable.

Modified Palpatory Methods

In order to overcome the unreliability of direct pulse palpation some authors have used electronic pulse detectors to detect the coccygeal pulse in horses. Using the 'Infration' pulse detector Brecht and Boucke (1952) developed for use in humans, Kunzle (1957), Grauwiler et al. (1958) and Engelhardt and Hampel (1962) measured systolic PBP in horses and Grauwiler et al. also attempted to measure diastolic pressure, using the beginning of maximal pulsations as their diastolic endpoint. However, while it is logical to assume that the beginning of maximal pulsations

occurs at diastole, this point is difficult to identify with modified palpatory methods (Geddes, 1970). Grauwiler et al. (1958) did not perform any verification studies on their diastolic values and so the accuracy of this instrument for diastolic PBP measurement remains unproven. The high cost and the complexity of the infration sphygmomanometer was noted by Grauwiler et al. (1958).

Bayer and Rheinlander (1967) developed an electronic pulse detector which they used in sphygmomanometric experiments on equine coccygeal arteries and although they claim to have successfully measured systolic pressure, they performed no verification studies on their results.

Smith (1969) attempted to measure PBP from the coccygeal artery with a variety of pulse detectors but found them unsuitable because of external motion artefacts and difficulties in placing the pulse detector immediately over the coccygeal artery.

The 'xylol pulse indicator' has been used to measure systolic PBP in anaesthetised horses by Glen (1970) and in conscious horses (Glen 1972). Glen (1970) verified his results by comparing them with directly obtained values in three anaesthetised horses and reported close agreement between the indirectly and the directly obtained systolic values. Glen claimed that this technique was consistent and accurate and he did not record any significant disadvantage associated with its use in horses. Ellis (1975) concluded from a literature survey that this simple and inexpensive apparatus was the most practical instrument for sphygmomanometry

in the horse but did not use it herself.

Using a piezocrystal pulse detector taped directly over the coccygeal artery, Ellis (1973) had limited success in measuring PBP. This was mainly due to the necessity of very exact positioning of the pulse detector over the artery and also due to artifacts caused by tail movements and even by respiratory movements.

The Auscultatory Method

The standard auscultatory method of measurement using a stethoscope has been attempted unsuccessfully from the horse's coccygeal artery by the following authors: Fontaine (1919), Schilling (1919), Covington and McNutt (1931), Schmidt (1946), Hildebrant (1950), Otte (1951) and Ellis (1973). The failure of the standard human sphygmomanometric technique appears to be due to the small size of the coccygeal artery which when compressed produces undetectable or weak Korotkoff sounds.

Modified Auscultatory Methods

Grauwiler et al. (1958) claimed to have recorded Korotkoff sounds from a horse's tail using an 'infration pulse detector', an instrument designed to detect movement rather than sounds, and which was also used by these authors as a pulse detector on the coccygeal artery. They reported difficulty in determining the diastolic endpoint in some animals because the recorded 'Korotkoff sounds' persisted throughout cuff deflation. It appears likely that these authors were not in fact recording Korotkoff sounds but were just recording arterial pulsatile movement, which would persist indefinitely on cuff deflation because with complete cuff deflation and consequently

no arterial occlusion, no Korotkoff sounds would be produced.

Using a piezocrystal microphone beneath the occlusive cuff, Dear (1968) recorded Korotkoff sounds in one anaesthetised horse. In a number of trials on this horse, he obtained a close correlation between direct and indirect systolic and diastolic PBP values. Similar modified auscultatory methods using a piezocrystal have been found satisfactory in the horse by Geddes and Moore (1968) and Desbrosse (1972) but these authors just used a single horse each in their experiments. Ellis (1973), using a piezocrystal microphone within the cuff sleeve measured PBP from the coccygeal arteries of 6 horses and found a highly significant linear relationship between 852 directly and indirectly measured paired values. Ellis mentioned that with this sphygmomanometric method, tail movement and incomplete tail muscle relaxation caused difficulties in some conscious animals and that the disappearance of the Korotkoff sounds in shocked horses made this method ineffective in some situations.

Doppler Ultrasound Method

The ultrasonic Doppler PBP measuring technique has been found to be satisfactory in the horse by Garner et al. (1972), Coffman et al. (1972), Hahn et al. (1973), Garner et al. (1975), Johnson et al. (1976), Sawazaki et al. (1976) and Gay et al. (1977A, B). Direct PBP comparisons have been performed by Hahn et al. (1973), Sawazaki et al. (1976) and Gay et al. (1977B) who have all shown this method to be accurate. Some disadvantages of this method noted by Garner et al. (1972) are very high cost and complexity of this equipment and the

necessity for accurate placing of the transducers over the coccygeal artery.

Oscillometric Method

This method has been used on the coccygeal artery of the horse by Götze (1916), Fontaine (1919), Schilling (1919), Lafaye (1932) and Fritsch (1965) who all visually judged the oscillations from a gauge. A single cuff oscillometer was used by many German workers including Hornung and Torgut (1930), Mglej (1930), Neumann-Kleinpaul et al. (1932), Schwartz (1933), Hofmann (1934) and Otte (1951). Lapras et al. (1971) used a double cuffed recording oscillometer in horses.

Although these authors have all reported that they could obtain both systolic and diastolic values by the oscillatory method, this method has fallen into general disrepute because no definite oscillometric criterion for diastole has yet been established (Geddes, 1970). In addition, the use of the single cuffed oscillometer normally used, did not even give a clear systolic value (Barry, 1950).

More recently, Geddes et al. (1970) and Geddes et al. (1977) have by direct comparison of oscillometry on equine coccygeal arteries established an oscillometric criterion for mean PBP but not for systolic and diastolic values.

OCCLUSIVE CUFF

Occlusive Cuff Width

Von Recklinghausen (1901) was the first to show that the relationship between the width of the occlusive cuff and the

size of the limb could affect the accuracy of the PBP measurement. He showed that Riva Rocci's original 5 cm wide cuff was too narrow for the average human adult arm, leading to an overestimation of PBP. With all occlusive methods of indirect PBP measurements the length of artery which is compressed is one of the more important factors in determining the accuracy of the measurement. The length of artery compressed is in turn determined by the width of the occlusive cuff (Geddes 1970). The term cuff as used here refers to the inner pneumatic cuff rather than to the outer non-distensible cover referred to as a sleeve.

In human medicine there have been many reports on the optimal relationship between cuff width and limb size including those by Ragan and Bordley (1941) and Pickering (1955).

Karvonen (1962) showed in man that whilst too narrow a cuff would cause an overestimation, too wide a cuff did not usually cause an underestimation of blood pressure. In the horse, Geddes et al. (1970) showed that a ratio of cuff width to tail circumference of approximately 0.5 gave accurate results and they used cuffs 7.5 - 12 cm wide. Glen (1970), using the 'xylol pulse indicator' on three anaesthetised horses found that a 5 cm wide cuff was too wide for the tail and caused an underestimation of systolic pressure, and he recommended that a 3.75 cm wide cuff should be used on horses' tails. Because of the very limited number of his observations which were only on systolic pressure and because of the large differences between his results and those

obtained from more comprehensive human and equine studies, the validity of his recommendation is doubtful. Garner et al. (1972) found by comparison with directly obtained values, that a 10 cm wide tail cuff gave accurate values in a wide range of horses and ponies. Ellis (1973) obtained similar findings in hundreds of observations in horses using a 13 cm wide tail cuff.

Occlusive Cuff Length

There appears to be no general agreement on optimal cuff length for use in man or in horses. An expert Committee of the American Heart Association has recommended the use of a cuff length that would half encircle the limb from which the PBP was being measured (American Heart Association, 1951), while a later Committee of this association stated that a cuff which fully encircled the limb would eliminate any risk of misapplication (American Heart Association, 1967). Geddes (1970) concluded that cuff length was not as critical for accuracy as cuff width and that a short cuff, if carefully placed over the artery, was satisfactory.

Occlusive Cuff Shape

The Riva Rocci cuff is normally rectangular in shape and the cuff shape effectively occludes arteries at most sites. However, some authors including Fontaine (1919) and Hornung and Torgut (1930) while attempting sphygmomanometry in horse using the median artery, just proximal to the carpus, found that when a rectangular cuff was inflated, it frequently slipped downwards due to the tapered shape of the limb and consequently, it failed to occlude the median artery. To

overcome this problem, later workers who used this site including Lafaye (1933), Schmidt (1946), Chowdhury and Banerjee (1960) and Ellis (1973) designed trapezoidal shaped cuffs and found that these would effectively occlude the median or the deep median metacarpal arteries.

CONCLUSIONS

From the survey of the literature, it appears that the arteries of the horse's head are not suitable sites for sphygmomanometry. This is because they are small and mobile and also because they cannot be occluded by a cuff due to the size and shape of the horse's head. Head movements induced by the procedure also introduce inaccuracies.

Similarly the equine limb arteries have been shown to be unsuitable as sphygmomanometric sites because they are neither large enough or superficial enough to allow accurate PBP measurement and also because of the leg movements frequently induced in the horses by the cuff inflation procedure.

The survey indicated that in horses, the proximal part of the middle coccygeal artery at the tail base is the most suitable sphygmomanometric site. The middle coccygeal artery at this site has the advantages of being superficial, backed by non-compressable tissue, i.e. coccygeal vertebrae and can be readily compressed by an occlusive cuff. At this site, cuff inflation does not appear to induce restlessness or movement as has been frequently recorded when occlusive cuffs were inflated on the limbs of horses. However this artery has the

major disadvantage of being small in diameter and subsequently having a weak pulse, which is difficult to detect by most sphygmomanometric methods.

The standard sphygmomanometric methods used in man, i.e. the auscultatory and palpatory methods have been shown to be unsatisfactory at all sites in the horse. The oscillometric method has been used by many authors but because no definitive diastolic endpoint has yet been established for this method its value is unproven. The modified auscultatory methods using the 'infratron pulse detector' and the 'xylol pulse detector' both appear to give satisfactory systolic values in the horse but neither of these methods can give diastolic values and the infratron pulse detector has the additional disadvantage of being a complex, expensive piece of equipment.

The modified auscultatory method utilising a piezocrystal microphone to detect the Korotkoff sounds has been shown by many authors to be an accurate method of equine sphygmomanometry. In addition, the equipment required for this method can largely be improvised from standard physiological recording equipment, i.e. a pressure recording system is necessary to record cuff pressure and a phonocardiograph or even electrocardiograph can be utilised to simultaneously detect the piezocrystal microphone's signal.

At the time of the original survey of the literature on equine sphygmomanometry in 1975, the Doppler ultrasonic sphygmomanometric method was not then established as a reliable method for equine work. The major disadvantage which this Doppler method has is the very high price of this specialised

equipment costing between £ 2,000 and £ 3,000 in early 1976. This very high cost would restrict its use to large institutions and in fact prevented the present author from using it. Since then numerous reports have verified the accuracy and consistency of this sphygmomanometric method in the horse.

The review of the literature indicated that a rectangular occlusive cuff of approximately 10-13 cm wide is satisfactory for use on the tails of adult horses and ponies. Consequently it was decided that a cuff width within this range would be used in the indirect PBP measurements envisaged. No conclusions regarding optimal cuff length can be drawn from the survey and it was decided to use a cuff similar in length to tail circumference. Ellis (1973) found a mean tail circumference of 22 cm in adult thoroughbred and thoroughbred cross horses and consequently a cuff of approximately this length was selected.

The coccygeal artery is the most suitable site for sphygmomanometry in horses and current authors, who invariably use this site, have published their results as coccygeal PBP without any correction of values to heart level. As it appears very likely that this site will continue as the sole equine sphygmomanometric site, the use of this hydrostatic baseline will not cause any variation between workers. Consequently, it was decided to adopt this procedure for the envisaged sphygmomanometric experiments.

CHAPTER II.

Pilot Experiment No. I.

SELECTION OF A PRACTICAL EQUINE SPHYGMOMANOMETRIC TECHNIQUE

INTRODUCTION

The survey of the literature indicated that a very wide variety of sphygmomanometric techniques, most of which were initially developed for use in man, have been used on the horse. Few of the authors who have performed equine sphygmomanometry have described disadvantages associated with their own particular sphygmomanometric techniques but in view of the fact that such a potentially useful clinical technique is virtually unused in any branch of clinical veterinary medicine, it appears likely that there are some inherent disadvantages with the techniques utilised to date.

It was therefore decided to carry out limited selection trials on those techniques which seemed to be potentially useful for work on the horse. For financial reasons, the Doppler ultrasound sphygmomanometric technique, which appeared to be one of the most promising techniques, was not included in these trials.

The sphygmomanometric techniques selected for trial were a modified palpatory method using the xylol pulse indicator and a modified auscultatory technique using a piezocrystal microphone. Both of these techniques had previously been used to measure PBP from the coccygeal artery of horses. Excepting the Doppler ultrasound technique, these two methods appeared to be the two most suitable sphygmomanometric techniques used to date in the horse.

A further technique which has had limited usage in man but had not apparently been used previously in veterinary work,

is the photoelectric sphygmomanometric technique. This technique was tried on some horses.

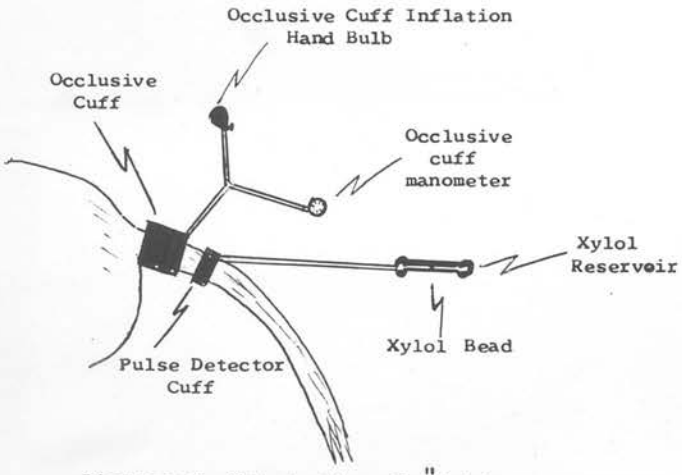
I XYLOL PULSE INDICATOR

INTRODUCTION

This technique, developed for paediatric use has been used in the dog and horse by Glen (1970, 1972). Ellis (1975) concluded from her review of the literature that this appeared to be the most practical sphygmomanometric technique for use in the horse.

Materials and Methods

A standard xylol pulse sphygmomanometer (see figure 2:1) as described by Ashworth et al. (1959) was used (Newcastle Sphygmomanometer, Chas. Thackray Ltd., Leeds) but its standard 2.5 cm wide paediatric occlusive cuff was replaced by a 13 cm wide and 23 cm long occlusive cuff, contained within a non-stretch and self-adhesive 14 cm wide and 51 cm long outer nylon sleeve ('Pre-gaged Adult Cuff', A. & C. Cossar, London). The instrument's standard pulse detection cuff was used. The preliminary experiments were performed on 5 conscious and 5 anaesthetised horses. As in all three indirect PBP measuring techniques used in this pilot experiment, the occlusive cuff was wrapped firmly around the base of the tail but not tight enough to cause arterial occlusion prior to cuff inflation. The detecting cuff was applied approximately 5 cm distal to the occlusive cuff. The sphygmomanometer was operated as described by Ashworth et al. (1959).



Diagramatic illustration of a "Xylol pulse indicator" applied to a horses tail.

Figure 2:1.

Results

It was found that even after hundreds of attempts on both conscious and anaesthetised horses there remained great technical difficulty in introducing a xylol bead into the capillary space at the appropriate stage of cuff deflation. Even after introduction of xylol beads into this space during cuff deflation, it was found that the beads tended to fall back into the reservoirs on either side of the capillary space. Due to these two technical difficulties, in many experiments no xylol bead pulsations could be detected and consequently no PBP could be measured.

During some attempts to measure blood pressure no xylol bead movement was detectable during cuff deflation even though some beads were within the capillary space throughout this time. In some instances a readjustment of the position of the pulse detecting cuff corrected this. Difficulty was also experienced in differentiating non-specific bead movements from the movements associated with a pulse return. These non-specific movements of the bead occurred more commonly in conscious horses and were sometimes associated with tail, leg or respiratory movements. Occasionally they were induced even at suprasystolic levels by the actual cuff deflation. These latter suprasystolic pulsations have also been observed in horses by Glen (1972) who used this same technique.

II PHOTOELECTRIC SPHYGMOMANOMETRY TECHNIQUE

INTRODUCTION

This technique which is potentially capable of giving a systolic and diastolic PBP values and pulse contours has apparently not been used previously in veterinary work.

Materials and methods

A standard human photoelectric PBP measurement instrument (Videograph phase III, Medical and Industrial Equipment Ltd., London) was used. This displayed the detected pulsations on a fluorescent screen. This instrument was used in conjunction with a standard 23 cm x 13 cm wide occlusive cuff previously described, an aneroid manometer and a rubber hand bulb for cuff inflation. This instrument has a plastic socket containing the photosensitive cell and light sources on opposite sides which is designed to accommodate and detect fluctuations in tissue density in a finger or thumb. It was decided to attempt to measure PBP from the shaved tip of a horse's tail using this socket, both because this was the only extremity which would neatly fit into the photoelectric socket and because the tail is the only site in the horse which can be reliably compressed by an occlusive cuff. Two normal adult hunter geldings (one chestnut and one grey) had the terminal 4-5 cm of their tail clipped and shaved. The occlusive cuff was applied to the base of the tail, the tip of which was placed within the photoelectric socket.

The occlusive cuff was inflated to above expected systolic PBP levels and then its pressure was decreased at a rate of

3-4 mm Hg/sec. while observing the fluorescent screen for changes in the photoelectric density of the tip of the tail.

Results

The shaved tip of the tail which was 2 cm in diameter fitted comfortably into the photoelectric cell socket. On lowering the occlusive cuff pressure to below predicted systolic and even predicted diastolic PBP values, no photoelectric pulsations were detected in more than 20 attempts on each of the two horses. This instrument worked satisfactorily on the fingers of two human volunteers before and after it was used on the horses. It was concluded that the tissues on the horse's tail possibly due to the skin thickness and/or pigmentation effectively blocked the passage of light across the tail and consequently made this method ineffective in the horse. Further evidence that this was the reason of the failure of this technique in horses was obtained by placing a light source on the far side of a horse's tail and observing that no transmitted light could be detected in contrast to the readily detectable transmitted light across a human finger in similar circumstances.

III MODIFIED AUSCULTATORY SPHYGMOMANOMETRIC TECHNIQUE

INTRODUCTION

A modified auscultatory sphygmomanometric technique utilising a piezocrystal to detect the low intensity Korotkoff sounds from the horse's coccygeal artery, has been used by Dear (1968), Desbrosse (1972), Geddes and Moore (1968) and Ellis (1973). Both Dear and Ellis have shown by simultaneous direct comparisons that this method is accurate in the

horse. It is, however, like all other equine sphygmomanometric techniques, not widely used.

Materials and Methods

In this experiment piezocrystals (6 x 6H, B.S.R. Ltd., Cradley Heath, Worcs.) removed from gramophone styluses were used. The two small electrodes from the piezocrystal were attached by lead solder to two electrical leads. The electrodes and 2-3 mm of the base of the piezocrystal were then embedded in epoxy resin (see Fig. 2:2) to protect the fragile electrodes from breaking away from the piezocrystal. The leads from the piezocrystal were attached to a phonocardiographic unit (Phono Function unit 3545, Devices Ltd., Welwyn Garden City, Herts.).

A 23 cm long and 13 cm wide occlusive cuff (Pre-Gaged, A. & C. Cossar Ltd., London) was pneumatically attached to a rubber inflation handbulb and also to a pressure transducer (Bell & Howell No. L 221-2-3, Basingstoke) which was connected to a pressure amplifier unit (Pressure Function Unit 3552, Devices Ltd., Welwyn Garden City, Herts.).

The outputs of the phonocardiograph and pressure amplifier units were simultaneously recorded on a multichannel hot stylus recording system (M19 Devices Ltd., Welwyn Garden City Herts.).

In this experiment the microphones were attached to the cuff in one of two ways. The microphone was placed either (1) directly on a mid-ventral aspect of the tail under the distal part of the cuff as originally described by Dear (1968) or (2) fitted within cuffs by a method similar to

that described by Geddes and Moore (1968). For the latter method, the rubber cuff was removed from its sleeve and an H shaped incision 5 cm wide and 7 cm deep was made on the wall. A piezocrystal mounted as previously described, was fitted to the medial aspect of the intact cuff wall by means of a 5 cm square perforated rubber patch which was glued around its periphery. The piezocrystal was left free within this perforated rubber pocket.

The leads from the piezocrystal were fed out through one of the two usual rubber tubes of the occlusive cuff and this tube was made airtight by tightly wrapping wire around it. By the use of a plastic T piece inserted into the other tube the pressure transducer and inflation bulb were pneumatically connected to the cuff. The cut surface of the cuff was then made airtight by a rubber patch over its outer surface. The rubber cuff was then replaced within the nylon outer sleeve so that the cuff wall on which the piezocrystal was mounted would be adjacent to the tail surface when in use (Fig. 2:3).

The pressure amplifier unit was calibrated and set for a pressure range of 1 - 200 mm Hg. The phonocardiograph unit was calibrated for piezocrystal microphone input and during the cuff deflation when Korotkoff sounds were being produced, various combinations of its input control adjustment (25 μv to 25 mv range) and of its input filtering adjustment (6 dB/ octave to 18 dB/octave range) were used until the settings which gave the greatest and most distinct Korotkoff sound recordings were obtained.

With the microphone in positions 1 and 2, PBP was measured from five normal horses. With the phonocardiograph output and

Figure 2:2. A piezocrystal mounted in epoxy resin, in position within an opened occlusive cuff.

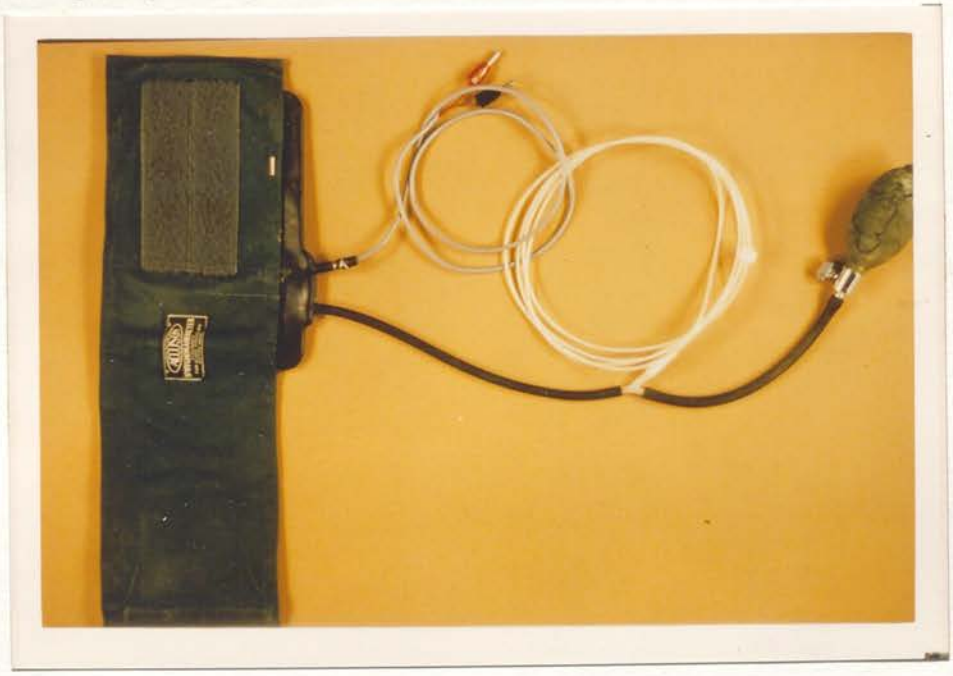


Figure 2:3. An assembled modified occlusive cuff, within a sleeve, with attached electrical and pneumatic connections.

cuff pressure being recorded, the cuff was inflated to above the expected systolic PBP level (approximately 175 mm Hg) and then the pressure was released at a rate of 3-4 mm Hg/sec.

Results

During most experiments with the microphone beneath or within the cuff, Korotkoff sounds were recorded along with cuff pressure. Loudest Korotkoff sounds were recorded with an input control setting of 2.5 mV and filtering of 6 dB/octave. The recorded Korotkoff sounds were interpreted as described by Ellis (1973) i.e. their initial appearance was taken as indicative of systolic pressure and their change from high to low amplitude which is equivalent to muffling on direct auscultatory method was taken as the diastolic criterion. A variable proportion of the recorded Korotkoff sounds were of poor quality because of superimposed interference on the Korotkoff sound recordings. These interference stimuli arose mainly from tail and body movement and less commonly from the cuff slipping down the tail. It was impossible to interpret these poor quality recordings accurately and they were disregarded.

I Microphone beneath the cuff

On cuff deflation to expected systolic PBP level (120 - 160 mm Hg), a series of Korotkoff sounds were recorded. The sounds gradually increased in amplitude and then began to fade out at about the expected diastolic PBP levels (70 - 90 mm Hg), and persisted below the expected diastolic value but disappeared totally before complete cuff deflation. In

general these sounds were low in amplitude and sometimes there was difficulty in deciding at which point they became reduced in amplitude.

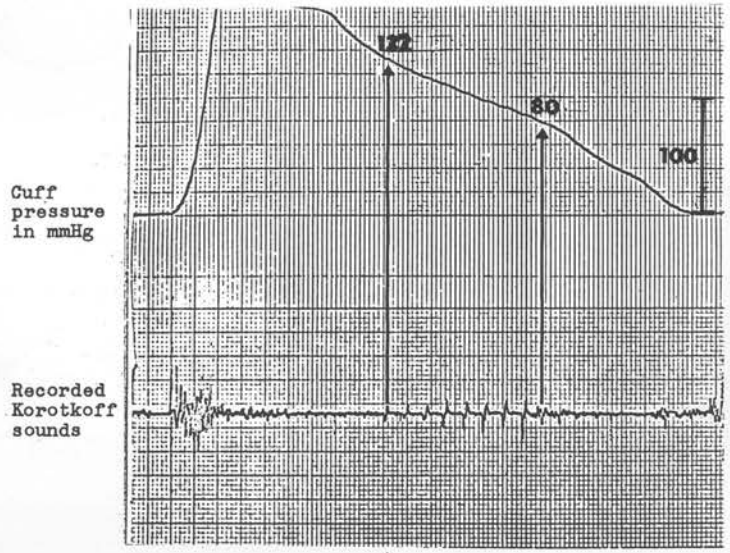
In 20% - 25% of experiments, no Korotkoff sounds were recorded at any stage of cuff deflation and their absence was generally found to be due to slight movement of the piezocrystal from it's midline position, which in turn was caused by cuff movement during inflation. With the microphone in this position, up to half of the Korotkoff sound recordings were of poor quality. On two occasions the delicate electrodes from the piezocrystals broke and so rendered them useless. On another occasion a piezocrystal broke possibly due to movement applied to it during cuff fitting or by tail movement.

2 Microphone within the cuff

Louder Korotkoff sounds were detected in the experiments with the piezocrystal within the cuff as compared to those with the microphone beneath the cuff. The positioning of the piezocrystal over the artery was also found to be less critical when the piezocrystal was within the cuff, therefore Korotkoff sounds were detected more reliably by this method with 90% success in recording these sounds and with 70-80% of the recorded sounds of satisfactory quality. No breakage of the piezocrystal or its mountings occurred. Figure 2:4 shows a recording of Korotkoff sounds obtained from a piezocrystal within the cuff and a simultaneous cuff pressure recording.

GENERAL DISCUSSION

Although the veterinary authors who have used the xylol pulse indicator technique did not mention any major disadvantages



Example of a recording of systolic (132 mmHg) and diastolic (80 mmHg) arterial blood pressures in a resting pony by modified auscultatory method.

Figure 2:4.

associated with its use, this method of PBP measurement is not widely used in the veterinary field. This lack of interest in such a simple method of PBP measurement may be in part due to the shortcomings described by the present observer, some of which have also been experienced by other observers both in the horse (Doddman, N., 1978, pers. comms.) and in the dog (Mackenzie, C.P., 1975, pers. comms.). The photoelectric sphygmomanometric technique was shown to be totally ineffective in horses.

These experiments showed that the modified auscultatory method of sphygmomanometry was feasible for use in the horse. It was also noted that using the piezocrystal within the occlusive cuff was the more effective sphygmomanometric technique because less piezocrystal damage occurred and more consistent and better quality Korotkoff sound recordings were obtained with the microphone at this site. In man, Geddes and Moore (1968) found that the Korotkoff sounds were more than three times louder within as compared to beneath the cuff and it appears that a similar situation occurs in the horse. Ellis (1973) found in horses that the microphone was less sensitive to external noises when fitted within the cuff's outer fabric sleeve. When fitted within the actual cuff itself as was done in these present experiments, it would be even more shielded from external noises and at the same time pick up louder Korotkoff sounds, therefore in this position a much more satisfactory signal to external noise ratio would be obtained which would increase the usefulness of this method.

Even the more effective modified auscultatory technique suffered the disadvantage that up to 10% of recordings were useless and up to 30% of remainder were of insufficient quality for PBP measurement.

CONCLUSIONS

This pilot experiment indicated that the modified auscultatory technique using a piezocrystal microphone within the occlusive cuff was a reasonably satisfactory equine sphygmomanometric technique and was the only technique which merited further consideration.

CHAPTER II

Pilot Experiment No. 2

DIRECT MEASUREMENT OF PERIPHERAL BLOOD PRESSURE (PBP) IN HORSES

INTRODUCTION

Because all sphygmomanometric techniques measure PBP intermittently, the diastolic pressure is measured from a much later pulse than the systolic pressure. To achieve accuracy the cuff pressure is slowly decreased at a rate of approximately 3-4 mm Hg/second and so these two measurements can be up to 20 seconds apart or in a normal horse about 15 pulses apart. The cuff must then be re-inflated and slowly deflated again before the pressure can be remeasured. In practice it is difficult to repeatedly measure PBP, faster than once every 30 seconds. For this reason it is impossible to study short term PBP changes by indirect methods and resort must be made to direct methods.

Besides the authors (Table 1:1) who have studied equine PBP indirectly, a large number have also done so directly. Ellis (1973) has comprehensively reviewed the works of 45 authors who have directly measured equine PBP prior to 1970 and since then direct PBP measurements have been performed in horses by several authors including Mordohovich (1971), Senta, et al. (1973), Bergsten (1974), Orr et al. (1975), Buss and Bisgard (1977), Fregin et al. (1977), Geddes et al. (1977) and Milne et al. (1977A, B).

Only two authors, using direct methods, have recorded the occurrence of physiological short term cyclic PBP variations. Gall (1967) and Senta, et al. (1973) observed cyclic variations in the PBP of most normal horses occurring in cycles of 1-3 per minute, with PBP variations of up to 35 mm Hg present.

Gall called these cycles "vasomotor waves" and Senta et al. (1973) called them "third grade waves". In addition Gall also observed a much shorter cyclic variation which she described as "staircase effect waves". These cyclic waves if present would be of major significance in both indirect and direct measurement of peripheral blood pressure. Because only two of more than 60 authors who have studied equine PBP directly have noted these cyclic waves it was decided to directly measure PBP and examine for their presence.

Because blood pressure waves are of a complex shape and rapidly fluctuate, the equipment required to accurately record the pressure levels and the wave forms must meet more exacting standards than equipment used to record slowly changing or static pressures. Criteria to be met by apparatus suitable for precise measurement of blood pressure have been discussed comprehensively by Fry (1960), Shirer (1962), Mendel (1968), Manktelow and Baird (1969) and Grossman (1974). They will be discussed in some detail at this point as they are also relevant to right heart blood pressure measurement which constitutes the major part of this thesis.

The four main requirements have been summarized by Manktelow and Baird (1969) as - sensitivity, linearity, stability and adequate frequency response.

1. Sensitivity: For the particular pressure being measured, the equipment must give a satisfactory deflection on the recorder.

2. Linearity: That the recorded deflection is simply and directly proportional to the pressure load applied to the transducer.

3. Stability: (a) With no pressure applied there should be minimal (less than 2% over 2 hours) baseline drift.

(b) Repeated application of the same pressure should consistantly produce the same deflection.

These three static requirements are usually adequate in modern manometers and amplifiers (Manktelow and Baird, 1969). Stability can be adversely affected however, by allowing inadequate warming up time for the manometer and amplifier or by housing these instruments in an environment with a fluctuating temperature (Fry 1960), (Manktelow and Baird 1969). Fry also suggests that the manometer should be minimally handled to prevent finger heat induced changes in the manometer's stability.

4. Frequency Response: The most difficult requirement to obtain is an adequate frequency response (Manktelow and Baird 1969). The complex pressure waves from a heart chamber or a great vessel are composed of a number of superimposed simple sine waves of differing frequencies. For a pressure measuring system to record both PBP wave form and pressure values accurately, the system must have a high enough frequency response to measure with equal amplitude and with equal time delay all of the component waves including those with a high frequency. (Shirer 1962). The natural frequency of modern strain gauge manometers is very high, up to 1000 hertz, which is

more than adequate for biological pressure measurements, but the necessary fluid filled catheters and connecting tubes greatly reduce the natural frequency of the entire catheter - manometer system. Among the factors that decrease the frequency response of a catheter-manometer system are the presence of air bubbles within the system, long or narrow catheters and connecting tubes, stopcocks, compressible and viscous fluid within the catheter system, and elastic walls on the catheter system (Manktelow and Baird 1969).

Manometer Damping

If the membrane of a manometer is displaced by the application and sudden release of pressure, the membrane will vibrate at its own natural frequency (Mendel 1968). If this same procedure is performed with a fluid filled catheter system attached, the diaphragm and fluid column will now vibrate at the natural frequency of the catheter-manometer system. In practice however friction between the fluid and the catheter will cause some damping of the transmitted waves in the fluid and so it is more correctly termed a damped natural frequency (Mendel 1968).

If the catheter-manometer system records a pressure wave which has a major frequency component similar to its own natural frequency, the entire system will resonate and consequently the recorded pressure wave will be distorted (Grossman 1974). To prevent resonance all catheter-manometer systems need extra damping. This damping can be affected by a physical constriction along the catheter system or by stepwise electronic filtering of the manometer output by the pressure amplifier

unit (Mendel 1968).

Theoretically, damping by means of a constriction in the catheter system is the more accurate as it prevents any resonance from developing, whereas electronic filtering allows the catheter manometer system to resonate but removes the effect of this resonance by damping the recorded signal. Electronic filtering is more convenient and more widely used because unlike constriction damping, it can be changed stepwise to adapt for different lengths or widths of catheter. A system can however be easily over damped and this will decrease its natural frequency below optimum (Mendel 1968) and the system will then give distorted rounded pulse waves due to omission of the higher frequency components of the pulse wave. With experience, damping can be performed by visual appraisal of the recorded pulse wave (Manktelow and Baird 1960) (Mendel 1968).

Connecting fluid

The purpose of the column of liquid within the catheter-manometer system is to transmit by its own movement, pressure fluctuations from the catheter tip to the manometer membrane. The connecting fluid is usually physiological saline (0.9% solution) with added heparin to prevent thrombus formation and consequent occlusion of the catheter. The most important requirement of the connecting fluid is that it be non-compressible and in practice this means air-free (Fry 1960) (Mendel 1968). This is achieved by boiling the fluid before use to remove its air content and then by slow, continuous flushing under low

pressure of the catheter manometer system to remove any small air bubbles from both the catheter and manometer (Mendel 1968). Air in the catheter-manometer system causes overdamping by lowering the natural frequency of the system (Manktelow & Baird 1969). Smaller amounts of air in the system can decrease the natural frequency of the system so that its natural frequency is the same as some of the more commonly recorded frequencies and thus resonance can be induced in the system (Mendel 1968).

Catheters

The catheters and connecting tubes which transmit the pressure fluctuation from the catheter tip to the manometer membrane must be non-elastic otherwise the wall would absorb some of the transmitted pulsations and distort the recording (Fry 1960, Mendel 1968).

Hydrostatic Baseline

When measuring PBP directly with a liquid filled catheter-manometer system, the recorded pressure is the absolute pressure within the transducer chamber $\pm$ the pressure of a saline column equal to the vertical distance between the catheter tip and the midpoint of the manometer membrane.

To objectively compare the results of different workers who use liquid filled manometric systems to measure blood pressures, all must use a common hydrostatic baseline reference point, i.e. the same height for the transducer relative to the subject whose blood pressure is being measured. Because the different cardiac chambers and great vessels are at different heights in the vertical plane and even different sites

within these chambers and vessels will vary in height there can be no ideal hydrostatic baseline for all catheterisation sites.

It is equally impractical to have separate baselines for each of these sites and consequently a single readily identifiable anatomical site close to all the chambers and great vessels is normally chosen as an alternative. It is particularly important that this reference point be level with the measurement site when a low pressure system is being examined e.g. atrial pressure, as hydrostatic error could be potentially greater in magnitude than the blood pressure at these sites.

One of the main advantages of a manometer tipped catheter is that they eliminate any potential hydrostatic baseline error either between or within cardiac chambers by having the manometer directly at the site of blood pressure measurement.

In man catheterisation is usually performed with the subject in a supine position and the reference site usually chosen is the mid-frontal plane at the second costochondral junction (Mendel, 1968). In veterinary medicine this important aspect of blood pressure measurement has been given little attention until recently, indeed some authors including Alexander (1959) and Geddes et al. (1965a, b) gave no details of the hydrostatic baseline they used. Others including Eberly et al. (1964, 1966) have used the dorsal aspect of the olecranon process which is anatomically ventral to the atria as a baseline and consequently some of their results appear

rather high. Other authors including Sporri and Schlatter (1959) and Bergsten (1974) have used the point of the shoulder (tuberositas lateralis of the humerus) as a baseline but did not state which intracardiac site it corresponds with.

Beltran (1973) has shown by angiographic studies, that the vertical midpoint of the right atrium is level with a site 2-3 cm above the point of the shoulder and he has suggested the use of this site as the hydrostatic baseline for all equine blood pressure measurements made by using direct methods. This baseline was used for direct PBP measurements in this thesis.

MATERIALS AND METHODS

Equipment: A 25 cm., 16 gauge nylon vascular catheter (Leader Cath. 120.15. Vygon U.K. Ltd.) - designed for insertion by the Seldinger method (see page 63), with a 7 cm, 16 gauge needle and a 40 cm guide wire, was used for the carotid catheterization.

The catheter was connected by a 1 metre long plastic connecting tube (Letrocath. 1150-20, Vygon U.K. Ltd.) to a strain gauge pressure transducer (L-221-2-3m, Bell and Howell, Basingstoke). The pressure transducer was connected to a pressure amplifier (3552, Devices Instruments Ltd., Herts.). The results were recorded on a hot stylus multichannel recorder (M19, Devices Instruments Ltd., Herts.).

The instruments which were maintained in a laboratory with a steady temperature of 20°C were switched on and allowed to warm up for a minimum of 2 hours before each experiment. The connecting fluid used was boiled 0.9% saline containing 25,000 I.U. Heparin (Pularin Heparin, Evan's Medical Ltd., Liverpool) per litre. This solution was kept refrigerated, but

before use was allowed to warm up to laboratory temperature to decrease its viscosity and also to prevent it causing any temperature induced changes in the catheter-manometer system's damping and stability characteristics (Mendel 1968). The connecting fluid was slowly aspirated into 20cc syringes, care being taken to avoid the introduction of any air bubbles. The catheter-manometer system was slowly and repeatedly flushed under low pressure until approximately 5 minutes after all visible air bubbles were removed from the system. The system was then calibrated stepwise, by electrical calibration signals. Periodically these electrical calibration signals were checked against a mercury U tube manometer.

The frequency response and damping characteristics of the pressure recording system were measured by studying its response to a square wave pressure change or "Pop testing" as described by Fry (1960) Shirer (1962) and Manktelow and Baird (1969).

A finger from a rubber surgical glove was tied tightly by silk thread to the catheter at 1 cm from its tip. This "balloon" was then inflated with connecting fluid through a stopcock at the manometer. With the recording paper at maximum speed (100 divisions/second) and with the minimal obligatory damping setting on the pressure amplifier i.e. 6 db./octave at 0.1 Hz, the balloon was burst by the heat of a match. The sudden drop in pressure and the subsequent oscillations induced in the catheter-manometer system were recorded. The rate of oscillations/second was taken as the damped natural frequency of the system and the damping of the

system was estimated from the initial overshoot below the baseline. Geddes (1970) states that a damping of 0.7 is optimal and this corresponds with a 7% overshoot on a square wave response (Mendel 1968). The procedure was repeated using different damping filters until the filter which caused damping closest to 0.7 was obtained.

Animals

Two adult hunter type geldings which were clinically and electrocardiographically normal were used in the experiments. The animals were brought to the laboratory on a number of occasions prior to the experiments to reduce the risk of excitement induced PBP changes occurring. During the experiments the horses were standing, non-tranquillised and restrained by a head collar.

Technique

The carotid artery was palpated deep in the jugular groove in the distal third of the horse's neck. In this position it feels hard with minimal or no palpable pulsations. The skin above the arterio-puncture site was swabbed with a 1% chlorohexidine B.P. solution and was subcutaneously infiltrated with 1 ml. of local anaesthetic, (2% xylocaine solution, Astra Chemicals Ltd., Watford).

The artery was then catheterized by the Seldinger technique. With this method the initial vessel puncture is made by a needle of smaller diameter than the catheter, so much less haemorrhage is likely from the puncture site during the catheterisation compared to that which occurs with other methods of catheter introduction.

The needle was inserted subcutaneously into the anaesthetised site and was then rapidly inserted into the artery in a ventro-caudal direction at an angle of 45 degrees. Successful arterial puncture was indicated by a flow of blood under high pressure from the needle. Immediately this occurred, the needle was redirected in a more ventral direction to prevent it transfixing the opposite side of the arterial wall. The guide wire was inserted through the needle into the arterial lumen and the needle was withdrawn. The catheter with its tapered tip was then inserted over the guide wire into the artery and the guide wire was withdrawn.

The connecting tube from the manometer was then attached by its luer fitting to the catheter, care being taken to ensure that no air bubbles were trapped between the fittings. Throughout the procedure the horses were kept as quiet as possible. The manometer was positioned at a site 3 cm above the point of the shoulder, a site level with the right atrium (Beltran 1973). PBP was recorded in horse A for 15 minutes, and in horse B for 25 minutes. During the measurements, the system was flushed with connecting fluid at five minute intervals to prevent thrombus formation in the catheter. On withdrawal of the catheters, finger pressure was applied to the arteriopuncture site for some minutes to reduce haematoma formation.

Results

The catheter-manometer system was found to have a damped natural frequency of above 25 Hz. which is adequate for equine blood pressure recording (Beltran 1973). Damping filtering

of 6 dB/Octave at 30 Hz was found to give closest to optimal damping. The arterio-puncture technique described, was successful in both horses.

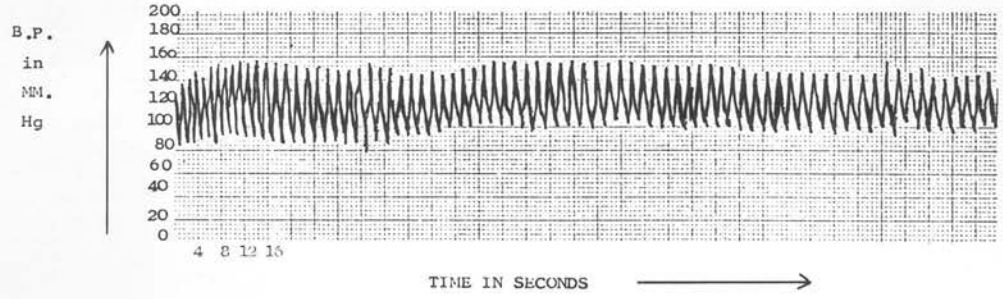
In horse A the mean systolic/diastolic PBP over a two minute period was 125/87 mm Hg with a mean heart rate of 42/minute. In horse B the mean systolic and diastolic pressure over a similar period was 152/97 mm Hg at a mean heart rate of 64/minute.

Undulating variations in pressure at the rate of 2-3 per minute were observed in both animals with maximum differences of 10-14 mm Hg in the systolic PBP and of 8-20 mm Hg in the diastolic pressure. Examples of this cyclic variation are shown in Figures 2:5 and 2:6 .

Discussion

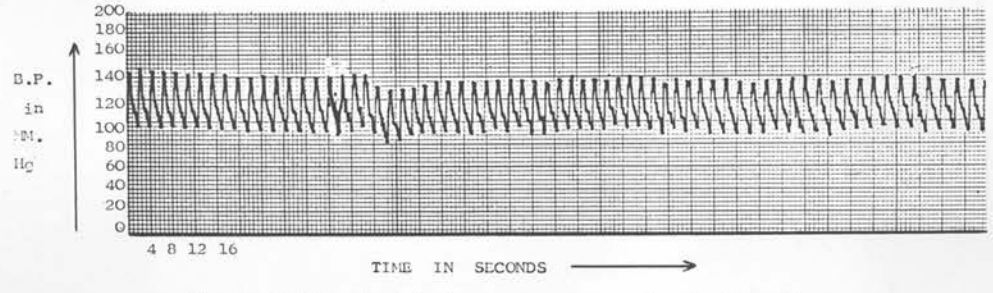
This experiment confirmed the presence of short term cyclic PBP variations in horses as previously described by Gall (1967) and by Senta et al. (1973). Other authors who have studied PBP directly have not reported this phenomenon. Cyclic variation, must therefore also be considered when indirect methods are employed. Changes of up to 20 mm Hg may occur in consecutive measurements which could cast doubts on the accuracy of the method in use. This very large physiological variation in peripheral blood pressure must be considered in any work in which equine PBP changes are being studied.

Direct PBP recording obtained in man usually show fluctuations synchronous with respiration and this variation is believed to be due to respiratory induced changes in stroke volume and in peripheral vascular resistance (Bell et al. 1972).



Direct carotid arterial blood pressure recording from Horse A.

Figure 2:5.



Direct carotid arterial blood pressure recording in Horse B.

Figure 2:6.

PBP recordings in man may also show variations caused by sinus arrhythmia and hypotensive individuals may also demonstrate oscillations at 20-40 second intervals which are known as Meyer (Mayer) waves (Ganong 1971).

Respiratory related PBP variations recorded in man include Traube-Hering waves

In addition, at least three non-respiratory related oscillations occur in man all of which have a cycle length of less than 1 hour. A major significance of these variable and frequently superimposed cycles is that their presence causes great difficulties in the development of automatic alarm systems for direct detection of significant PBP changes in critically ill patients (Taylor, D.E.M. 1975 pers. comms.).

Gall (1967) showed by simultaneous PBP measurements and pneumography that neither of the two types of PBP waves she observed in horses were directly respiratory related. Desliens (1935) and Carraud (1971) have also shown that there is normally no respiratory variation in the cardiac rhythm of horses. In these present experiments the horses' respiratory rate varied between 15-20/minute and so no relationship can be established between respirations and the slower (2-3/minute) cyclic PBP variations.

It is possible that multiple wave types also occur in the horse but to critically examine for their presence, mathematical analyses of a large number of longer term PBP records would be required. It does however appear that the cyclic variation(s) observed in the studies of Gall (1967), Senta et al. (1973)

and in this present study are not of respiratory origin. Senta et al. (1973) found equal systolic and diastolic variation in their PBP waves but Gall (1967) found greater systolic PBP changes. In the present limited study, the diastolic PBP changes observed were greater than the systolic ones.

The elevated heart rate recorded in horse B (64/minute) was significantly above his pre-experiment heart rate of 46/minute and the tachycardia persisted throughout the experiment, consequently the recorded PBP in this animal cannot be described as a resting value. The moderate tachycardia and hypertension recorded may have been due to pain from a small haematoma which developed at the arterio-puncture site during the measurements.

The percutaneous carotid-puncture technique used proved to be satisfactory, although this method is seldom used and carotid puncture in horses for experimental purposes is now generally performed through carotid loops or subcutaneously translocated carotid arteries. Both of these methods have the disadvantage of requiring considerable surgical intervention at some date prior to the PBP measurement. A possible reason why the percutaneous carotid puncture technique worked successfully in this experiment is that the author was familiar with this technique from using it to obtain arterial blood samples for blood gas analyses from horses undergoing examination of respiratory system.

CONCLUSIONS

Short term cyclic PBP variations occur in normal horses and its presence should be considered during direct or indirect PBP measurements.

CHAPTER 3

STUDIES OF NORMAL PERIPHERAL BLOOD PRESSURE VARIATION IN HORSES

INTRODUCTION

During the pilot experiment designed to assess practical indirect methods of measuring PBP in horses, it was observed that in an individual animal much variation occurred between the values obtained during a single recording session, and to a lesser extent between the mean values obtained during different recording sessions. In addition, much variation was observed between the individual animals. In a further pilot experiment using direct PBP measurements, marked short term cyclic variation was observed in two normal horses.

Most authors who have studied equine PBP directly or indirectly have observed variation between different animals (see Table I:I) but very few have recorded variation in the individual animal. The vast majority of authors who have studied equine PBP give just a single systolic and diastolic value for each animal as if the parameter being measured was a fixed one such as height or weight.

A small number of workers, however, have observed PBP changes in horses, induced by fear or excitement, from causes such as rough handling or the presence of unfamiliar attendants, (Hiepe and Gurtler, 1955) (Carraud, 1971) (Bergsten, 1974). Only Hiepe and Gurt ler (1955) and Choudhury and Banerjee (1960) have recorded variations in PBP in undisturbed normal horses.

It has been known since the introduction of routine

sphygmomanometry in human medicine that the PBP of normal humans can fluctuate widely and rapidly (Norris et al. 1928). This has been recently well demonstrated by Bevan et al. (1969) who placed miniature direct PBP recorders in normal individuals for periods of days and showed that frequent and massive PBP changes occur in normal adults throughout the day. Most of the subjects showed changes of more than 100% throughout the day with peak pressures occurring during periods of emotional stress and the lowest pressures occurring during sleep.

Addis (1922) is credited with the introduction into human medicine of the term basal PBP which refers to PBP measured from an individual not exposed to any physical or emotional stress. Desliens (1935), a French veterinary practitioner, has also used this term in relation to horses. Desliens performed thousands of direct carotid punctures on horses and the very low heart rates (32/minute) he frequently recorded would indicate that the animals he examined were in a true resting state. The low mean pressure values he recorded (90/70 mm Hg), while probably partly due to the resting state of the horses is also partly due to his use of an aneroid manometer to measure PBP. This instrument has too low a frequency response to accurately measure PBP (Geddes 1970) and so would underestimate systolic pressure.

It is well recognised in humans that fear induced by the actual measuring procedure can be an important hypertensive factor (Addis, 1922) (Norris et al. 1928) (Smirk, 1957).

Kapsaamer (1899) stated that a 'true' PBP value in man could only be obtained after many repeated measurements, when the subject had lost all fear of the sphygmomanometric procedure. Masters et al. (1952) and Pickering (1974) also state that in man, repeated measurements at future dates would give progressively lower values, which Pickering concluded was due to adaptation of the patient to the sphygmomanometric procedure. Masters noted that even after more than 100 sessions, some individuals still remained apprehensive of the procedure with consequently persistently elevated PBP values.

In this present experiment, PBP measurements were obtained from horses to look for short term PBP variation and measurements were repeated at intervals of two to three days and the mean results of each session were examined for the presence of longer term variations. Blood pressures were examined in some horses for a trend towards decreasing PBP levels over a long series of measurement sessions.

It had been observed in earlier experiments that the sounds of horses incidentally trotting at a distance from the laboratory appeared to have a marked hypertensive effect on the horses whose PBP was being measured even though the measurements were made in a laboratory with the doors closed. It was also planned to verify this observation.

MATERIALS AND METHODS

Animals

Seven animals were used; two adult hunter type geldings,

a 6 year old hunter type mare and four 2 year old Shetland ponies (three geldings and one filly).

Method

PBP was measured from the middle coccygeal artery by the modified auscultatory method described in pilot experiment No. 1, Chapter 2. The pressure recording unit was operated as previously described for the direct PBP measurement experiment (pilot experiment No. 2) except that for the present experiments the frequency response and damping level of the pressure recorder were not critically adjusted, because of the even and slowly changing nature of the pressure being measured. The phonocardiograph unit was allowed to warm up for two hours before the start of each experiment and its frequency range and filtering were adjusted to those settings which gave optimal Korotkoff sound recording in the pilot experiment.

Prior to obtaining any PBP measurements, horses 1, 2 and 3 were repeatedly brought to the laboratory to get them accustomed to the handler, operator and sphygmomanometric procedure. It was hoped that by frequently applying and inflating the tail cuff at this stage, these 3 horses would become accustomed to the sounds and sensations of the sphygmomanometric procedure and that the PBP values when obtained would represent true resting values. Horses 4-7 were examined without any previous familiarisation period. All animals were standing quietly before any recordings were taken.

Peripheral Blood Pressure Measurement

The cuff was firmly applied to the base of the tail with

the microphone in a mid-ventral position. If the animal tensed or moved its tail, the recording was delayed until the tail muscles were relaxed, as tensing of tail muscles would necessitate extra occlusive pressure to compress the coccygeal muscles before any occlusive pressure was applied to the artery itself and thus would cause an over-estimation of PBP. The cuff was inflated to approximately 175 mm Hg as indicated on the pressure recording, and then deflated at approximately 3-4 mm Hg/second by the valve on the inflation bulb, until the first Korotkoff sounds were recorded, indicating systolic pressure.

Just prior to cuff deflation, the microphone was connected to the phonocardiograph unit and during cuff deflation the phonocardiograph recording was continually observed for the appearance of Korotkoff sounds. If the Korotkoff sounds were absent or were weakly recorded, the cuff was adjusted slightly to bring the microphone to an exactly ventral midline position. If the sounds still remained absent or weak after adjusting the microphone position, the cuff was removed and re-applied slightly more firmly. Provided that the microphone and its electrical connections were intact, it was found that these two corrective procedures would usually result in satisfactory Korotkoff sound recordings.

At a recording session each animal's PBP was measured 12-15 times to ensure a minimum of 8-10 satisfactory recordings for each session. Two horses (nos. 2 and 3) had their PBP repeatedly recorded while a horse was trotted outside about 30 metres from the laboratory. The PBP of animal No. 1 was

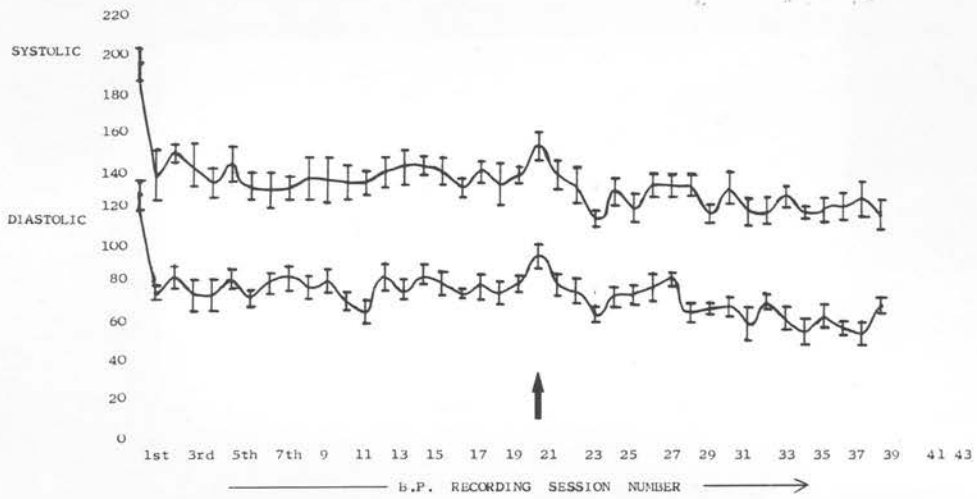
recorded satisfactorily for 38 sessions at 2-3 day intervals and the results were examined both for variations during and between the different recording sessions. The PBP's of animals Nos. 2 and 3 were similarly satisfactorily measured on 9 and 10 occasions respectively.

The PBP's of animals Nos. 4 - 7 which were unaccustomed to the measurement procedures were measured on five occasions at intervals of 2 - 3 days. The PBP (mean + S.D.) and the mean heart rates, as calculated from the recorded Korotkoff sound rate of each session were compared, to examine for any changes in PBP or heart rate between the different PBP measuring sessions.

In these four animals, which had not been familiarized with the measurement procedure, the mean of the first two measurements at each session was compared with the mean of the last two measurements to see if the PBP decreased over these recording sessions, as the horses became accustomed to the procedure. PBP values are given as uncorrected coccygeal PBP. The vertical difference between the point of the shoulder and the mid-point of the tail cuff was 23 cm in horses No. 1 - 2, 24 cm in horse No. 3 and 18 cm in horses Nos. 4 - 7.

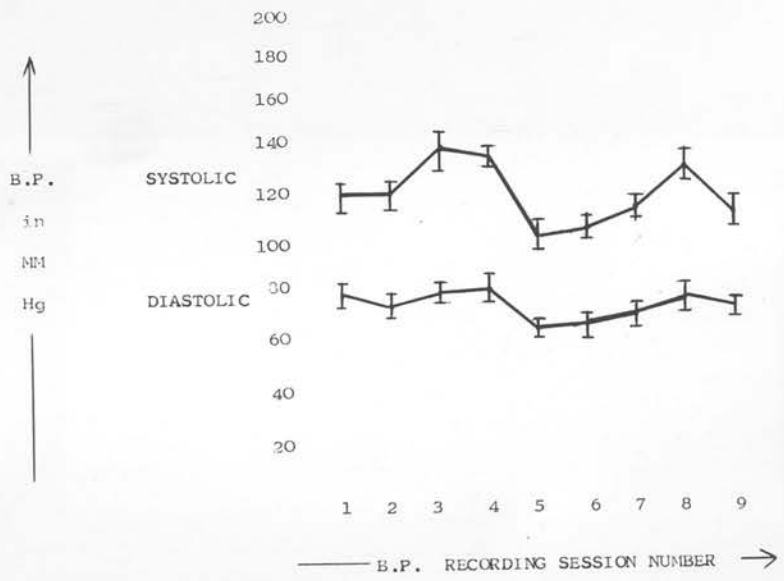
RESULTS

PBP values obtained in horses 1 - 3 are presented in figures 3:1, 3:2 and 3:3. In animal No. 1, despite the initial familiarisation period, a markedly raised value was recorded at the 1st recording as compared to subsequent recordings and no obvious explanation for this hypertension could be found.



SYSTOLIC AND DIASTOLIC B.P. (MEAN ± S.D.) OF HORSE NUMBER 1.

Figure 3:1



SYSTOLIC AND DIASTOLIC B.P. (mean ± S.D.)
OF HORSE NUMBER 2.

Figure 3:2

Comparison of the mean PBP and H.R. values obtained at the 1st recording session with those obtained at the last session by Students 't' test in all seven horses showed a significant decrease in animal No. 1 only, and this was due to the abnormally high value recorded in the horse on day I (Fig. 3:1). Because of the absence of any other significant individual change, the mean values of the other six animals are presented together below.

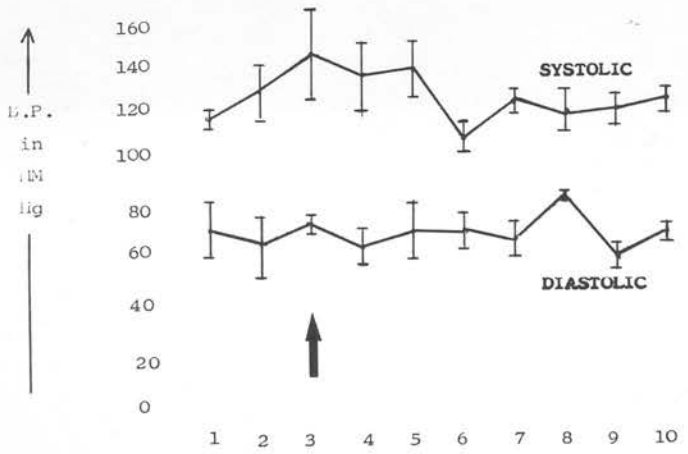
	1st Session	Last Session	
Systolic PBP in mm Hg ($\pm$ S.D.)	119.3 $\pm$ 6.50	120.6 $\pm$ 10.36	NS
Diastolic "	67.1 $\pm$ 8.35	67.2 $\pm$ 10.25	NS
Heart rate/min.	46.0 $\pm$ 7.44	49.8 $\pm$ 3.40	NS

NS = $P > .05$

In animals Nos. 3 - 7, comparison of the mean PBP values of the 1st two readings of each recording session with those of the last two readings of each session by Student's 't' test showed no significant individual variation and the mean results of these four animals are:-

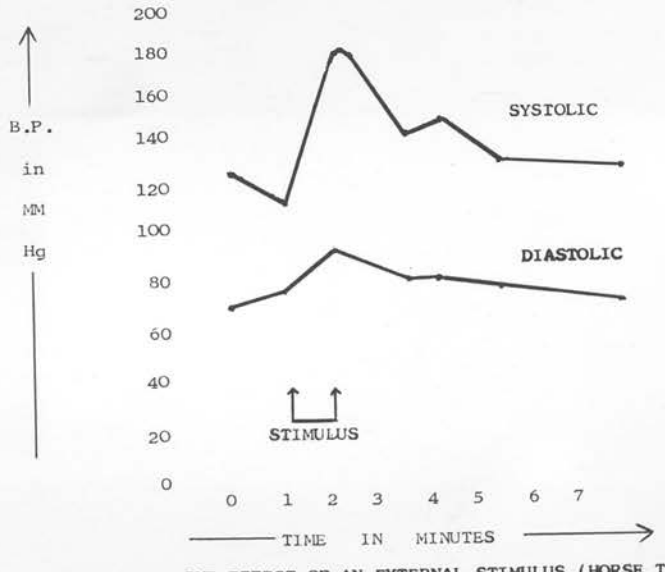
	1st two readings	Last two readings
Systolic PBP in mm Hg	122.9 $\pm$ 12.46	119.6 $\pm$ 9.59
Diastolic "	64.6 $\pm$ 9.14	65.5 $\pm$ 7.53

Although all measurements were made under conditions planned to minimise mental and physical stress to the horses, on some occasions e.g. the 20th recording session of animal



SYSTOLIC AND DIASTOLIC B.P. (mean $\pm$ S.D.)
OF HORSE NUMBER 3.

Figure 3:3



THE EFFECT OF AN EXTERNAL STIMULUS (HORSE TROTTING OUTSIDE) ON THE B.P. OF HORSE NUMBER 3.

Figure 3:4

No.1 (Fig. 3:1) and the 3rd recording session of animal No.3 (Fig. 3:3), a horse incidentally trotting outside caused increases in PBP. A significant ($P<.01$) increase in blood pressure and heart rate was induced in horses No. 2 and 3, when a horse was trotted at a distance from the laboratory. The PBP values obtained from animal No. 2 during this procedure are shown in Figure 3:4.

DISCUSSION

In all experiments variation was observed between values obtained at a single recording session (see Figs. 3:1, 3:2, 3:3). Lesser variation was observed between the mean values of different recording sessions (see Figs. 3:1 - 3:4). The consistent short term PBP variations observed throughout this experiment could be readily explained as being mainly due to the physiological PBP waves described by Gall (1967) and Senta et al. (1973) and also observed in pilot experiment No. 2. That the mean values of repeated PBP measurements tend to show much lesser variation, also supports this hypothesis. It is also probable that experimental error caused some of this variation. All indirect methods of PBP measurement have some inherent inaccuracy (Shirer, 1962) and the auscultatory method in particular has constant small inaccuracies (American Heart Association 1951).

In addition to the small inherent inaccuracy of the auscultatory method, it was observed in these experiments that extraneous sounds caused by tail or body movement or poor

Korotkoff sound production caused by improper cuff application could also potentially cause errors of measurement with the present method.

The longer term blood pressure variation observed in these experiments, i.e. the variation in the mean PBP values between the various measurement sessions, is similar to the PBP variation described in horses by Hiepe and Gurtler (1955) and by Chowdhury and Banerjee (1960). Hiepe and Gurtler measuring PBP indirectly in normal horses observed daily variations of between 110 - 124 mm Hg in systolic, and between 72 - 93 mm Hg in diastolic PBP.

Chowdhury and Banerjee recorded the PBP's of six horses on five occasions over a month-long period and they observed systolic variations of 5 - 15 mm Hg and diastolic variations of 4 - 18 mm Hg in individual animals over this time. It appears from the reports of both of these groups, that just a single measurement was recorded on each occasion and so the variations they have observed may have been due to normal cyclic PBP variation rather than to any other factor.

A reduction in recorded PBP levels after repeated recording sessions as commonly occurs in man, was only observed in animal No. 1 (Fig. 3:1). The absence of a consistent decrease in levels in animals 2 and 3 (Figs. 3:2, 3:3) was believed to be due to the preliminary familiarisation procedures these animals underwent. But animals 4 - 7 showed no tendency towards decreasing PBP levels despite the fact that they had not become accustomed to the procedure before any recordings were started.

The further decrease in PBP levels observed in animal No. 1 after approximately 3 months' recording may have been due to a further lowering of this horse's fear of the measurement procedure. It is possible that if the remaining animals had their PBP measured for as long a period as animal No. 1, a similar decrease in their PBP might also have occurred.

The coccygeal PBP values obtained from normal horses in this experiment were lower than those values obtained in horses by most other authors (Table 1:1). This may have been due to the more optimal conditions under which the present measurements were made. Even allowing for hydrostatic differences between authors, there is a great deal of variation among the indirectly reported PBP levels of horses (Table 1:1).

Some of the reported values appear to be very high including those obtained indirectly by Gotze (1916) and by Chowdhury and Banerjee (1966) (Table 1:1) and directly by other authors.

Examples of the latter are; 169/105 mm Hg obtained by Osman (1963), mean PBP values of 160 mm Hg by Geddes et al. (1965A, B) and 195/160 mm Hg by Hoff et al. (1965). The apparently high values obtained by all of these authors except by Gotze (1916) and Osman (1963) could possibly be explained by the improper baseline they used. They measured PBP directly with a liquid filled catheter at a site below heart level and made inadequate or even no compensatory hydrostatic adjustment to their results.

In addition to hydrostatic error it is possible that the high values obtained by some workers might be attributed to the fact that their horses were not in a true resting state during the measurements. Gall (1967) states that she saw no advantage in allowing the horses to get adapted to the PBP measuring technique even though she carried out the measurements in a horse abbatoir, by a direct method without local anaesthesia. Amend et al. (1972) stated that they 'lightly' restrained ponies during PBP measurement yet recorded 'resting' heart rates of up to 96/minute during their measurements. Eberly et al. (1964), when measuring PBP directly in horses, used the animal's heart rate as an indicator of its nervous state, but nevertheless regarded pressures from horses with heart rates of up to 72/minute as resting PBP values. It is unlikely that true resting values were obtained in any of these three studies and that fear, with it's attendant hypertensive effects was present in the horses during the measurement of their blood pressure.

CONCLUSIONS

These results further demonstrated the presence of short term cyclic variation in the systemic arterial blood pressure of horses and showed that use of the mean value of repeated measurements at each session can eliminate most of this variation. The variation observed between the mean values of the different recording sessions was found to be mainly due to excitement and if this was minimised, the mean values of the sessions showed little variation. The results indicate that PBP measurements obtained from horses in a true resting state would have lesser variation and lower levels than values obtained from horses not so stabilised.

CHAPTER 4.

STUDIES ON THE EFFECT OF SUBMAXIMAL EXERCISE ON THE PERIPHERAL BLOOD PRESSURE OF UNTRAINED PONIES

INTRODUCTION

Although exercise testing of horses has long been employed in the practice of veterinary medicine, only recently has there been any real interest in the physiological or the biochemical effects of exercise in this species. PBP increases due to exercise have been recorded in man by many authors, including Addis (1922), Thacker (1940), Korner (1952), Astrand and Rodahl (1970), Bevan, et al. (1969) and in the dog by Vogel, et al. (1967) and Vatner et al. (1970). Although exercise related PBP increases have also been recorded in the horse (Gehring, 1939; Laskov et al. 1960; Hornicke et al. 1971), the recent study of the effect of exercise on PBP in the horse by Bergsten (1974) showed no such PBP increase during exercise. There remains some doubt as to the PBP response to exercise in the horse.

The present experiment was designed to examine the effect of submaximal exercise on the indirectly measured PBP of untrained ponies by measuring their PBP immediately before and immediately after a period of exercise.

MATERIALS AND METHODS

Animals

The animals used were three Shetland ponies (two geldings and one mare) and one Welsh pony (gelding), all between 2.5 and 3 years old. These untrained animals had been confined in pairs, in loose boxes measuring 5 m by 5 m, for 2 years, but due to their small size they did manage to get

exercise within the boxes. Two weeks before the beginning of the experiments, the ponies were daily walked 30 metres to the laboratory where the PBP was to be measured and were made accustomed to the operator, groom and the PBP measurement procedure, to reduce the possibility of hypertension induced by excitement. To obtain basal PBP and heart rate values, all measurements were performed in a quiet laboratory.

Technique of Blood Pressure Measurements

Blood pressure was measured from the coccygeal artery by the modified auscultatory method previously described in Chapters 2 and 3. The heart rate was calculated from the Korotkoff sound rate. While in situ, the mid-point of the tail cuff was 18 cm and 20 cm above the level of the point of the shoulder (tuberositas lateralis of the humerus) in the Shetland and Welsh ponies respectively. PBP levels were measured at approximately 30-second intervals throughout the monitoring period. As this is an intermittent measuring method, the times of each reading vary due to differences in the PBP level being measured and to slight variation in the rate of cuff deflation.

For each experiment resting PBP values were obtained by repeated measurements over a period of 5 to 10 minutes. The animal was then taken to an indoor riding school and lunged on a rein for 8 minutes at a speed of approximately 2.5 metres/second, as calculated from time of circuit. After exercise the animals were immediately trotted back to the laboratory and their PBP was measured immediately post-exercise and

monitored over a period of 20 minutes. The first measurement was usually recorded within 30 seconds post-exercise, this being the time required to affix and inflate the tail cuff and to attach its pneumatic and electrical connections. No more than one experiment was performed on each animal daily and all experiments were performed at least 4 hours after feeding to prevent any postprandial cardiovascular changes (Bevergard and Shepherd, 1967).

Serum Enzyme Measurements

To examine changes in serum creatine phosphokinase (CPK) and glutamine oxaloacetic transaminase (GOT) levels associated with exercise in these animals, paired blood samples were obtained from each pony by jugular venipuncture into evacuated glass tubes (Vacutainer, Becton-Dickinson Co., Rutherford, New Jersey) at their first two and their last two experiments. The blood samples were obtained immediately prior to exercise and 5 hours after exercise at which time, exercise related CPK changes are maximal (Anderson, 1975). These enzyme levels were measured by an ultraviolet spectrophotometric method at 340 nanometers and 30°C (Calbiochem, La Jolla, California).

Statistical Analysis of Results

The difference between resting and post exercise enzyme levels were compared by the Students' 't' test as applied to paired observations. For each experiment, PBP and heart rate were plotted against time and the mean and standard deviation (SD) of these parameters were calculated from the 8 experiments on each pony. For each pony, mean differences

between the systolic and diastolic PBP levels before and 30 seconds after exercise were compared by Students' 't' test as applied to paired observations (Snedecor and Cochran 1971).

RESULTS

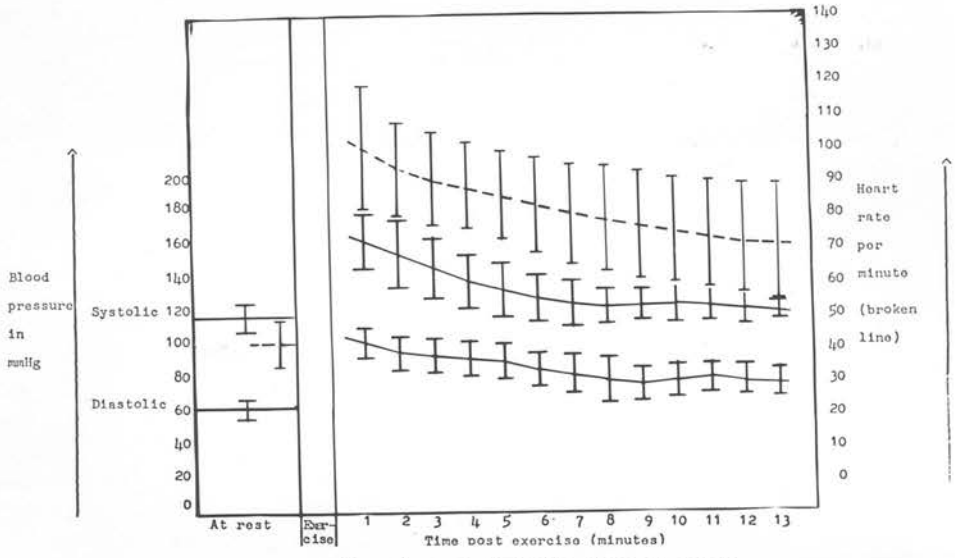
The PBP and heart rate values (mean ± S.D.) recorded before and after exercise from the 4 ponies are presented in Figs. 4:1 - 4:4. The mean PBP values obtained at rest and 30 seconds after exercise from the 4 ponies are presented in Table 4:1. The serum CPK and GOT levels obtained before and after exercise are presented in Table 4:2.

TABLE 4:I

Diastolic and systolic peripheral blood pressures (mean ± S.D.) in mm Hg from the 4 ponies before and 30 seconds after 8 minutes of exercise.

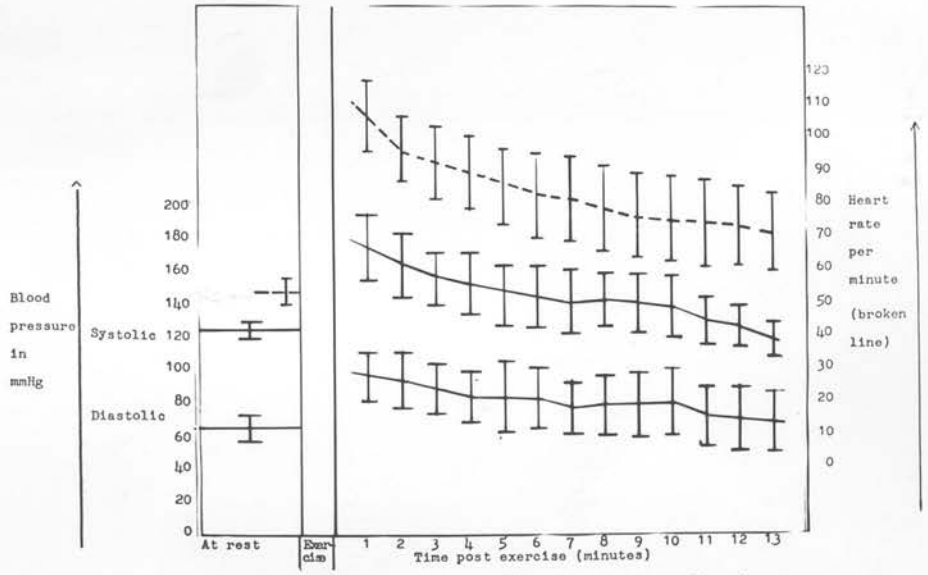
Pony	Diastolic PBP		Systolic PBP	
	pre-exercise	post-exercise	pre-exercise	post-exercise
1	65.6 ± 7.80	98.40 ± 14.80***	125.1 ± 5.44	175.4 ± 19.83***
2	59.5 ± 5.59	98.90 ± 21.58***	120.7 ± 5.57	167.9 ± 6.71***
3	67.4 ± 8.48	94.25 ± 17.38***	118.3 ± 11.79	150.8 ± 18.45**
4	64.6 ± 5.45	105.90 ± 10.78***	119.3 ± 8.14	165.8 ± 16.58***

** = $P < 0.01$ *** = $P < 0.001$



Mean values and standard deviations of systolic and diastolic blood pressure and heart rate before and after exercise (animal No. 1).

Figure 4:1



Mean values and standard deviations of systolic and diastolic blood pressure and heart rate before and after exercise (animal No. 2).

Figure 4:2

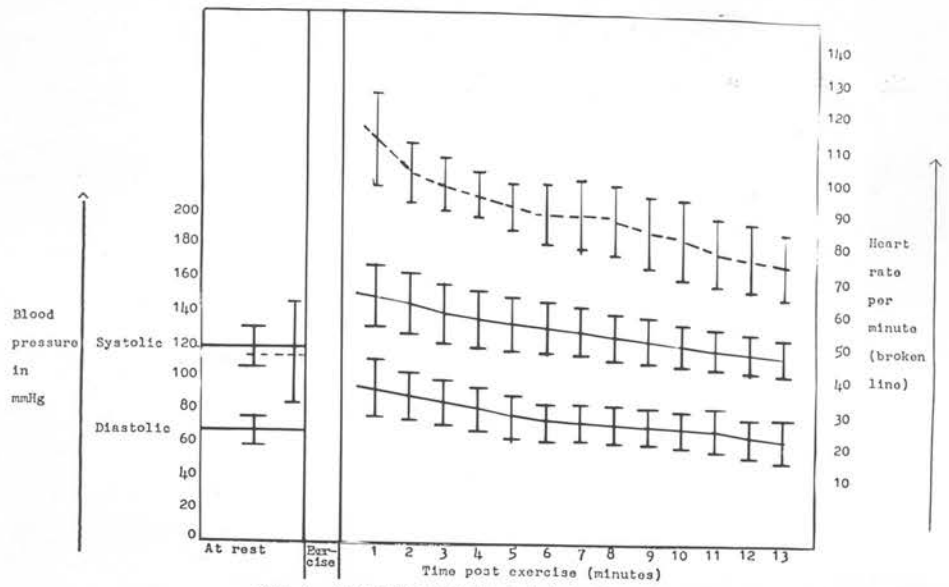
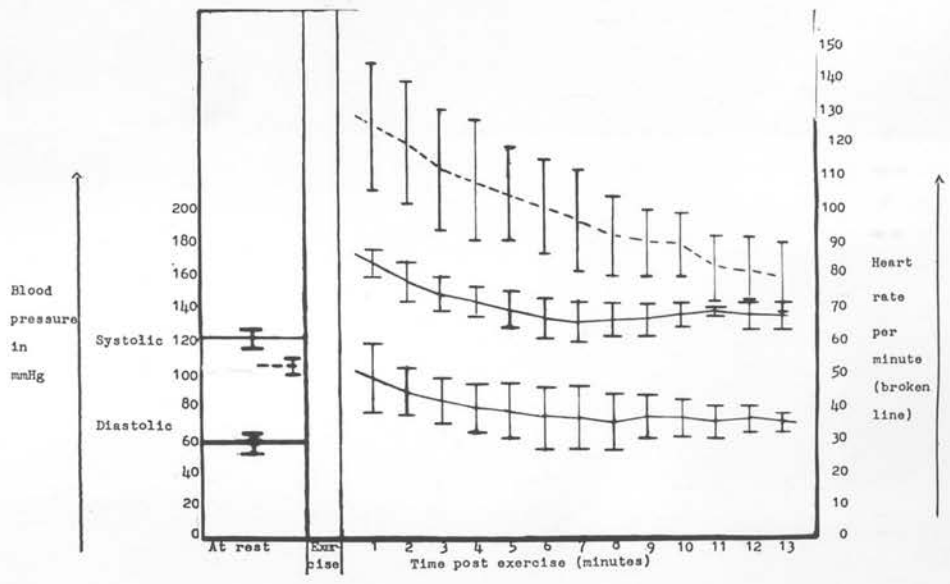


Fig. 1. Mean values and standard deviations of systolic and diastolic blood pressure and heart rate before and after exercise (animal No. 3).

Figure 4:3



Mean values and standard deviations of systolic and diastolic blood pressure and heart rate before and after exercise (animal No. 4).

Figure 4:4

The resting PBP levels were relatively stable and low indicating that the ponies were in a true resting state prior to the exercise. Statistical analysis showed that post-exercise diastolic and systolic levels were significantly raised ($< .01$) in each animal (Table 4:1). The post-exercise fall in PBP occurred in two stages. A rapid initial fall for approximately 3 minutes was followed by a slower decrease to near resting levels about 15 minutes post-exercise (see Figures 4:1 - 4:4). The recorded Korotkoff sounds postexercise were much increased in amplitude as well as in frequency (Figure 4:5), compared with those at rest. (Figure 2:4).

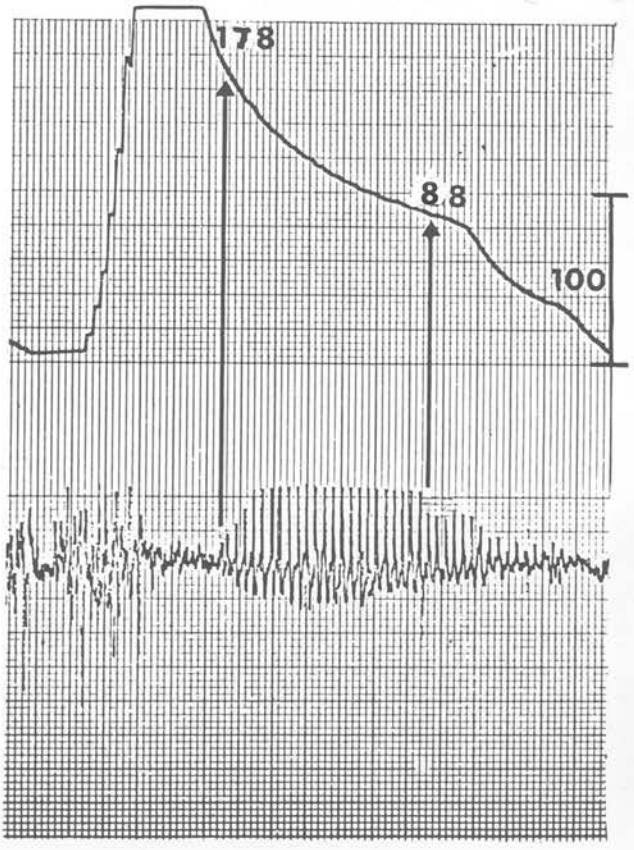
The serum CPK and GOT levels showed no significant changes ($P > .05$) associated with exercise and the results are presented in Table 4:2.

TABLE 4:2

Mean serum creatine phosphokinase and glutamine oxaloacetic transaminase levels before and after exercise.

SERUM CPK LEVELS IN I.U./L.			
	Pre-exercise	Post-exercise	
First two experiments	96.8 ± 49.27	131.17 ± 92.04	NS
Last two experiments	79.33 ± 8.41	101.5 ± 22.39	**
SERUM GOT LEVELS IN I.U./L.			
	Pre-exercise	Post-exercise	
First two experiments	162.25 ± 54.31	182.0 ± 38.95	NS
Last two experiments	152.8 ± 28.62	174.4 ± 41.91	NS

NS = $P > .05$ * = $P < .01$



Example of a recording of systolic (178 mmHg) and diastolic (88 mmHg) arterial blood pressures by modified auscultatory method in a horse post-exercise.

Figure 4:5

DISCUSSION

An increase in blood flow is required by the body and particularly by the skeletal muscles to cope with the increased metabolic rate associated with exercise. This is normally fulfilled by a reflex induced proportionate increase in cardiac output (Herd 1970).

During exercise, increased cardiac output is accomplished by an increase in heart rate and to a much lesser extent by an increase in stroke volume. A close correlation between heart rate and cardiac output during exercise has been demonstrated in man by Bevergard and Shepherd (1967); in dogs by Khouri et al. (1965) and in horses by Bergsten (1974). During maximal exercise in horses, the heart rate may be increased by more than seven-fold, Hall et al. (1976) Marsland (1968) so contributing to a vastly increased cardiac output.

Increased cardiac output would cause a proportionate increase in PBP unless a simultaneous decrease in peripheral vascular resistance occurred. The balance between these two opposing forces is the basis on which the PBP depends during exercise. During exercise massive dilation occurs in the muscle vasculature which is both centrally and locally controlled. This causes an overall decrease in peripheral vascular resistance despite the constriction of nearly all non-muscular vascular beds (Astrand and Rodahl 1970) (Silber and Katz 1975).

In exercising horses a marked splenic contraction occurs

thus greatly increasing the haematocrit and consequently the oxygen carrying capacity of the blood (Swenson 1977). Exercise induced haemoconcentration has also been recorded on a lesser scale in dogs (Khouri et al. 1965), but it does not appear to be a significant occurrence in man. Haemoconcentration causes an increase in blood viscosity which necessitates a higher PBP to pump the blood through the vessels (Herd 1970). It has been demonstrated in dogs that the haematocrit rise is regulated so that the cardiac work load and oxygen transfer are optimally balanced (Khouri et al. 1965) and the same may hold true for the horse. Thus along with the increased cardiac output, the haemoconcentration which occurs in horses will further tend to raise the PBP during exercise.

Increased PBP due to emotional effects has been recorded in athletes just prior to exercise (Detweiler, 1973). This is due to central stimulation of the cardiovascular system by corticohypothalamic pathways, which overides the normal cardiovascular reflex mechanisms and thus enables an anticipatory increase in cardiovascular performance ahead of metabolic needs. (Silber and Katz 1975). In man, excitement during exercise can potentiate the hypertensive effect of the exercise (Barger et al. 1956). In thoroughbred horses Hall et al. (1976) and Krzywanek et al. (1970) have recorded excitement induced increases in heart rates of 300 - 400% of resting rates just prior to racing. The possibility that the increased PBP recorded in the present experiments was due to excitement rather than to exercise, was considered. However, tachycardia was not recorded on any occasion prior to

exercise, which indicated a lack of excitement at this stage.

During exercise blood pressure raising reflexes originating from muscles, stimulated by an accumulation of exercise metabolites within the muscles might contribute to the rise in PBP (Smirk 1957). If there is failure to disperse the exercise metabolites from muscles post-exercise, continued hypertensive inducing reflexes from the muscles can delay the fall of blood pressure by causing temporary arrests of blood flow within the vascular beds of the musculature (Korner 1952). This phenomenon could account for the continous increase in blood pressure for 1 minute post exercise recorded in dogs by Khouri, et al. (1965). It is possible that the post-exercise peripheral hypertension recorded in the present experiment was due to blood pressure raising reflexes from muscles since these untrained ponies might have inefficient exercise related muscle vasodilation.

The louder Korotkoff sounds recorded post-exercise Fig. 4:5 are due to increased cardiac output (Ur and Gordon, 1970). There is no evidence that these louder sounds occur at an earlier stage during cuff deflation, thus giving erroneously higher PBP readings by auscultatory methods of measurement.

Of the authors who have recorded PBP increases in the horse during exercise, Gehring (1939) used tonoscillography, a method which was subsequently shown to be unreliable for measurement of diastolic PBP (Collins and Magora, 1963), Laskov et al. (1960) did not report the number of horses studied, the method used or the values obtained and Hornicke

et al. (1971), using 3 horses, gave neither the method used nor the values obtained.

Bergsten (1974), using 20 Swedish standardbred riding horses on treadmill exercises at 4 metres/second and recording the PBP directly by carotid catheterisation, found no increase in mean PBP during exercise. It is possible though, that an increase in systolic pressure occurred without affecting the mean pressure, because with tachycardia the systole is often very peaked and, even if increased, it might not significantly raise the mean PBP.

Bergsten's failure to show an increase in mean PBP with exercise may have been due to the relative fitness of his horses because of their training for treadmill exercises with fixed short arterial catheters. Speeds of 4 metres/second would be very submaximal for this breed of horse, whose maximal speed is greater than 12 metres/second (Lindholm and Saltin, 1974). Bergsten recorded a mean resting heart rate of 47/minute and a mean rate of 135/minute during exercise. In well trained human athletes, submaximal exercise may have little effect on PBP (Detweiler, 1973). Cardiovascular changes due to training have also been recorded in dogs (Vogel and Hannon, 1966) and in horses (Milne et al. (1977A). Thus, the difference between Bergsten's results and those reported here may be partly due to the fitness of the animals. Another possible reason for the differences between the present results and Bergsten's is a breed difference. It has been observed in this laboratory that ponies have higher resting heart rates and slightly lower PBP than horses of the larger breeds and there may also be a difference in their physiological response to exercise.

Strenuous exercise elevates certain blood enzyme levels in animals, particularly (CPK), a skeletal and cardiac muscle enzyme (Blackmore and Elton 1975). Other serum enzymes which have been noted to increase post exercise are glutamic-oxaloacetic-transferase (GOT), lactic dehydrogenase (LDH), aldolase (ALD), (Blackmore and Elton 1975) (Anderson 1975). These serum enzyme increases as a result of exercise, are greater in unfit than fit horses (Anderson 1975). Training in humans and rats has been shown to reduce or even eliminate these post exercise serum enzyme level increases by making the muscle cell membrane less responsive to the exercise induced increase in permeability.

CPK measurement post exercise has been suggested as the basis of a test for assessing fitness in the horse. CPK increases of 50 - 300% had been observed in trained thoroughbreds and hunters after 10-20 minutes of exercise. These increases are proportional to the duration rather than to the amount or severity of the exercise (Anderson 1975). Our results showed small increases post exercise in both GOT and CPK levels in all experiments. Due to the large variations between the individual animals and between the individual experiments on the same animals, little trend was seen in these enzyme level changes. Only the CPK levels in the last two experiments on each of the 4 animals showed significant change (see Table 4:2).

These small increases in serum enzyme levels taken along with the relatively rapid post exercise return of heart rate

to resting levels (less than 15 minutes) and also the observed absence of any physical signs of fatigue in the ponies during or post-exercise, indicates that this exercise was not very stressful to them and therefore could be classified as submaximal.

CONCLUSION

Although this study was on a limited number of animals and the PBP was measured after exercise, the results demonstrate a consistent hypertensive effect of submaximal exercise in untrained ponies. The variation between these findings and those of other authors may be due to differences in the fitness and breed of the animals used in the different studies.

INDIRECT MEASUREMENT OF PERIPHERAL BLOOD PRESSURE IN HORSES

GENERAL DISCUSSION AND CONCLUSIONS

The main reason for the restricted use of sphygmomanometry in equine medicine, is the lack of a suitable artery from which to measure this parameter. The photoelectric and modified palpatory sphygmomanometric techniques are impractical in horses, but the modified auscultatory technique was shown to be reasonably effective though, despite inherent technical difficulties. These latter were such that its use for routine purposes could not be recommended.

The results obtained with this modified auscultatory technique indicated that a great deal of short term variation (i.e. less than 15 minutes), occurred in the peripheral blood pressure (PBP) of resting horses and this observation was substantiated by a number of direct PBP recordings. Some longer term variations were also noted, as was the lability of PBP to stimuli caused by excitement. It was shown that the PBP of ponies significantly increased with submaximal exercise, although recent work by Bergsten (1974) suggested that equine PBP remains stable during exercise.

It is interesting that none of the four authors who previously utilized this same modified auscultatory technique in horses have published further reports about this method, although none of them have described any significant technical difficulties associated with its use. It is perhaps

significant that the clinic where Ellis (1973) published comprehensive report on the accuracy of this technique, now uses the "doppler ultrasound technique" about which, there have been several recent favourable reports by other authors.

The expense and bulk of the "doppler ultrasound" sphygmomanometer will undoubtably preclude its use by veterinary practitioners and consequently its use is likely to be restricted to large institutions. It is also possible, that in time some inherent disadvantages will be shown to be associated with this method as eventually occurred with all previous methods, despite initial optimistic reports.

Since there was also a need for more information on the haemodynamics of the right heart circulation, attention was then turned to investigating right heart blood pressures.

SECTION II

MEASUREMENT OF RIGHT HEART BLOOD PRESSURE IN HORSES

RIGHT HEART BLOOD PRESSURE MEASUREMENTS

GENERAL INTRODUCTION

Although the first recorded cardiac catheterisation was performed on the right heart of a horse by Chaveau and Marey (1861) who noted the technical ease of the procedure, for the next 100 years, cardiac catheterisation studies were virtually ignored in all species. In the last two decades there has been a revival of interest in this technique especially in right heart catheterisation.

These recent right heart studies have included blood pressure and pulse contour recordings both in normal horses and in horses suffering from chronic pulmonary disease. Clinical right heart catheterisation for the investigation of cardiac disease and particularly of congenital disease has also been recently performed in the horse (Critchley, 1976; Dixon et al., 1977), and is likely to assume greater importance in the future.

The aim of this work, is to review the literature concerning right heart catheterisation of normal horses and horses suffering from chronic pulmonary disease, to assess areas where further study would be beneficial and then to investigate these areas.

CHAPTER 5

REVIEW OF THE LITERATURE

1 RIGHT HEART BLOOD PRESSURE MEASUREMENTS IN NORMAL HORSES

A. TECHNIQUES

The first recorded cardiac catheterisation in any species was performed in 1861 by two French workers, Chaveau a veterinary surgeon, and Marey a physician. Using a curved air-filled metal catheter with two rubber balloons a few centimeters apart at its tip, they catheterised the right atrium and right ventricle of a standing horse. The proximal ends of the two catheter lumens had diaphragms which were attached by amplifying levers to a smoked drum recorder. Remarkably, the pressure values and pulse contours which these authors published are similar to those obtained today with the most sophisticated modern pressure recording apparatus. These authors noted in their report the technical ease and lack of complications associated with right heart catheterisation in the horse (Chaveau and Marey, 1861).

Fick (1864) introduced the use of the Bourdon Gauge as a manometer for intracardiac pressure measurements. He was the first author to damp the catheter/manometer system to prevent resonance induced distortion of the pressure recording. The optical manometer developed by Frank (1903) was an improvement on the previous mechanical manometers because of its increased frequency response. Frank realised that the optical manometer and all earlier pressure measuring systems had one severe limitation. They all utilised energy from the pressure being measured and could not therefore measure this pressure accurately.

All the systems to that date, utilised gases rather than liquids as a connecting medium between the catheter tip and the manometer membrane, and this predisposed to potentially large temperature induced volume changes in the connecting fluid which could distort the pressure recording. The introduction of liquid filled catheter systems while greatly decreasing the chances of volume change error, introduced the possibility of hydrostatic error in the pressure recording which would occur unless the manometer membrane and the catheter tip were at the same level in the horizontal plane.

A significant advance in intracardiac manometry was made by Schütz (1931) who developed an accurate electrolytic manometer, a pressure transducer which was small enough to be fitted on the tip of a cardiac catheter. This type of manometer converted the blood's pressure into an electrical signal and so did not abstract substantial energy from the event being recorded. It also had the advantage of eliminating hydrostatic error by having the manometer at the actual site of blood pressure measurement. This potentially useful form of manometer had very limited usage, however, because of the instability of the chemicals within the manometer and because of frequent electrode polarisation and overloading during pressure measurement (Geddes, 1970). Other types of manometers including electro-optical, capacitance, inductive and mechano-electronic systems have been utilised briefly for cardiac pressure measurements and the relative advantages and disadvantages of these various manometer

systems have been comprehensively discussed by Geddes (1970).

The strain gauge manometer is currently the most widely used manometer for blood pressure measurements. This manometer acts on the principle that stretching a wire will increase it's electrical resistance. Movement of a strain gauge manometer membrane causes stretching or relaxation of wires attached to it and the subsequent changes, induced in these wires' electrical resistance is proportionate to the pressure applied to the manometer membrane.

This type of manometer was first introduced by Simmonds (1942) and rapidly gained popularity because of it's inherent properties of high sensitivity and high frequency response and also because of it's relatively low commercial production costs. Miniature strain gauge manometers have also been developed for use on catheter tips and their use at this position increases the frequency response and sensitivity of the pressure recording above that of an external strain gauge manometer used with a liquid filled catheter system. However, these miniature catheter tipped strain gauge manometers have the disadvantages of high cost and fragility.

B. RIGHT HEART CATHETERISATION IN HORSES

Some details of right heart catheterisations in normal horses performed by previous authors are given in Table 5:1.

In the early twentieth century despite many developments in manometers potentially useful for cardiac catheterisation, very little interest was shown in cardiac catheterisation in any species. An exception to this was Desliens, a French veterinary practitioner who catheterised the right heart of

Table 5 : 1. Summary of right heart blood pressures obtained from normal horses by previous authors.

Author	Number of horses	Hydrostatic baseline	Drugs administered	Blood pressure in mm Hg (mean or range)								
				Pulmonary artery			Right ventricle			Right atrium		
				Syst.	Diast.	Mean	Syst.	Diast.	Mean	Syst.	Diast.	Mean
Chaveau & Marey (1863)	1	NR	No	-	-	-	-	-	27	-	-	2.5
Alexander (1959)	1	?	T	42	20	-	-	-	-	-	-	-
Sporri & Schlatter (1959)	2	POS	?	-	-	-	45	1	-	-	-	-
Ruckebusch et al. (1960)	1	?	?	-	-	27	-	-	-	-	-	-
Sporri (1962)	10	POS	?	-	-	-	39.5	-1.5	-	-	-	-
Eberly et al. (1964)	12	OLEC	T	-	-	34	59	13	25	-	-	-
Geddes et al. (1965a)	?	?	GA	70	30	-	80	5	-	-	-	-
Geddes et al. (1965b)	?	?	GA	70	30	-	80	5	-	-	-	-
Sporri (1965)	?	NR	?	-	-	-	-	20-30	-	-	-	13
Eberly et al. (1966)	24	OLEC	T	-	-	34	64	15	28	-	-	-
Gall (1967)	15	NR	No	36	21	-	49	14.5	-	16	4	12
Wagenaar et al. (1967)	?	?	?	30-53	-	-	-	-	-	-	-	-
Mordohovich (1971)	1	?	?	-	-	-	57.8	16.3	-	-	-	-
Detweiler & Patterson (1972)	7	POS	?	39	16	22	46	1	11	20	0	6
Beltran (1973)	17	2-3 cm above POS	No	30	13.8	-	30.8	2	-	9.9	1	-
Bergsten (1974)	30	POS	No	45	22	30	51	11	-	-	-	10
Bisgard et al. (1975)	6	POS	No	-	-	25.1	-	-	-	-	-	-
Milne et al. (1975)	14	POS	No	42	18	26	46	6	-	-	-	6
Orr et al. (1975)	17	POS	No	33.6	14.5	22.7	-	-	-	-	-	-
Buss & Bisgard (1977)	6	POS	No	-	-	20	-	-	-	-	-	-
Milne et al. (1977b)	5	POS	No	-	-	26.8	-	-	-	-	-	11.4

Hydrostatic baseline : POS = Point of shoulder
OLEC = Dorsal aspect of olecr. process
NR = Not required. Pneumatic system or transducer tipped catheter used.

Drugs : T = Tranquillised (standing)
GA = General anaesthesia (lateral recumbent)

standing horses (Desliens, 1935). Using a Bourdon gauge he measured RAP and RVP in these animals, but he does not appear to have measured PAP. Desliens gave no further information about his catheterisation or manometric techniques and did not publish his recorded pressure values.

Using a primitive manometric system, which they described as 'Marey's tambour', Ruckebusch et al. (1960) catheterised the right ventricle of one horse. In this short report they did not discuss the catheterisation technique or the hydrostatic baseline used. See Table 5:I. Grover (1959) measured PAP from one normal horse while simultaneously recording intrapleural pressure. He did not describe the equipment or techniques used for these measurements.

A further catheterisation of a single horse was reported by Sporri and Schlatter (1959), who employed a conventional catheter system (i.e. external manometer) and used the point of the shoulder as a hydrostatic baseline reference point. Sporri (1962) studied the timing of cardiac events by simultaneously recording ECG's and cardiac pulse contours from the right and left cardiac chambers. In this study he used a transducer tipped catheter and he appears to be the first veterinary author to have done so. Sporri reported the right heart pressure values from 10 normal horses and also published a record of equine right ventricular pulses, obtained simultaneously by a conventional catheter system and by a transducer tipped catheter. Examination of the published recording would suggest that the conventional catheter system was underdamped and this tends to exaggerate the advantages of

the transducer tipped catheter.

Eberly et al. (1964) measured right heart pressures in 10 thoroughbred horses with a conventional catheter system, using the top of the olecranon process as a hydrostatic baseline. All horses were tranquillised with propiopromazine hydrochloride before the catheterisation. The use of the olecranon process, which anatomically lies below the atria, as a hydrostatic baseline appears to have resulted in their published values being raised. These authors also noted the difficulty of establishing basal blood pressure values especially with nervous thoroughbred horses and stated this was the reason they tranquillised their horses before cardiac catheterisation. However during PBP measurements, three of their horses had heart rates of above 60/min. despite the tranquillisation.

Sporri (1965) studied cardiac dynamics in 9 normal horses, but he did not give any right heart pressure values or details of the technique and equipment used. Using a conventional catheter system Geddes et al. (1965 a, b) catheterised the right heart of an unspecified number of anaesthetised horses, but they did not specify the hydrostatic baseline used. They reported right ventricular systolic values of between 70 to 80 mm Hg which appear high in comparison with other author's normal values (Table 5:I) although their mean right ventricular diastolic value of 0 mm Hg would indicate that improper baseline selection was not responsible for the apparently raised systolic pressure. The right heart blood pressure contours these authors

published have multiple afterwaves in the diastolic period, which Geddes et al. considered to be due to the marked elasticity of the equine pulmonary vascular bed. It appears more probable that these afterwaves are in fact artifacts, caused by underdamping of their pressure recording system. These authors like all preceding veterinary authors did not describe the frequency response or the damping characteristics of their pressure recording equipment.

Eberly et al. (1966) studied right heart pressures in 24 normal horses. They used the top of the olecranon process as a hydrostatic baseline and also tranquillised an unspecified number of the horses with a phenothiazine type ataractic before catheterising them. Despite tranquillisation, some of the reported pressure values appeared high, one normal horse having a systolic right ventricular pressure of 109 mm Hg. These authors do not appear to have considered the cardiovascular effects of tranquillisation with this type of drug, which has proven hypotensive activity in horses (Gabel et al. 1964).

Gall (1967) performed right heart catheterisation on 15 horses and in a comprehensive study utilised a transducer tipped catheter, which eliminated any possible pressure recording artifacts due to frequency response, damping or hydrostatic baseline errors. Because this type of pressure measurement equipment gives a more accurate pulse contour recording than the conventional catheter system, this author devoted much of her study to this aspect of cardiac catheterisation. Gall noted very significant differences between the right atrial,

right ventricular and pulmonary artery pulse pressure contours of the individual horses studied. She described the common characteristics of the various equine right heart pulse contours.

Mordohovich (1971) performed right heart catheterisation on 8 horses some of which he stated were suffering from various cardiac valvular and conduction defects. In a confused report this author published the mean RV pressure values from all 8 horses. The reported mean pressure values appear to be well outside the commonly accepted range (see Table 5:I) and this is probably a reflection of the diseased state of the horses used by Mordohovich.

Beltran (1973) catheterised the right hearts of 17 normal horses. Using a conventional catheter system he described in detail his system's damping and frequency characteristics. He also performed angiographic studies during right heart catheterisation and was the first author who attempted to establish a definitive hydrostatic baseline in horses for fluid filled catheter systems. This baseline which corresponds in the horizontal plane with the mid-point of the right atrium, is 2-3 cm above the point of the shoulder. This author devoted a great deal of his study to the detailed description of the pulse contours of the right heart cardiac chambers and pulmonary artery. He was apparently unaware that this work had been performed by Gall (1967) using the more suitable manometer tipped catheter.

However, Beltran was aware of the limitations of the conventional catheter system and stated that some extra peaks

which he occasionally recorded on the systolic pulmonary arterial pulse were probably artefacts resulting from catheter movement, due to the myocardiac contractions or from tricuspid or pulmonary valve movement. Beltran performed many of his right heart catheterisation recordings while simultaneously recording a pneumogram and ECG. He found no evidence of any respiratory related cardiac arrythmias in the horse. A pneumographic recording while indicating the stage of respiration cannot show the magnitude of the intrathoracic pressure changes.

Beltran's published right heart pressure values are generally lower than those of most other authors probably because of his use of a higher hydrostatic baseline than that of all other authors, and also because he took great care to ensure that the horses were in a fully resting state prior to the pressure recordings.

Beltran found no evidence of increased RVP after exercise in normal horses, but he did not specify the state of fitness of the horses used, the speed of exercise, nor the actual RVP levels recorded before or after the exercise. Because of these omissions this finding must be cautiously interpreted.

Right heart catheterisation investigations usually refers to blood pressure, gases and pH, studies of the right atrium (RA), right ventricle (RV) and pulmonary artery (PA). A less commonly studied right heart site is the pulmonary arterial wedge (PAW) site. The PAW site is obtained by advancing a sufficiently long catheter with a single opening at its tip into the PA until it enters and occludes a terminal pulmonary arteriole of its own diameter (1-2mm). This arteriolar

occlusion causes the development of a physiological shunt between the catheter tip and the pulmonary venous circulation, but the exact mechanism of this shunt is not understood (Mendel, 1968; Grossman, 1974). The blood gas characteristics and the mean blood pressure at a pulmonary arterial wedge site are very similar to those at a pulmonary venous site, consequently PAW pressure values are used to indirectly estimate pulmonary venous or left atrial pressures.

Beltran appears to have been the first author to study pulmonary arterial wedge pressures in horses. For these pressure measurements, he used a 110 cm long balloon tipped Swan-Ganz catheter of a type originally described by Swan et al. (1970). In many instances this length of catheter proved too short to occlude a terminal pulmonary arteriole and consequently a conventional pulmonary wedge pressure was unobtainable. In these situations Beltran inserted the catheter as far as possible into a pulmonary artery and then inflated the balloon which would occlude an end artery of up to 10 mm diameter. He appears to have concluded that occlusion of an end artery of this size, was physiologically similar to the occlusion of an arteriole 1-2 mm in diameter. The results obtained using the conventional technique and the modified wedge technique were presented as equivalent even though he could not consistently aspirate from his modified 'wedge' site a sample of blood with the blood gas characteristics of a normal wedge sample.

Using a conventional catheter system Bergsten (1974) catheterised the right hearts of 30 normal horses. In this report he did not give the details of the damping or

frequency characteristics of his system and some of his published pulse pressures, particularly his pulmonary arterial pulse contours appear slightly under-damped. This author used the point of the shoulder as a hydrostatic baseline reference point.

Bergsten noted increased pulmonary artery pressure in normal horses during exercise, but as previously noted in Chapter 4 he observed no significant increase in mean peripheral blood pressure in these same horses during exercise.

Further right heart pressure studies in the horse have been published by Bisgard et al. (1975), Milne et al. (1975), Orr et al. (1975), Buss and Bisgard (1977) and Milne et al. (1977B). All of these authors except Milne et al. (1977B) have used in their studies ponies of the grade breed weighing less than 200 kilograms as adults and have reported relatively high heart rates in the ponies during the right heart blood pressure measurements (Table 5:1). This apparently high heart rate may be normal for this small type of pony and the relatively low blood pressures recorded would indicate that it was not due to a fright induced tachycardia. The right heart pressures reported by these five groups of authors (Table 5:I) are similar to those obtained by Gall (1967), Beltran (1973), and Bergsten (1974).

CONCLUSION OF LITERATURE SURVEY

Over 100 years ago workers showed that right heart catheterisation and blood pressure measurement are easily performed in horses. Despite the technical ease of the procedures, very little interest was shown in this field until two decades

ago. Since then right heart cardiac catheterisation has been performed in normal horses by many authors and some of these studies, particularly those by Gall (1967), Beltran (1973) and Bergsten (1974), have been performed using acceptable equipment and techniques and these authors values for normal right heart pressures and pulse contours are in close agreement. Bergsten (1974) has shown that the pulmonary arterial pressure of normal horses increases significantly during the exercise, in contrast with the situation in man.

II THE RELATIONSHIP BETWEEN CHRONIC RESPIRATORY DISEASE AND ALTERATIONS OF THE RIGHT HEART CIRCULATION

Physicians have realised for many centuries, that many patients with chronic pulmonary disease developed a certain type of cardiac disease at a later date, but the relationship between the two diseases was not then understood. This secondary cardiac disease was known by many names, including 'pulmonary heart disease' and 'emphysema heart' and was manifested as RV hypertrophy often leading to right heart failure (Brill 1958) (World Health Organisation 1963). The exact incidence of this form of cardiac disease among the human population is unknown, but some hospital reports show that more than one third of all cardiac patients admitted, suffer from cardiac disease secondary to chronic respiratory disease (World Health Organisation, 1963). Chronic pulmonary diseases in man in which airway obstruction occurs, include chronic bronchitis, pulmonary emphysema, asthma and bronchiectasis and these diseases are frequently classified together as Chronic Obstructive Lung Disease (COLD) Thurlbeck (1976). Secondary right heart circulatory disorders are particularly common with these respiratory diseases (World Health Organisation 1963).

At the beginning of this century, workers correctly surmised that this cardiac disease was basically due to increased pulmonary arterial pressure (pulmonary hypertension), leading to an increased RV workload which eventually caused RV hypertrophy. The term 'cor pulmonare' was introduced by White (1931) to describe this disease. More recently an expert

committee was instigated by the World Health Organisation, to review the then confusing and frequently conflicting information on this disease and to establish a definite nomenclature for it.

This committee suggested that the term 'chronic cor pulmonare' should be used for this condition, which they defined as "hypertrophy of the right ventricle resulting from diseases affecting pulmonary function or structure except where these pulmonary alterations are the result of diseases that primarily affect the left side of the heart or of congenital heart disease" (World Health Organisation 1963).

Despite the effort of the World Health Organisation committee, there still remains amongst the different medical disciplines some confusion regarding the term cor pulmonare as many clinicians do not use this term until patients are showing clinical signs of right heart failure, whereas pathologists still use this term to denote anatomical RV hypertrophy (Thurlbeck 1976). Because of this ambiguity some authors have suggested that the term cor pulmonare should be dropped and the disease be known by clinical terms such as 'pulmonary hypertensive cardiac disease' (Silber and Katz, 1975) or 'pulmonary hypertension' (Thurlbeck, 1976). In this thesis Thurlbeck's recommendations will be followed.

Since the advent of routine clinical catheterisation in man over the last three decades, the functional disturbances which occur in pulmonary hypertension have begun to be understood. It was at first believed that the pulmonary

hypertension demonstrated in this disease was due to an anatomical reduction in the pulmonary vascular bed, caused by the primary pulmonary disease.

Euler and Liljestrand (1948) using cats as experimental models were the first to show that experimentally, hypoxia could cause an increase in PAP. Later studies showed that a hypoxia induced pulmonary vasoconstriction was the main cause of this pulmonary hypertension (Lloyd, 1964) as well as a hypoxia-induced increase in cardiac output and myocardial contractility (Aviado, 1965).

It is currently believed that structural vascular changes are of little significance in the development of pulmonary hypertension, but severe or prolonged pulmonary hypertension can eventually induce anatomical changes such as sclerosis, fibrosis and hyperplasia of the pulmonary vasculature. These anatomical changes will then add a mechanical obstruction to the pre-existing functional vasoconstriction. A similar hypoxia-induced pulmonary vasoconstriction has also been shown to cause brisket disease in cattle. This disease which is normally manifested as congestive right heart failure induced by severe pulmonary hypertension, occurs in cattle suffering from hypoxaemia caused by movement to high altitudes (Bisgard 1977).

Despite numerous studies, the exact mechanism of the hypoxic induced pulmonary vasoconstriction remains unresolved. It is believed however that the effect is induced by local alveolar hypoxia rather than by hypoxaemia in the alveolar arterioles or venules (Harvey 1965, Bisgard, 1977).

It is believed that the main purpose of this effect is to divert blood from local diseased and consequently hypoxic areas of the lung to areas which are better aerated. This is thus apparently beneficial to a subject with focal pulmonary disease, but in case of diffuse pulmonary disease with consequent generalised pulmonary hypoxia, the general pulmonary vasoconstriction is detrimental to the subject.

Although it appears to be a local effect, Kazemi et al. (1972) found that cervical sympathectomy partly decreased the response and they concluded that it had two components, one local and one mediated through the sympathetic system. However, Malik and Kidd (1973a) found that α or β adrenergic blockade had no effect on the hypoxic response suggesting that the effect was purely local. As the effect has been well demonstrated in isolated perfused lungs and even in isolated pulmonary vascular tissues, it appears that it is primarily a local one (Bisgard, 1977). In humans only the smaller pulmonary arterioles with a lumen diameter of 100 - 1,000m μ have any appreciable muscle and these muscular arterioles are the likeliest site of this pulmonary vasoconstriction (Bristow et al. 1966).

Humans clinically affected with chronic obstructive lung diseases (COLD) are frequently hypercapnic and acidotic as well as being hypoxaemic (Thurlbeck 1976), pulmonary hypertension in these patients is probably related to all three factors as hypercapnia and acidosis are also believed to cause pulmonary vasoconstriction (Harvey 1965, Rudolph and Yuan 1966).

The effects of this reflex are well understood in man and as the results of more long term pathophysiological studies become available, it appears that even mild pulmonary hypertension of a level once believed not significant can cause RV strain if persistent (Silber and Katz, 1975). This is believed to be due to the inability of even mildly constricted pulmonary vasculature to accommodate normal increases in blood flow such as occurs during exercise, without then developing pulmonary hypertension.

In most cases of pulmonary hypertension, congestive heart failure does not occur, because the RV can compensate for the increased workload by developing a higher systolic pressure to adequately perfuse the pulmonary vascular bed, despite its increased resistance. The diastolic right ventricular and right atrial pressures remain at normal levels in these cases. In most cases however this RV and pulmonary hypertension are completely reversible and besides some possible hypertrophy the RV myocardium shows no permanent adverse changes (Bristow et al. 1966).

For a variety of reasons including the occurrence of very raised or very prolonged pulmonary hypertension or intercurrent disease, RV compensation is inadequate in some subjects despite RV hypertrophy. RV end-diastolic volume and RV diastolic pressures will then become raised and clinical right heart failure will ensue (Bristow et al. 1966).

III CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN THE HORSE

INTRODUCTION

Chronic obstructive pulmonary disease has been recognised for many years as being one of the major afflictions of horses (Axe, 1906). It is believed that Aristotle in 333 B.C. recorded the first description of this disease, when he described an incurable disease of horses associated with a drawing in of the flanks (Smith, 1924). This disease has been known by many names including in English language 'broken wind', 'heaves', 'emphysema', 'chronic alveolar emphysema', and 'pulmonary emphysema', in German 'Dämfigkeit', and in French 'pousse' (Sasse, 1971). More recently on the basis of respiratory function studies in affected horses, which indicated that airway obstruction played a major role in this disease, the term 'chronic obstructive pulmonary disease' (COPD) has been adopted (Sasse, 1971; Beltran, 1973; McPherson et al., 1978). In contrast to human chronic obstructive lung disease (COLD) which refers to a group of chronic pulmonary diseases with similar functional disturbences, equine COPD appears to refer to a single pulmonary disease.

Over the last two centuries there have been numerous publications dealing with this disease but they were largely confined to descriptions of clinical signs and empirical treatments. Until recently there have been no critical studies dealing with the aetiology, functional disturbances or pathology of this syndrome. Most authors have without any evidence compared equine COPD with the chronic and incurable pulmonary emphysema syndrome of man.

AETIOLOGY

In the past COPD was believed by many to result from over-work while on a high roughage diet, which distended the animal's abdomen and prevented complete diaphragmatic expansion. When the working horse tried to forcibly expand its lungs against this obstruction it allegedly caused alveolar rupture and emphysema.

A later theory suggested by Gillespie and Tyler (1969) was that a hereditary deficiency of alpha-1-antitrypsin which predisposes to the development of panacinar emphysema in man might also predispose to COPD in horses. However studies by Breeze et al. (1977) have shown no evidence of alpha-1-antitrypsin deficiency in COPD affected horses.

It was suggested by Larsson (1936), Cook (1965) and Eyre (1972) and later shown by McPherson et al. (1978, 1979A, B) that COPD is due to a hypersensitive type reaction, in susceptible horses, to the inhalation of fungal antigens, particularly those of Micropolyspora faeni and Aspergillus fumigatus. These moulds commonly occur on hay or straw which has been stored with an excess moisture content, with subsequent overheating and mould growth. McPherson et al. (1979B) have shown that exposure of asymptomatic COPD affected horses to these moulds can induce the clinical disease. This can be done naturally by stabling them in an environment contaminated with dust from mouldy hay or straw, or by artificial inhalation challenge with nebulised mould extracts.

EPIDEMIOLOGY

It appears that COPD was of great significance in the 18th and 19th centuries especially amongst draught horses (Axe, 1906; Smith, 1924). With the decline in the large stables of draught horses due to the development of the internal combustion engine, the prevalence of this disease has decreased somewhat but in the few remaining stables today where large numbers of draught horses are maintained in crowded conditions, the author has observed that this disease can still be widespread and severe.

Cook (1965) has observed that COPD is also very common in ponies, hunters and show jumpers and attributes this to the high proportion of their time which these groups of horses are stabled, as compared to thoroughbreds in which the incidence of COPD is very low. The current investigation of the Edinburgh workers suggests that stabling under overcrowded conditions or with poor ventilation predisposes to COPD, probably because this increases the exposure of the horse to moulds in the hay or bedding (McPherson et al., 1979B).

Clinical Signs

A classical and near pathognomonic clinical sign of COPD is an increased and usually biphasic abdominal expiratory action often called a 'heave'. Other major clinical signs associated with COPD are decreased work performance, chronic cough, increased and/or wheezing respiratory sounds, chronic nasal discharge (Cook, 1965; Sasse, 1971; McPherson and Lawson, 1974; McPherson et al., 1978).

Respiratory Function Disturbances

It was formerly believed that the respiratory function disturbances in COPD were irreversible. Obel and Schmiterlow (1948) showed by intrapleural catherisation that increased intrapleural pressures changes (MAX Δ Ppl) occurred in this condition, presumably caused by increased airway resistance. More significantly they showed that this airway obstruction could be partially reversed by atropine, thus indicating that it was at least a partly functional obstruction.

Amonst other authors who have since found increased intrapleural pressure in this condition are Gillespie et al. (1966), Sasse (1971) and Muylle and Oyaert (1973). Arterial blood gas studies by Gillespie and Tyler (1969), Sasse (1971), Beltran (1973) and Bergsten (1974) have shown that a normocapnic hypoxaemia is present in clinically affected horses. The results of the Edinburgh workers have confirmed these findings and they have additionally shown that remission of these functional disturbances can be induced in a high percentage of clinically affected horses by removing them from contact with the aetiological agents. This can be achieved most effectively by bedding them on peat and feeding them a proprietary complete cubed diet, or less effectively by use of mould free hay and stray or by keeping the horses fully outdoors.

Ancillary Diagnostic Tests

The main parameters currently used for COPD diagnosis by the Edinburgh workers, are intrapleural pressure (Ppl) measurements by use of an intraoesophageal balloon and

arterial oxygen partial pressure ($P_a O_2$) measurement. This group have found a maximal intrapleural change (MAX $\triangle$ Ppl) of $\geq$ 6 mm Hg and $P_a O_2 \leq$ 82 mm Hg in COPD affected horses. Chest radiography has also been used as an aid to diagnosis. Further tests used to determine the aetiology in particular cases, include intradermal testing and inhalation challenge with the aetiological agents and examination for serum precipitins against these agents.

Pathology

Possibly because of the longstanding but unproven analogy between equine COPD and human pulmonary emphysema, most authors have recorded that pulmonary emphysema is the major pathological lesion in COPD (Alexander, 1959; Cook and Rossdale, 1963; Gillespie and Tyler, 1969; Jubb and Kennedy, 1973). However, objective studies by Thurlbeck and Lowell (1964), Sasse (1971) and recently by Nicholls (1978) who used COPD affected horses referred by the Edinburgh group, have shown that diffuse bronchiolitis is the main and usually the sole lesion in this disease, with some limited secondary pulmonary emphysema in a proportion of cases.

IV RIGHT HEART BLOOD PRESSURE MEASUREMENTS IN HORSES AFFECTED WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

The relationship between chronic pulmonary disease and secondary cardiovascular disease appears to have been ignored until recently in veterinary work, but in the last few decades some reports have been published on cardiovascular changes in horses suffering from COPD. In the majority of these studies terms such as heaves and emphysema have been used to describe this syndrome, but in this review the term COPD will be used regardless of the authors' original terminology.

Using a conventional saline filled catheter and an aneroid manometer Desliens (1935) measured vena caval, right atrial and right ventricular blood pressures of horses suffering from COPD, but does not appear to have measured the potentially more useful PAP. He thus appears to have been the first author to have studied in horses the relationship between pulmonary disease and alterations of the right heart circulation. Desliens gave no details of how he selected his COPD affected horses and whilst he noted elevated right ventricular pressures in this disease he did not give the normal right heart pressures used for comparison.

He noted that right heart pressure changes in the COPD affected horses were due as much to respiratory related intrapleural pressure changes as to cardiac contractions. He recorded diastolic right ventricular pressures of between -10 mm Hg to +20 mm Hg and right ventricular systolic pressures of between 60 to 100 mm Hg. These pressure values must be

interpreted with caution, because the type of manometric system used has inadequate frequency response to accurately measure blood pressure and would overdamp the recordings, leading to an underestimation of systolic pressures and an overestimation of diastolic pressures.

Alexander (1959) noted that horses with longstanding COPD could eventually develop clinical right heart failure including ventral oedema, but he did not specify whether this statement was made on personal experience. In the appendix of Alexander's article, Grover (1959) described some cardio-pulmonary measurements made on one normal horse and on one horse stated to be suffering from COPD. No clinical details about the COPD affected horse were given. Grover recorded a PAP of 88/35 mm Hg in the COPD affected horse and 42/20 mm Hg in the normal horse. Grover appears to be the first author to have recorded pulmonary hypertension in equine COPD, which he suggested was due to a loss of pulmonary capillaries in the affected lungs, causing increased pulmonary vascular resistance.

Studying right ventricular pressures of three normal horses and three COPD affected horses Sporri and Schlatter (1959) found systolic right ventricular hypertension (mean 73/-6.0 mm Hg) in the diseased horses, as compared to the controls (mean 45/+1.0 mm Hg). No clinical or respiratory function details of these horses were given, but the authors state that post mortem examination of two of the COPD affected horses revealed marked emphysema, bronchiolitis and right ventricular hypertrophy in both animals but no details of ventricular weights or wall thicknesses were given. The occurrence of

right heart failure in horses with advanced COPD was reported by Salutini (1959) who used the term cor pulmonale to describe this cardiac disease. As Salutini did not perform any respiratory function tests or cardiac catheterisation, his diagnosis of COPD and particularly of cor pulmonale must be cautiously interpreted.

Eberly et al. (1966) measured systolic and diastolic right ventricular pressures, mean pulmonary artery pressures and cardiac output in 24 normal and twelve COPD affected horses. The COPD affected group was selected on clinical grounds only. These authors found a mean PAP in the diseased group of 45.9 mm Hg as compared to 34.0 mm Hg in the normal group yet surprisingly they did not observe corresponding differences in systolic RVP. This apparent discrepancy may be partly due to the raised systolic RVP they observed in normal horses (mean 63.9 mm Hg) which is a higher value than that recorded in normal horses by most other recent authors (Table 5:I) and was similar to the mean systolic RVP obtained in the COPD group (65.1 mm Hg).

Another possible explanation might be that the raised mean PAP was primarily due to increased diastolic PAP with little systolic PAP increase and consequently little systolic RVP increase. These authors used a site level with the dorsal aspect of the olecranon process as a hydrostatic baseline for all their measurements and as this site is anatomically lower than the pulmonary artery, (Beltran, 1973) this would cause an overestimation of the recorded PAP

values. These authors found that increased pulmonary vascular resistance occurred in the COPD, group which could account for the observed pulmonary hypertension.

They also tranquillised 16 horses, including six of the COPD affected horses with Proiopromazine before the measurements and the possible hypotensive effects of this drug on the recorded pressure measurements was apparently not considered. Despite tranquillisation their COPD affected horses had elevated heart rates (mean 63/minute) during the measurements unlike their control horses (mean heart rate 44/minute). These authors also studied peripheral blood pressures (PBP) in the control and in the COPD affected horses and observed no differences in PBP or in peripheral vascular resistance between the two groups.

Beltran (1973) studied right heart pressure in an unspecified number of horses which were adjudged by clinical and respiratory function tests to have COPD. A pneumograph recording obtained from a facemask was simultaneously made with the blood pressure recording in many instances. The pneumograph recording, while indicating increased intrapleural pressure changes in the COPD affected horses, could not quantify these changes. His right heart blood pressure records of COPD affected horses indicate the presence of marked respiratory related changes, particularly in PAP and to lesser extent in RVP and RAP. Unfortunately many of his published records have no pressure reference tables and therefore the actual blood pressure levels recorded cannot be ascertained.

Whilst he published the RVP values obtained from normal horses, he did not publish any normal pulmonary arterial pressure values, or RVP or PAP results obtained from COPD affected horses, although he stated that pulmonary hypertension occurred in these COPD affected animals.

Beltran noted that fright increased the RVP of normal horses and caused proportionally larger increases in the RVP of COPD affected horses. He also noted that RVP was raised after exercise in COPD affected horses but found no such RVP increase after exercise in normal horses. He concluded that the post-exercise increase in RVP in the COPD affected horses was due to an inability of the vascular bed in the diseased lungs to accommodate any large increases in cardiac output. Beltran did not state the speed of exercise or the degree of fitness of the horses used in these experiments.

Beltran also studied pulmonary arterial wedge (PAW) pressures in COPD affected horses and as discussed previously (Chapter 5 section I.) he frequently had to use a modified pulmonary wedge technique.

Despite the shortcoming of Beltran's technique, his studies consistently showed that no differences occur between the pulmonary arterial wedge pressures of normal horses and COPD affected horses. As the COPD horses had pre-existing pulmonary hypertension, his results indicate that a greater pressure gradient and consequently a greater pulmonary vascular resistance existed in the diseased group.

A comprehensive study of right heart blood pressures was

performed by Bergsten (1974) on twelve COPD affected horses. These animals were diagnosed as being COPD affected on the basis of clinical signs and arterial blood gas studies. Bergsten found that COPD affected horses had increased systolic, diastolic and mean pulmonary arterial pressures. He found pressures of 60/28 mm Hg with a mean of 44.0 mm Hg in COPD affected horses compared with levels of 45/22 mm Hg and a mean of 30 mm Hg in his control horses.

He also noted that at rest, systolic right ventricular pressures were elevated in his COPD affected horses but that their diastolic right ventricular and right atrial pressure values were similar to those of control horses. During treadmill exercises, PAP increases were recorded in both groups, but to a much greater degree in the COPD affected horses. Bergsten concluded that even in horses moderately affected with COPD, the pulmonary circulation was severely affected and that exercise further aggravated this secondary circulatory disorder. He showed by cardiac output studies that the pulmonary hypertension of COPD affected horses was primarily due to increased pulmonary vascular resistance and found no evidence of increased cardiac output in these COPD affected horses. Bergsten in addition found no change in the peripheral blood pressure or peripheral vascular resistance of the COPD affected horse.

DISCUSSION

This review suggests that COPD affected horses suffer from secondary pulmonary arterial and systolic right ventricular hypertension, which is primarily due to increased pulmonary vascular resistance, associated with this disease.

However, in most studies COPD was diagnosed on clinical grounds only and in some later reports including those of Beltran (1973) and Bergsten (1974) incomplete respiratory function studies and no fungal inhalation, skin or serology testing was used for COPD diagnosis.

It is therefore probable, particularly in the earlier studies, that some of the horses studied suffered from a respiratory disease other than COPD. McPherson et al. (1978) in a detailed study of 46 horses showing clinical signs suggestive of COPD found that only 75% of them could be definitely classified as being affected with COPD using their current classification parameters.

Although the relationship between the blood gas changes in chronic pulmonary disease and the secondary cardiovascular changes had been well established in man, no detailed study of their relationship has yet been reported in horses.

Whilst veterinary authors recording pneumographs along with blood pressures have noted large, respiratory related, right heart blood pressure changes in COPD affected horses, only a single concurrent intrapleural pressure recording has been performed and consequently no one has yet quantified the intrapleural pressure - right heart blood pressure relationship in this disease.

None of those who have observed pulmonary hypertension in COPD affected horses have tried to relate the degree of the hypertension to the severity of the clinical disease. All appear to assume that the severity of each animal's pulmonary

disease and right heart cardiovascular parameters are fixed but no evidence has been shown to substantiate this assumption, e.g. by repeating pulmonary function tests or right heart blood pressure measurements at intervals or attempting to influence the clinical disease by moving affected animals to different environments.

The reports have indicated that as in man the secondary cardiovascular alterations are confined to the right heart circulation and that the peripheral circulation is unaffected in COPD. Whilst some authors have recorded the occurrance of RV hypertrophy in COPD, little information is available regarding the incidence of RV hypertrophy amongst horses suffering from COPD.

CHAPTER 6.

MATERIALS AND METHODS

I RIGHT HEART CATHETERISATION AND BLOOD PRESSURE MEASUREMENT TECHNIQUES

INTRODUCTION

Detailed descriptions of techniques for right heart catheterisation in horses have been published by Gall (1967) who used a manometer tipped catheter and by Beltran (1973) who used a balloon tipped catheter but most right heart catheterisation studies in horses including those by Eberly (1964, 1966), Bergsten (1974) and Milne et al. (1975, 1977B) have been performed using non-balloon tipped, flow directed catheters. However none of these authors have given detailed descriptions of the techniques they used for their catheterisation and blood pressure measurements.

Because right heart blood pressures are much lower than peripheral blood pressures, the need for an accurate hydrostatic baseline assumes even greater importance when right heart pressures are being measured. Hydrostatic baseline establishment for right heart pressure measurements is discussed more fully in the angiography experiment in the following chapter (Chapter 7). An additional factor to be considered in establishing a baseline for right heart catheterisation is that the vascular chamber whose pressure is being measured is also subject to intrapleural pressure (Ppl) changes. Ideally both the vascular chamber and the external pressure reference point should be at the same atmospheric pressure. Because the continually changing Ppl cannot be duplicated on the external manometer, there cannot be an ideal external hydrostatic baseline for right heart blood pressure measurements (Beltran 1973). As many subjects with respiratory disease have greatly

increased Ppl, consequently Ppl related blood pressure change is of greater significance in these cases.

MATERIALS AND METHODS

Animals

Because previous studies (Chapter 3) indicated the lability of peripheral blood pressure and because Beltran (1973) has observed similar excitement induced right heart hypertension of horses, great care was taken during all catheterisations to prevent excitement. The horses were made accustomed to the laboratory, personnel and to the catheterisation technique before any pressures were recorded. Each horse, throughout its stay in the hospital was looked after and handled by the one attendant. For four hours prior to PBP measurements, horses were not fed any concentrates and those horses on a complete cube diet were starved, to prevent postprandial cardiovascular changes.

During recordings horses were loosely restrained by a halter only. Any horses selected for cardiac catheterisation which could not be adequately restrained by this means alone were omitted from all further cardiovascular investigation. It was felt that further restraint such as twitching or tranquilliser administration which could in themselves influence the blood pressure being measured would invalidate the measurements. Additionally the risks which fractious horses would pose both to personnel and equipment in the confined space of the laboratory also necessitated the policy of omitting such animals.

Equipment

The pressure recording system previously described for

direct PBP measurements (Chapter 2) was used. Two types of flow directed right heart catheters were used (Cardioflex 1150-09, and Normacath 115-20, Vygon U.K. Ltd.). The equipment was calibrated and operated as described for direct PBP measurements, except that a pressure range of 0-100 mm Hg was used for right heart pressure measurements. In addition to recording maximum-minimum values, mean blood pressure recordings were also obtained at the PA site. These mean pulmonary artery pressures, more correctly termed electronically integrated mean pressures, were obtained by electronically overdamping the pressure recordings to such an extent that cyclic blood pressure variation was suppressed. These mean pressure recordings were made at slow paper speeds as is customary (Mendel 1968). All measurements were made to the nearest mm Hg using the mean of ten consecutive pulse waves.

Catheter Insertion

The jugular vein was identified in the lower third of the neck and if the animal's coat was long, an area over the vein was clipped. The area was then swabbed with a 0.5 % w/v hibitane (chlorohexidine gluconate PBP) solution and subcutaneously infiltrated with local anaesthetic (2% lignocaine, Astra Chemicals Limited, Watford). Both types of catheters used (Normacath and Cardioflex) were supplied with a percutaneous introducer kit consisting of a 9 cm long plastic cannula with a tapered distal tip, fitted over a removable metal

trocar. The trocar had an external diameter equal to that of the cardiac catheter.

After preparing the catheterisation site, the operator's hands were scrubbed with an iodised soap (Pevidine surgical scrub, Berk Pharmaceuticals Ltd., Surrey). The sterile catheter and introducer kit were slowly flushed with connecting fluid. The jugular vein was distended by manual occlusion below the venipuncture site. The attached introducer trocar and catheter were percutaneously inserted into the jugular in a posterior direction.

The trocar and catheter were fully inserted into the vein and the trocar was then removed while keeping the insertion catheter fixed. The connecting fluid filled cardiac catheter was then fully inserted through the introducer catheter down the jugular vein and was then flushed with 20cc of connecting fluid and its proximal end was connected to the connecting tube by their luer fittings. Continuous low pressure flushing with connecting fluid was carried out from the manometer during this time, to prevent air bubbles trapping between the fittings.

Once assembled the manometer - catheter system was flushed with a further 60-80 cc of connecting fluid through a manometric stopcock. During PBP recordings, the manometer - catheter system was flushed at five minute intervals with 10-20 cc of connecting fluid both to remove air bubbles that may have come out of solution on to the internal catheter walls and also to prevent thrombus formation in the distal catheter lumen.

Pressure recording

After insertion of the catheter the recording initially obtained was from the pulmonary artery site, which was recognised by the characteristic triangular shaped pulse wave contour and the raised diastolic pressure levels (▷ 15 mm Hg) recorded. After positive identification of the PA site the catheter was slowly withdrawn into the right ventricle (RV), which was recognised by its characteristic rectangular shaped pulse wave contour and by its large rapid pressure fluctuations and low diastolic pressure levels. In larger breeds of horses, e.g. draught, as little as 10 cm of catheter had to be withdrawn before the change from PA to RV occurred, while in small ponies up to 40 cm of catheter had to be withdrawn.

After identifying the RV site, the catheter was again slowly withdrawn until a change in pulse contour and pressure level to those of the right atrium (RA) occurred. The RA site was identified by its low blood pressure levels and its very irregular pulse contour.

For PAP measurements the catheter tip was slowly moved back through the RV into the PA. The catheter was advanced 2-3 cm after the initial registration of a PA pulse to ensure that the catheter tip would definitely remain in the PA trunk. Depending on the temperament of the horse, the catheter was left in this position for up to 2-3 minutes until the animal settled down after the catheter manipulations, as adjudged by the animal's appearance and heart rate, before pressure levels were recorded.

To measure the pressure in the right ventricle, the catheter was slowly withdrawn from the PA trunk until the appropriate contoured RV recording was first registered. The catheter was then withdrawn a further 6 cm, and after allowing the animal to settle down and to allow any induced pressure oscillations to fade, right ventricular pressure (RVP) was measured. The site for recording the right atrial pressure was obtained by withdrawing the catheter until a RA pulse first appeared then further withdrawing it by 2-3 cm.

After the required recordings were obtained, the cardiac catheter was withdrawn through the insertion catheter which was then withdrawn. A swab was then pressed over the venipuncture site for some minutes to prevent haemorrhage. The manometer was repeatedly flushed with distilled water after use and was then filled with a 2% roccal solution which was left in situ until the manometer was again required. On the morning of catheterisation, the manometer was flushed with sterile distilled water to remove the disinfectant and was then slowly flushed with connecting fluid.

TECHNICAL RESULTS

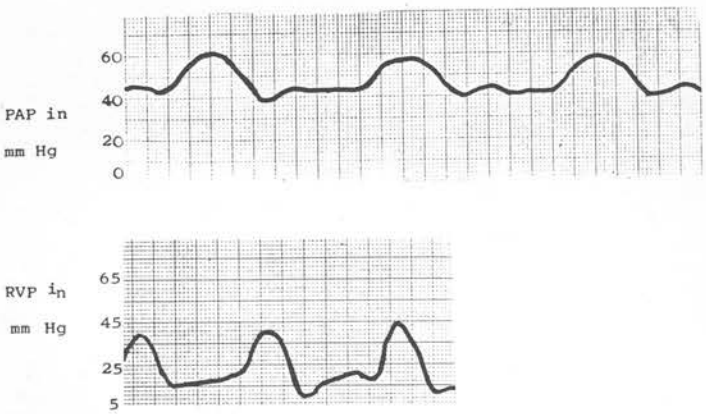
It was found that the familiarisation procedure was very effective, with most horses standing quietly during the catheterisation and pressure measurements. It was observed that tachycardia seldom occurred during the recordings except

during catheter manipulations and in these instances pressure recordings were delayed until the heart rate and blood pressure levels returned to resting values.

The catheterisation technique described proved satisfactory. Initially there was some difficulty in definitively identifying these different cardiac sites but this was mainly due to unfamiliarity with the normal pulse contours and pressure levels at the right heart sites. Another factor which made recognition of pulse contours difficult was over rapid (> 5 cm/second) or too slow (< 2 cm/second) recording paper speeds.

The most frequent artefact encountered was overdamping of the pressure recording, caused in most instances by small air bubbles trapped within the lumen of the manometer - catheter system (see Figure 6:1). This could normally be corrected by low pressure flushing of the system, from the manometer down the connecting tube and catheter. Less commonly, overdamping was found to be due to a loose connection between the manometer and the connecting tube or between the connecting tube and the catheter. On two occasions leaking stopcocks at the transducer were found to be at fault.

Frequently during PBP recordings, movement was induced in the connecting tube and the exteriorised catheter by the catheter manipulations and also in some animals by head movement. These connecting tube movements caused continuous irregular oscillations of the pressure recording,



Pulmonary artery pressure (PAP) recording from a symptomatic COPD affected horse and a right ventricular pressure (RVP) recording from a normal horse. Both recordings are grossly overdamped due to the pressure of air bubbles in the manometer-catheter system, consequently causing the recorded pulse contours to be rounded and flattened.

Figure 6:1.

PAP, PpL and ECG recording from a COPD affected horse. The PAP recording shows artefacts induced by connecting tube movement induced by the horse's head movement.

Figure 6:2.

Pulmonary arterial pressure (PAP), intrapleural pressure (Ppl) and electrocardiograph recording from a symptomatic COPD affected horse. The PAP recording is underdamped and the recording shows large oscillations, particularly during systole.

Figure 6.3.

Figure 6.4.

A flow directed right heart catheter which developed a knot intravascularly.

(see Figure 6:2). Occasionally, similar artefacts were observed in PBP recordings which could not be attributed to movement of the external parts of the catheter. It is possible that these oscillations were due to catheter tip movement induced by blood flow, a phenomenon commonly described as 'catheter whip' (Mendel, 1968). Another artefact less frequently encountered was oscillation in the pressure recording which occurred mainly during cardiac systole, see Figure 6:3. It was invariably found that these oscillations were due to underdamping of the pressure measurement system and this was caused by a recalibration error occurring after the system had been deliberately overdamped to record mean blood pressures.

On three occasions out of 170 right heart catheterisations, knots developed in catheters intravascularly. This was initially recognised during catheter withdrawal by increased resistance before withdrawal should have been completed, followed by complete resistance to further withdrawal. It is likely that the initial increased resistance was caused by the knot tightening at the venipuncture site. These knotted catheters were removed by first pulling laterally on the exteriorised catheter so that the skin and venous wall were distended outwards. At this stage the catheter knot could be palpated beneath the venipuncture site.

An area beneath the original venipuncture site was infiltrated with 1 cc of local anaesthetic. A stab incision was then made with a scalpel to enlarge the

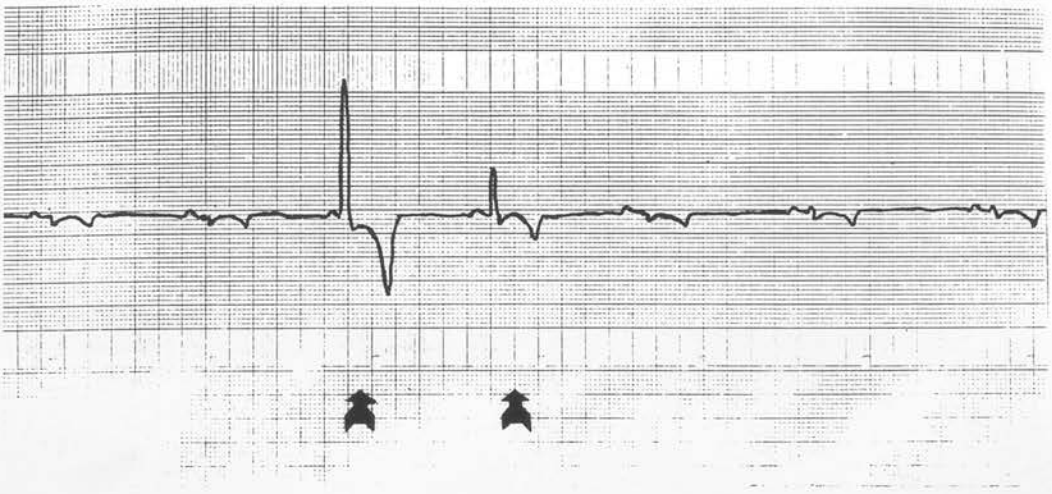
initial venipuncture site ventrally, taking care not to transect the catheter. The knot in the catheter was then smartly withdrawn through this incision and the remaining catheter was withdrawn. A single simple suture of monofilament nylon was inserted into the skin wound and local antibiotic ointment ('Streptopen', Glaxo Laboratories Ltd., Middlesex) was administered. No untoward sequelae developed in any horse. Figure 6:4 shows one of these catheters with a knot.

ECG recordings obtained during the cardiac catheter insertion usually showed the presence of ventricular extrasystoles (Figure 6:5), occuring at a time when the catheter tip was passing through the heart. In all cases this arrhythmia was transient and no clinical signs were associated with it.

No local or systemic infections were recorded after catheterisations even though the catheters' sterility could not be guaranteed during repeated or prolonged catheter manipulations and though antibiotics were not normally administered after catheterisations.

DISCUSSION

The catheterisation and pressure measurement technique described was found to be satisfactory, except for the high incidence of cardiac arhythmias during catheter manipulations and the relatively high (1.6%) incidence of intravascular catheter knotting.



ECG recording (LEAD I) obtained during the insertion of cardiac catheter. Two ventricular extrasystoles are present (See arrows)

Figure 6:5.

It is believed that catheterisation related arrhythmias are due to endocardial irritation by the catheter tip and they have been associated with transient collapse in horses (Bergsten, 1974). The use of balloon tipped catheters which have a softer tip and are flow directed to a much greater degree than the type used, in the present experiment also reduces the risk of catheterisation induced arrhythmias in horses (Beltran 1973, Milne et al. 1975), The high incidence of intravascular knotting recorded is also possibly related to the catheter type used, as Beltran using a balloon tipped catheter, did not record any intracardiac knotting during a large number of equine right heart catheterisations.

II INTRAPLEURAL PRESSURE MEASUREMENTS

INTRODUCTION

Intrapleural pressure (Ppl) measurements can be performed directly by percutaneous cannulation of the thorax as was performed by Gillespie et al. (1966) and Sasse (1971), or indirectly by using an intra-oesophageal balloon as described by McPherson and Lawson (1974) and McPherson et al. (1978). McPherson and Lawson (1974) have shown the indirect technique to be technically simpler and equally as

accurate as Ppl measurement by thoracopuncture. The potentially less dangerous indirect Ppl measurement technique was used in this thesis.

MATERIALS AND METHODS

A stomach tube with a thin rubber balloon attached to its distal tip was passed down the oesophagus in the conventional manner, until the balloon was in a mid thoracic position as adjudged by the length of stomach tube passed. The balloon was then slightly inflated by blowing into the proximal end of the stomach tube. The stomach tube was then quickly connected by plastic tubing to a pressure recording system similar to that described for blood pressure measurements (Chapter 2).

For Ppl recordings, zero baseline was set in the middle of the paper to enable both positive and negative pressure fluctuations to be recorded. The recording equipment was electronically calibrated with a 10 mm Hg signal and atmospheric pressure was used as zero baseline. The position of the oesophageal balloon was adjusted until maximal Ppl fluctuations were recorded.

TECHNICAL RESULTS

The Ppl recording system described proved satisfactory. Examples of Ppl recordings from a normal and symptomatic COPD affected horse are given in Figure 6:6. As well as the increased magnitude of Ppl recording in diseased horses, a notch frequently occurs in its ascending shoulder (see arrow in Figure 6:6) which corresponds with the 2nd part of the biphasic abdominal expiratory action (heave) of these horses.

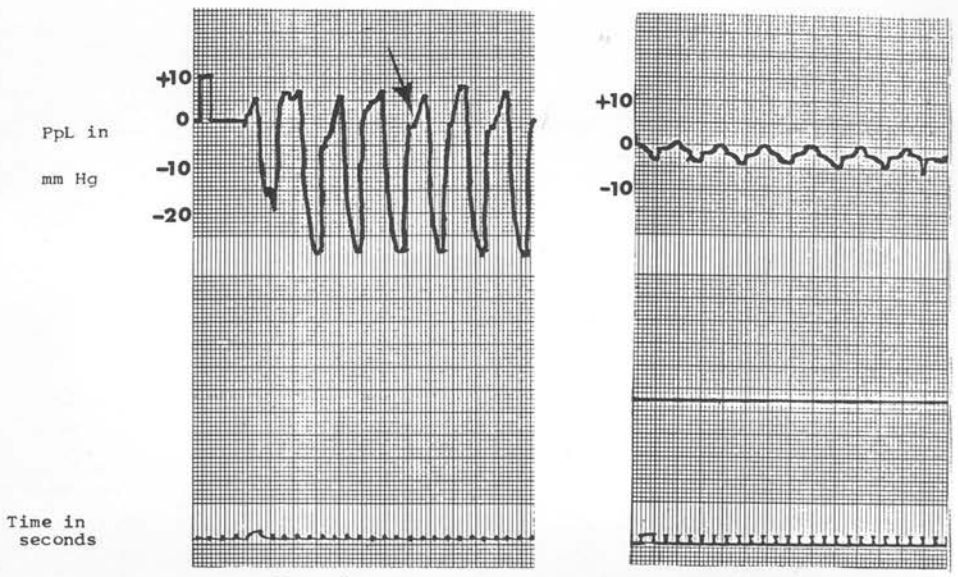
It was found that the intraoesophageal positioning of the balloon was critical and very slight positional adjustments could cause very large differences in the quality of the Ppl recording (see Figure 6:7). Occasionally oesophageal contractions caused artifactual increases in the Ppl recordings (see Figure 6:8). Coughing caused very large and mainly positive Ppl changes which also caused large and sudden increases in right heart blood pressures (Figure 6:9).

III ARTERIAL BLOOD GAS AND pH MEASUREMENTS

MATERIALS AND METHODS

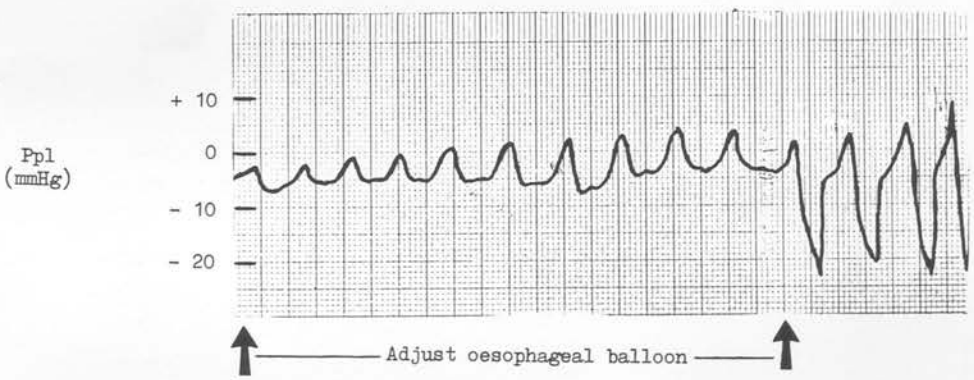
Arterial blood samples for P_aO_2, P_aCO_2 and pH analyses were obtained by carotid puncture in the lower neck using a 4 cm, 21 gauge hypodermic needle, after preparation of the site by swabbing with a 1% chlorohexidine PBP solution. Carotid puncture was indicated by a high pressure flow of bright red blood from the needle. The needle was then connected to a 20 cc glass syringe which had been flushed with sterile heparin 25,000/I.U./L (Pularin heparin; Evan's Medical Ltd., Liverpool), both to act as an anticoagulant and to eliminate airspace within the syringe. The syringe contained a brass washer to facilitate mixing of the heparin with the blood.

The sample was taken over a period of 30-60 seconds to allow several respiratory cycles to occur during the collection and to prevent the introduction of air at the



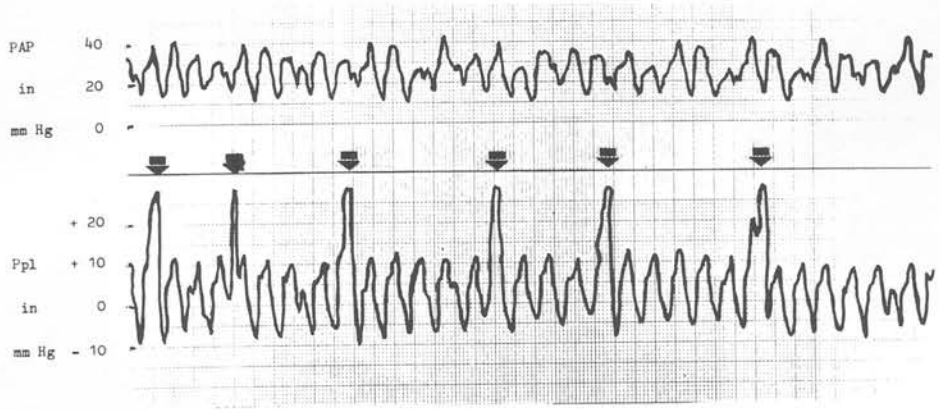
Ppl recordings obtained by intraoesophogeal baloon from a normal horse and a symptomatic COPD affected horse.

Figure 6:6.



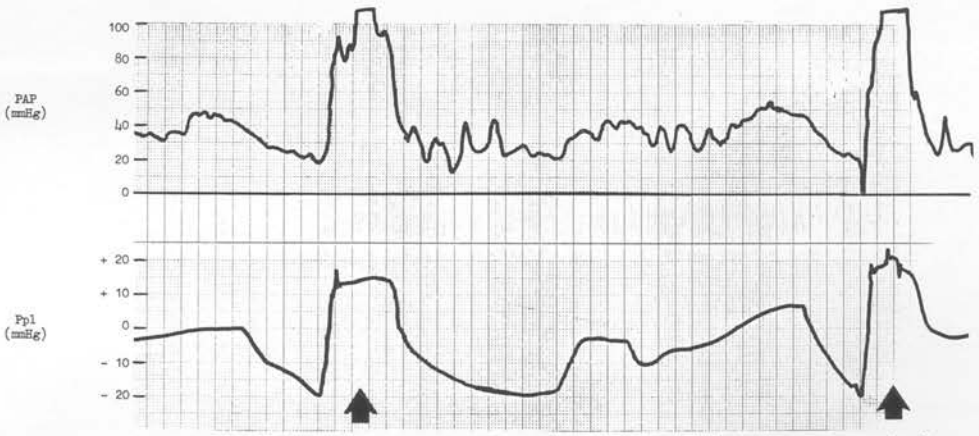
The effects of altering the position of the intra-oesophageal balloon on the quality of the intrapleural pressure recording.

Figure 6:7.



Simultaneous pulmonary artery pressure (PAP) and intrapleural pressure (Ppl) recordings from a symptomatic COPD affected horse. Oesophageal contractions in this horse causes artefactual increases in the Ppl recording (see arrows), but causes no changes in the PAP record.

Figure 6:8.



Simultaneous pulmonary arterial pressure (PAP) and intrapleural pressure (Ppl) recordings from a symptomatic COPD-affected horse. Coughing (at arrows) causes large positive Ppl changes which induce large sudden increases in PAP.

Figure 6:9.

syringe - needle junction which could occur with rapid high pressure aspiration. Approximately 15 cc of blood was collected and the syringe was then disconnected and sealed with a plastic cap and was shaken to mix the blood with the anticoagulant. The needle was then withdrawn and digital pressure was applied over the carotid-puncture site for some minutes to reduce haematoma formation.

The blood sample was normally analysed within minutes of collection using a blood gas and pH analyser (Corning 161, Corning Ltd., Essex). If any delay occurred between collection and analysis, the sample was stored in an ice bath. The altitude of the laboratory is 200 m. The blood gas and pH analyses were performed by the technical staff of the Department of Veterinary Medicine.

TECHNICAL RESULTS

It was found that the described carotid-puncture technique was very reliable and in the vast majority of horses a satisfactory sample was obtained on the first attempt. Most horses developed a haematoma about 3-7 cm in diameter after carotid-puncture but this invariably disappeared within 24-36 hours and no longer term adverse effects were observed, even after repeated carotid puncture. The blood gas analyser proved reliable and gave consistent results with duplicate samples.

IV ELECTROCARDIOGRAPHIC RECORDING

MATERIALS AND METHODS

Electrocardiographic (ECG) recordings were satisfactorily

obtained from standard leads using plate electrodes and electrode jelly (Camjel electrode jelly, Cambridge Instruments, Herts.) and an ECG recorder (ECG Function Unit 3442 Devices Ltd., Herts.).

DISCUSSION

ECG signals are electrically transmitted from the animal to the recorder and are therefore recorded almost instantly. Changes in blood and intrapleural pressures are transmitted from the animal to the pressure transducer by relatively slow pressure waves and consequently a time lag develops between the occurrence and the recording of a pressure event (Mendel 1968). This lag time must be borne in mind when correlating E.C.G., intrapleural pressure and blood pressure events.

CHAPTER 7.

Pilot Experiment No. 1.

I PULMONARY ARTERIAL WEDGE PRESSURE MEASUREMENT IN HORSES

INTRODUCTION

As noted in Chapter 5, pulmonary arterial wedge (PAW) pressures have been measured in the horse by only two authors, Beltran (1973) and Milne et al. (1975); both adopted modified wedge techniques using balloon tipped catheters.

MATERIALS AND METHODS

Four horses were used in this study; two normal Shetland geldings approximately 300 kg weight (Horses A and B) and two adult hunter mares one normal (Horse C) and one symptomatically affected with COPD (Horse D), (weights 520 and 550 kg respectively). Swan-Ganz, 110 cm balloon tipped catheters (Swan-Ganz model number 93-111-7F, Edwards Laboratories, Inc. Santa Anna, California) were used along with the pressure measurement system described in Chapter 6, using the Seldinger technique. The catheters were percutaneously passed into the jugular vein, at as low a site as possible.

I Conventional PAW Site

From the jugular vein the catheter was advanced to its full length into the pulmonary artery and pressures were then recorded and during the withdrawal of the catheter by 10-20 cm.

II. Modified PAW Site

The catheter was advanced fully into the pulmonary artery and its balloon then inflated with 1 cc of air. Pressures were then recorded with the balloon inflated and also during its deflation, while keeping the catheter position stationary.

Additionally blood samples were aspirated from the catheter before and after balloon inflation, with care being taken to fully remove all connecting fluid from the catheter before collecting the blood samples. Two conventional and two modified PAW pressure measurements were attempted on each of the four horses.

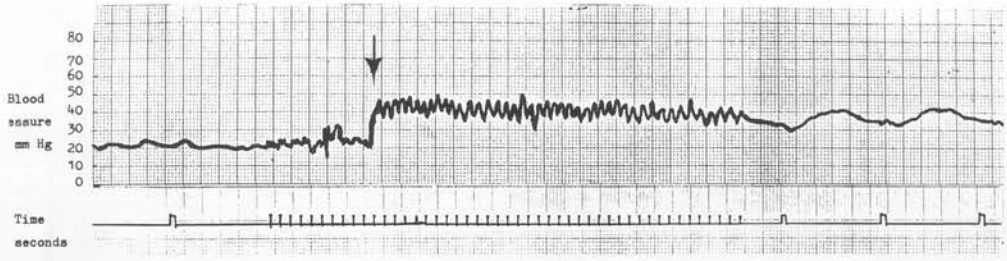
RESULTS

I. Conventional PAW site

When the catheter with its balloon uninflated was advanced to its full extent into the PA, normal pulmonary arterial pressure levels and contours were obtained in all experiments before and after the catheter withdrawal.

II. Modified PAW site

With the catheter fully advanced into the PA, when its balloon was inflated and subsequently deflated, normal PA pulses and contours were obtained in all attempts on horses A, B and C. In Horse D (COPD affected) one recording initially showed a low pressure (mean 18 mm Hg) recording with an irregular contour, which on balloon deflation assumed the pressure (mean pressure 35 mm Hg) and pulse contour characteristics of a P.A. pulse (see Figure 7:1). Attempts to repeat this modified wedge pressure position were unsuccessful. Analysis of blood aspirated from the modified pulmonary wedge site revealed blood gas levels of P_aO_2 66.2 mm Hg P_aCO_2 43.2 mm Hg and pH 7.391 and of blood from the P.A. gave P_aO_2 of 39.1 mm Hg, P_aCO_2 of 61.2 mm Hg pH of 7.361.



Modified pulmonary wedge pressure recording from a symptomatic COPD affected horse.
On deflation of the catheter tip balloon (see arrow) the recording changes to
a pulmonary arterial pressure recording.

Figure 7:1.

DISCUSSION

This experiment suggested that PAW measurements using 110 cm long catheters is unreliable in horses and even in small ponies. The reason for this is believed to be the inadequate length of the catheter, which is too short to enter and subsequently occlude a terminal pulmonary arteriole. Further support that this was the cause can be obtained from examination of radiographs obtained in the angiography study (Figure 7 :4). This catheter which was also 110 cm long was fully advanced into the PA and as can be seen in the figure its tip still lay in a relatively large vessel. It appears that when the catheters are advanced into the PA they tend to flow in a posterior direction and consequently to the most distant pulmonary arterioles.

Analyses of the blood aspirated from the modified pulmonary wedge site showed that its blood gas and pH composition was not that of pulmonary venous blood (i.e. fully oxygenated), as would be expected from a true pulmonary arterial wedge position but was a mixture of pulmonary arterial and pulmonary venous bloods. Beltran (1973) found similar blood gas and pH results using this technique. It appears possible that a fundamental difference exists between the normal and the modified PAW site.

Beltran (1973) used a similar length of catheter for his modified wedge measurements and he also found the technique unreliable even though all his studies were on small ponies. Milne et al. (1975) used both 130 cm and 160 cm balloon tipped catheters in adult horses (weight 431-545 kg) and found that

the 130 cm long catheter was frequently too short to obtain a modified PAW position and eventually these authors only used the 160 cm long catheter. It would appear that these authors had the catheters made to their own requirements as the largest human size available is 110 cm long.

PAW measurements would have been of benefit to indirectly assess pulmonary vascular resistance in the envisaged experiment on normal and COPD affected horses because facilities to measure cardiac output and thus to conventionally measure pulmonary vascular resistance were unavailable. The single modified PAW pressure obtained in this experiment (Figure :1) obtained from the symptomatic COPD horse and showed a large pressure gradient (17 mm Hg) between the PAW and PA pressures which indicates the presence of increased pulmonary vascular resistance in this horse. Similar findings were obtained by Beltran (1973) in COPD affected horses.

CONCLUSIONS

Pulmonary arterial wedge pressure measurements cannot be satisfactorily obtained in horses, using standard human right heart catheters.

Chapter 7.

Pilot Experiment No. 2.

RIGHT HEART ANGIOGRAPHY

INTRODUCTION

Because of the technical difficulties associated with the radiography of large tissue masses, thoracic radiography of horses is not widely used. Partly for this reason thoracic angiographic studies in horses have been greatly neglected. Detweiler and Patterson (1972) reported that they were unsuccessful in performing angiocardiography in horses. Beltran (1973) using contrast medium injected through a balloon tipped catheter, performed some limited angiocardiographic studies of horses. These studies were primarily to establish a hydrostatic baseline for intracardiac pressure measurements in this species. There appear to be no further reports of angiocardiography in the horse.

The aims of this pilot experiment were threefold.

1. To confirm that Beltran's hydrostatic baseline (2-3 cm above the point of the shoulder) is suitable for all right heart sites in which blood pressure was to be measured in the envisaged studies.

2. To visually examine the intravascular position of the catheter body while its tip was in the RA, RV and PA.

3. To assess the potential value of the technique to radiographically outline the cardiac chambers, e.g. to examine for possible RV or PA dilatation.

MATERIALS AND METHODS

Two normal 3 year old Shetland geldings and two normal

adult hunters (one mare and one gelding) were used in this experiment. The catheter used (Normacath 115-20, Vygon U.K. Ltd., 150 cm, 13 gauge) incorporated a radiopaque strip in its wall to allow radiographic observation of its position. The catheter was directed into the PA trunk by the previously described technique (Chapter 6). The catheter was then disconnected from the connecting tube and the proximal catheter end was sealed. The horse was walked 30 m to the radiography room. Radiographs of the horse's anterior thorax were obtained with the catheter in the PA site. Further radiographs were obtained 2 -3 seconds after the injection of 10 cc of sodium iothalamate, 70% W/V solution, a radiopaque angiography solution (Conray 420, May & Baker, Dagenham) into the catheter.

The radiographs were obtained using 115 kV and 300 mA for 0.04 seconds, using 'fast' films (Trimax XM, 100 NF, International Medical Technology Inc. Santa Clara, California) with an intensifying screen. Further radiographs were obtained of the anterior thorax with the contrast filled catheter's tip in the RV and RA sites.

In one horse, an attempt was made to radiographically outline a PA branch. The catheter was advanced to its full length and the posterior chest was radiographed while 50 cc of the contrast media was injected through the catheter with maximum manual force.

RESULTS

In the experiments where the 'radiopaque' catheter in the PA was not filled with contrast medium, the catheter could

not be radiographically identified. In these same radiographs the heart and great vessels were clearly outlined (see Fig. 7:2).

After injecting contrast medium into the catheter without altering its position, the catheter was clearly radiographically detectable except at its distal tip (Figure 7:3). The catheter is shown to enter the RA then bend ventrally into the RV and then loop dorsally to the PA before coursing posteriorly in the PA.

When the catheter was fully advanced into a PA branch and the contrast medium forcibly injected, the catheter tip is clearly defined (Figure 7:4). However, the objective to outline the PA branch was unsuccessfull and just a small stream of the contrast media can be seen flowing in the vessel. This was because a very slow injection rate < 4 cc/second was achieved, despite maximum pressure with both hands during the injection.

Examination of figures 7:2 and 7:3 indicates that Beltran's hydrostatic baseline (2-3 cm above point of shoulder), which can be adjudged from the radiographs as being above the scapulo-humeral joint, is level in the standing horse with the PA, RA and the root of the aorta. However, it is above the level of the RV and consequently the use of this baseline for RVP measurements would lead to an underestimation of RVP.

The study showed that during catheter insertion, the catheter tip moving ventrally into the RV, touches the RV apex and is then reflected dorsally with the blood flow to the PA. This was indicated by the consistent finding of a

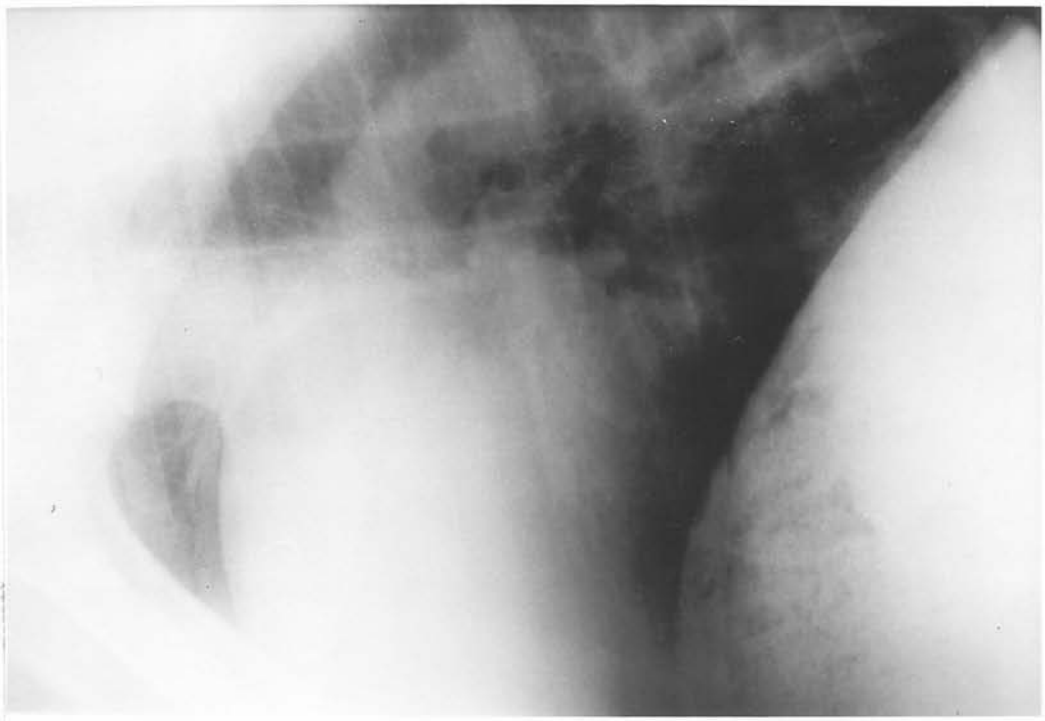


Figure 7:2.

Figure 7:3.

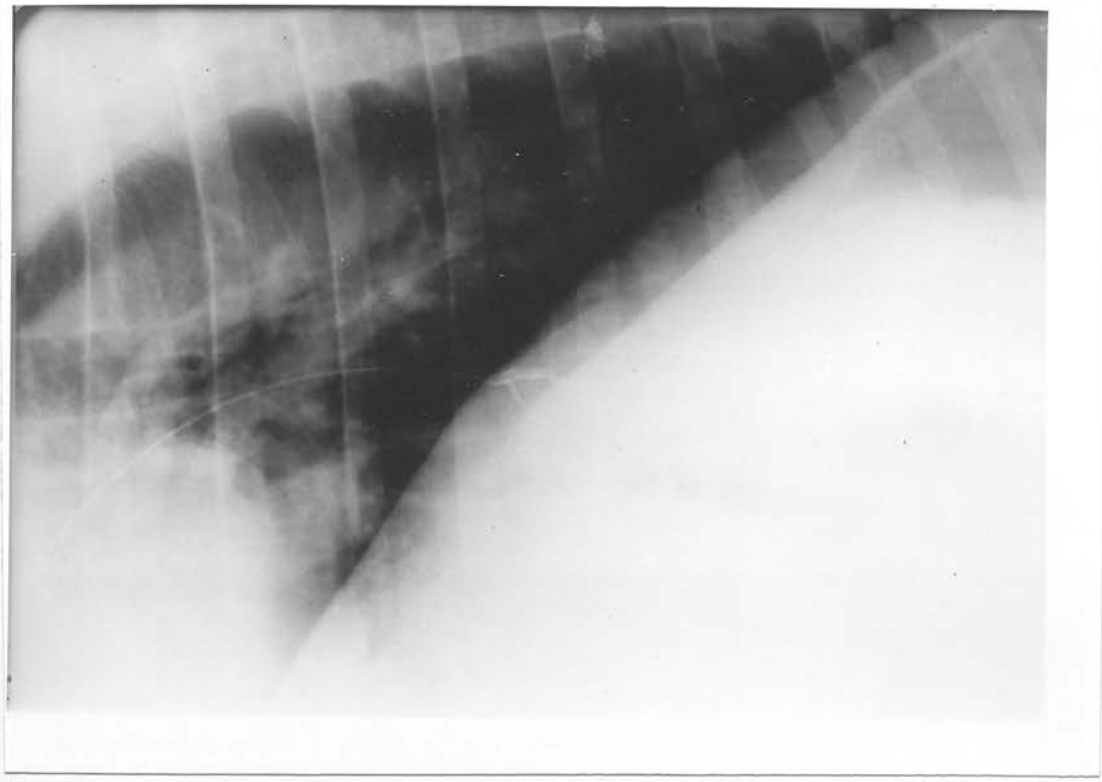


Figure 7:4.

catheter loop in the RV apex, whereas if catheter movement was fully flow directed, it probably would have looped dorsally in to the PA immediately after entering the RV base, without passing through the full depth of the RV chamber.

DISCUSSION

The results show that because of the large size of the horses' heart and because of its vertical disposition in the standing animal, there are significant differences between the horizontal levels of the RV and the RA, PA and aorta. Therefore a single hydrostatic baseline as is used in man and has been used to date in horses is unsatisfactory. The use of a single baseline is satisfactory in man because of the smaller cardiac size and more significantly because humans are normally catheterised while supine and thus the greatest intraventricular distance, i.e. base to apex is in the horizontal plane, in contrast to the situation in the horse.

It was decided to continue to use Beltran's hydrostatic baseline for PAP and RAP measurements. For the envisaged RVP measurements it was planned to place the catheter tip in the PA trunk and to withdraw it slowly into the RV. Once the change in the pulse and pressure from PA to RV was observed, the catheter would be withdrawn a further 6 cm to ensure that it would remain within the RV. The angiographic studies indicated that the catheter would be moving ventrally at this stage and consequently the catheter tip would then lie in the RV, 6 cm ventral to the PA trunk. It was planned to measure the RVP at this site without adjusting the transducer

height, but to add a correction of + 5 mm Hg to the recorded pressure, to compensate for the 6 cm baseline error (60 mm normal saline approx. = 5.0 mm Hg).

The radiographs indicate that the catheter tip touches the RV apex before being reflected dorsally into the PA and this could predispose to endocardial irritation and arrhythmias. In man, prior to the development of balloon-tipped catheters by Swan et al. (1970) PA catheterisation usually involved the use of radiography while directing the catheter tip, by using a variety of guide wires with various fixed bends. The apparent ease of PA catheterisation in horses with non balloon tipped catheters is possibly due to the greater blood flow and to the larger RV chamber which allows the catheter to loop readily after it reaches the RV apex.

The study showed that the angiography technique used would not be useful for outlining intracardiac structures because a sufficient volume of the contrast medium could not be injected fast enough. This was due to the resistance caused by the length and bore of the catheter. In man angiocardiography is normally performed using pressure pumps which can inject the contrast medium rapidly enough to outline any chamber. In order to obtain similar results in horses large bore, side holed catheters and larger volume, higher pressure angiographic pumps would require to be developed. Detweiler and Patterson (1972) have suggested that a contrast medium flow rate of 500 cc second would be required to outline the cardiac chamber of an adult horse and such pumps

are as of yet unavailable.

As noted the 'radiopaque' catheter used was not radiographically detectable on thoracic radiographs of adult horses unless filled with contrast medium. This is probably due to the relatively low radiodensity of the catheter, compared to the equine thorax. When filled with contrast medium the catheter was clearly outlined except at its distal tip. It was observed that delays between injection of the contrast medium and radiography would decrease further the radiographic clarity of the distal catheter. It would seem that in a catheter even with its proximal end sealed that considerable interchange occurs between the catheter contents and the blood stream at the distal catheter tip.

CONCLUSIONS

1. The use of a single hydrostatic baseline for right heart pressure measurements in horses, causes an underestimation of RVP and consequently a separate baseline has been established for this site.

2. Non balloon tipped, flow directed right heart catheters loop at the RV apex before being reflected dorsally into the PA.

3. Angiography of right heart vessels or chambers, using manual injection of the contrast medium is unsatisfactory.

CHAPTER 8.

STUDIES OF RIGHT HEART BLOOD PRESSURES IN NORMAL HORSES

INTRODUCTION

The survey of the literature indicated that right heart blood pressure measurements have been recorded by many authors (Table 5:1). Most of these studies have been satisfactorily performed although the results of the angiographic studies (Chapter 7) suggested that most previous author's right ventricular values are slight underestimates because of hydrostatic baseline error. As previously noted, simultaneous right heart blood pressure and Ppl measurements have only been performed previously in a single normal horse.

The present right heart blood pressure measurements from control horses were made to establish normal values under our experimental conditions and to examine the effects of Ppl changes on the right heart pressures and contours in normal horses.

Materials and Methods

Some details of the 12 horses used in this experiment are given in Table 8:1. These 12 horses had no history of chronic respiratory disease and no clinical signs of respiratory or cardiac disease. Additionally each animal's P_aO_2 and MAX Δ Ppl values were within the normal range, i.e. > 82 mm Hg and < 6 mm Hg respectively. Right heart blood pressures, Ppl and ECG recordings were obtained using previously described techniques (Chapter 6).

Results

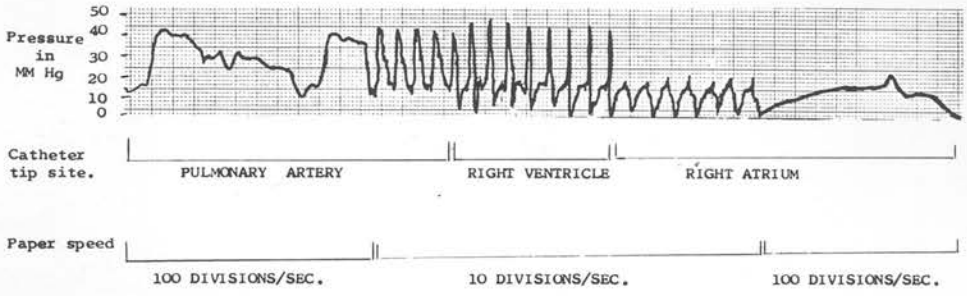
The recorded right heart blood pressures are presented

TABLE 8:1

Right heart blood pressure values obtained from normal horses.

Horses				Blood pressure in mm Hg						
No.	Breed	Age	Sex	Pulmonary artery			Right ventricle		Right atrium	
				Systolic	Diastolic	Mean	Systolic	Diastolic	Systolic	Diastolic
1	Hunter	8	Mn	28	12	18	34	12	8	1
2	Pony	3	F	39	12	25	45	11	9	3
3	Hunter	7	F	34	9	18	39	11	11	2
4	Pony	4	F	32	19	24	39	11	10	5
5	Pony	4	Mn	32	18	24	40	9	12	3
6	Pony	Aged	F	34	15	25	40	9	12	3
7	Pony	5	F	29	13	18	43	11	14	7
8	Thoroughbred	3	Mn	32	10	25	38	5	9	3
9	Pony	5	F	30	18	23	37	16	12	2
10	Pony	4	F	32	14	24	35	10	10	0
11	Pony	3	Mn	30	14	23	36	9	10	2
12	Hunter	3	Mn	32	12	24	37	8	10	1
Mean				32.0	13.77	22.50	38.58	10.17	10.58	2.67
+ - S.D.				2.14	3.06	2.84	3.18	2.62	1.68	1.87

(RV pressures corrected, see page 166)

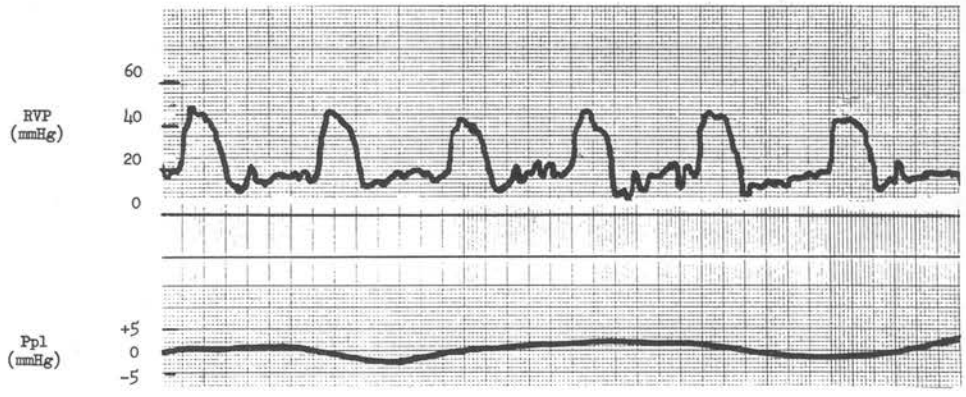


Pressure tracing from a catheter being withdrawn from the pulmonary artery trunk to the right atrium, recorded at two different paper speeds.

Figure 8:1.

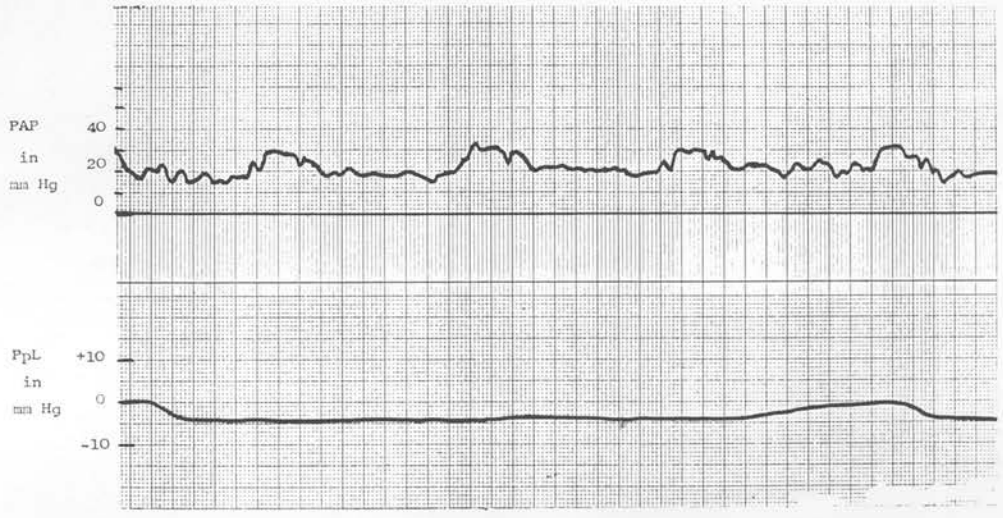
Simultaneous right atrial pressure (RAP), intrapleural pressure (Ppl) and ECG recordings from a normal horse. The small and negative Ppl changes have little effect on the level of contour of the right atrial blood pressure recording.

Figure 8:2.



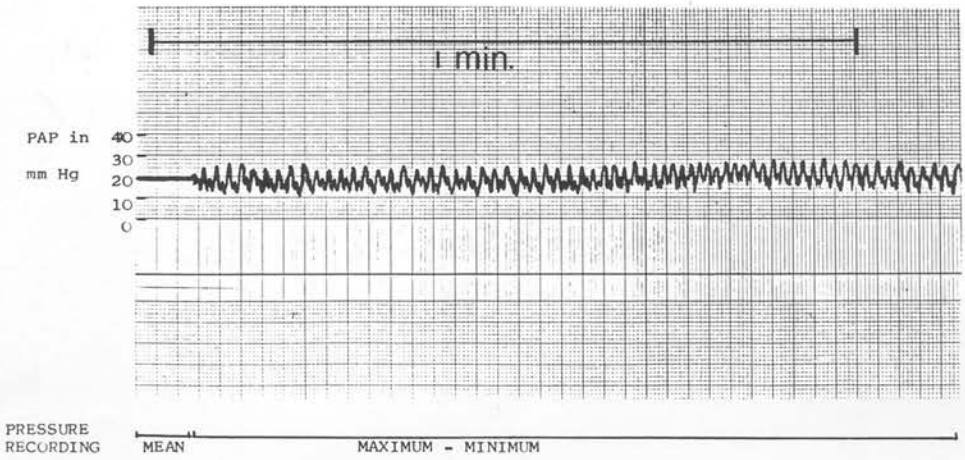
Simultaneous right ventricular pressure (RVP) and intrapleural pressure (Ppl) recordings from a normal horse.

Figure 8:3.



Simultaneous pulmonary artery pressure (PAP) and intrapleural pressure (PpL) recordings from a normal horse. The recordings show the negligible affects of normal PpL changes on the P.A. countour or pressure levels.

Figure 8:4.



Pulmonary artery pressure (PAP) recording from a normal horse. The PAP recording (mean PAP followed by maximum/minimum levels) shows the stability of PAP levels in normal horses.

Figure 8:5.

in Table 8:1. A heart rate of 46.0 ± 4.9/ per minute was recorded from these horses during the right heart blood pressure measurements. A pressure recording obtained during catheter tip withdrawal from the pulmonary artery to the right atrium (Figure 8:1) shows pressure recordings from PA, RV and RA sites. Simultaneous RAP, Ppl and ECG recordings from the right atrium showed respiratory related RAP variations of 1-4 mm Hg associated with Ppl changes of similar magnitude, e.g. Figure 8:2.

RVP and Ppl recordings showed RVP variations of 1-4 mm Hg associated with similar Ppl variation, e.g. Figure 8:3. Simultaneous PAP and Ppl recording e.g. Figure 8:4 shows pressure variations of 1-4 mm Hg in PAP associated with Ppl changes of 2-4 mm Hg. A further slower PAP record (Figure 8:5) shows the stability of normal PAP levels. As seen in Figures 8:2 - 8:5, blood pressure at all sites increased during expiration, and decreased during inspiration. Some slight respiratory related changes in the various pulse contour can also be seen in these Figures (8:2 - 8:4).

Discussion

The right heart blood pressure values obtained in this experiment (Table 8:1) are similar to those obtained by most of the recent authors who have measured these parameters (Table 5:1).

During inspiration, increased ventricular filling occurs and this induces a higher systolic RVP and consequently

increased PAP. However, inspiration also increases the capacitance of the pulmonary vascular bed which causes a PAP decrease. Additionally, the negative Ppl changes during inspiration have an equal pressure decreasing effect on intrathoracic vascular pressures, including PAP (Silber and Katz 1975).

An additional respiratory related factor which can significantly effect PAP, particularly in subjects with respiratory disease, is the effect of intra-alveolar pressure on the alveolar capillaries and consequently on pulmonary vascular resistance (Robbard et al. 1956, and Whittenberger et al. 1960). During expiration, increased intra-alveolar pressure obstructs the alveolar capillaries and causes increased pulmonary vascular resistance which increases PAP. The converse occurs during inspiration. In normal individuals, the overall effect of inspiration therefore is to cause a reduction in PAP. The converse occurs during normal expiration (Silber and Katz 1975).

In the present experiment, the small normal Ppl changes were shown to cause changes in pulse pressures of a somewhat similar magnitude at the various right heart sites. The pulse contours recorded are similar to those obtained by Gall (1967), Beltran (1973) and Bergsten (1974), Gall (1967) using a manometer-tipped catheter which can reproduce the pulse contours more accurately than a conventional catheter.

CONCLUSIONS

The right heart blood pressure values obtained by the author are similar to those obtained by most recent authors who have used acceptable measurement techniques. The recorded pressure levels and pulse contours at all sites were found to be stable except for small respiratory related variations in pressure levels of 1 - 4 mm Hg.

CHAPTER 9.

STUDIES OF RIGHT HEART BLOOD PRESSURES IN SYMPTOMATIC COPD AFFECTED HORSES

INTRODUCTION

The survey of the literature indicated that horses suffering from COPD develop pulmonary and systolic RV hypertension but in many of these reports the diagnosis of COPD was inconclusive. Additionally no author has referred to the actual stage of COPD during the blood pressure measurements. In this experiment it was planned to examine RAP, RVP and PAP values from horses which were conclusively shown to be affected with COPD and which were fully symptomatic at the time of the right heart blood pressure measurements, as adjudged by clinical and respiratory function examinations.

Other than the single recording of Grover (1959), there are no reports of simultaneous intrapleural pressure and right heart pressure recordings from horses affected with respiratory disease and consequently the relationship between these two parameters is not clearly understood in the horse.

MATERIALS AND METHODS

The COPD affected horses used in this experiment (Table 9:1) had been referred to the Department of Veterinary Medicine by veterinary practitioners for investigation of chronic respiratory disease. All the animals were affected with COPD as judged by the objective methods previously outlined (Chapter 5 and 6) i.e. all animals were showing clinical signs of COPD and had a MAX Δ Ppl $>$ 6 mm Hg and P_aO_2

<82 mm Hg at the time of cardiac catheterisation. The duration of the disease varied but most horses had been affected for many years. In these 10 symptomatic COPD affected horses alternate PAP, RVP and RAP recordings were simultaneously obtained along with Ppl and ECG recordings, using previously outlined methods (Chapter 6). The right heart blood pressure values obtained from these symptomatic COPD affected horses were compared by Student's 't' test with the pressure values obtained from the 12 control horses in the previous chapter (Chapter 8).

RESULTS

A heart rate (mean $\pm$ S.D.) of 41.6 $\pm$ 4.7 per minute was recorded during these blood pressure measurements.

Intrapleural pressures:

Mean intrapleural pressure levels recorded were MAX $\triangle$ Ppl 14.4 mm Hg, (MAX Ppl Exp. 9.1 mm Hg, MIN Ppl Insp. -5.3 mm Hg).

Blood pressure levels

The PAP, RVP and RAP values recorded are presented in Table 9:1. The results of the comparison between right heart blood pressures of normal and symptomatic COPD affected horses are presented in Table 9:2, and these show that maximum, minimum and mean PAP, maximum RVP and maximum RAP are significantly elevated in the diseased horses. Minimum RVP and minimum RAP levels did not differ significantly between the two groups ($P > .05$). As well as being elevated these right heart blood pressures

TABLE 9:1

Pulmonary arterial pressures (PAP), Right Ventricular pressures (RVP) and Right Atrial Pressures (RAP) (Maximum (MAX), Minimum (MIN) and Mean Pressures in mm Hg values from 10 symptomatic COPD affected horses.

Horses				Pressure in mm Hg			
Animal number	Breed	Age	Sex	PAP MAX/MIN	Mean	RVP MAX/MIN	RAP MAX/MIN
B 1	Hunter	Aged	F	43/23	30	60/7	21/3
B 2	Pony	10y	F	59/22	38	56/11	15/3
B 3	Pony	8y	Mn	60/40	46	70/11	20/8
B 4	Hunter	Aged	Mn	44/26	38	54/5	18/0
B 5	Hunter	8y	F	46/22	34	60/14	16/2
B 6	Polo Pony	6y	F	64/15	40	76/5	15/1
B 7	Hunter	9y	Mn	52/18	36	64/11	17/3
B 8	Draught	12y	Mn	45/22	34	51/10	12/4
B 9	Draught	15y	Mn	40/17	35	52/8	7/0
B 10	Hunter	12y	F	104/61	75	116/5	17/2
Mean				55.7/26.6	40.6	66.5/8.7	15.8/2.6
$\pm$ S.D.				18.85/13.91	12.82	18.89/3.16	4.0/2.3

(RV pressures corrected, see page 166)

TABLE 9:2

Comparison by Students' 't' test of pulmonary arterial pressures (PAP), right ventricular pressures (RVP) and right atrial pressures (RAP) obtained from 12 normal horses and from 10 horses symptomatically affected with chornic obstructive pulmonary disease.

Right heart blood pressure (mean ± S.D.) in mm Hg.				
	Control horses		Symptomatic COPD affected horses	
MAXIMUM PAP	32.0 ± 2.7	v	55.7 ± 18.85	**
MINIMUM PAP	13.8 ± 3.1	v	26.6 ± 13.91	**
MEAN PAP	22.5 ± 2.8	v	40.6 ± 12.82	**
MAXIMUM RVP	38.6 ± 3.2	v	66.5 ± 18.89	**
MINIMUM RVP	10.2 ± 2.6	v	8.7 ± 3.16	NS
MAXIMUM RAP	10.6 ± 1.7	v	15.8 ± 4.0	**
MINIMUM RAP	2.7 ± 1.9	v	2.6 ± 2.3	NS

** = $P < 0.01$ NS = $P > .05$

vary greatly from animal to animal (Table 9:1) with the greatest pressure variation occurring in maximum PAP and maximum RVP values.

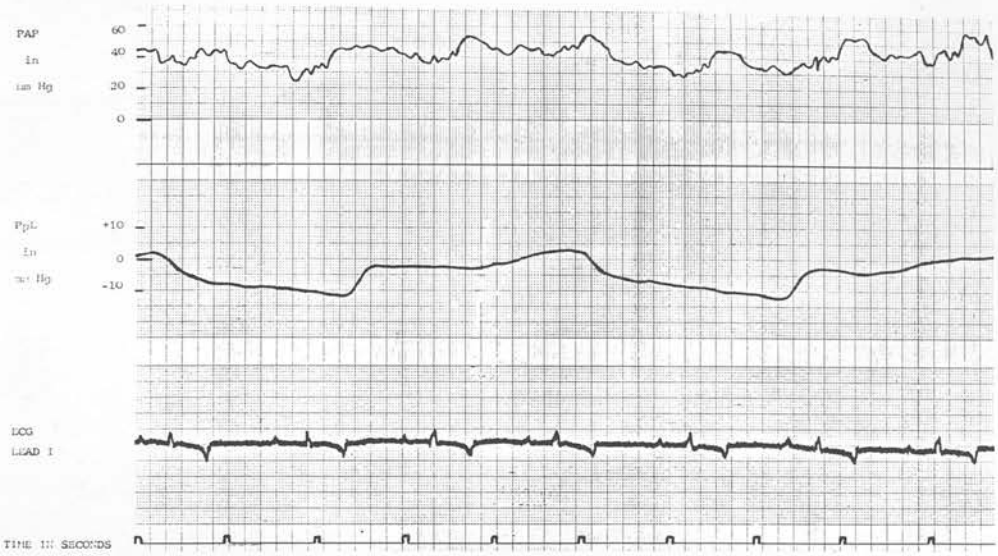
Respiratory related pressure and pulse contour variations

Pulmonary Artery

As well as the presence of inter-individual pressure variation, the blood pressure levels in individual animals varied from pulse to pulse. Figure 9:1, a simultaneous PAP, Ppl and ECG recording shows the elevated PAP with large variations in pressure levels between different pulses. In this recording the PAP contour is so influenced by the increased Ppl changes that the ECG recording is required to definitively identify the distorted PA pulse contours.

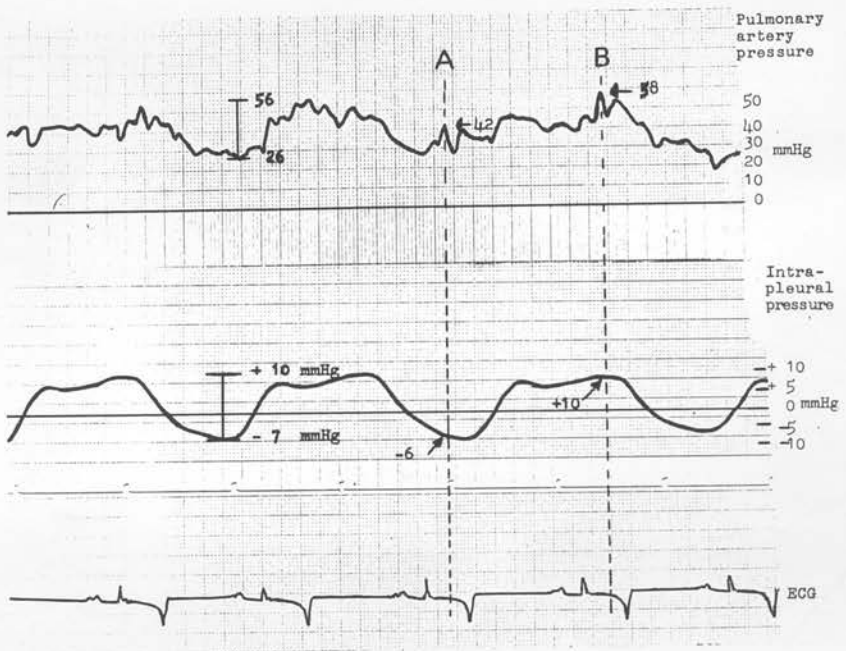
It can be seen that the highest PAP levels are obtained during peak expiration i.e. at MAX Ppl Exp. Conversely lowest PAP levels were obtained during peak inspiration (MIN Ppl Insp.). It is seen that if peak expiration does coincide with systole that highest PAP levels are obtained because of synergism between these two blood pressure increasing influences i.e. systole and raised positive Ppl changes.

It is difficult to accurately quantify the separate influences that Ppl changes and cardiac contractions have on PAP. However examination of a PAP, Ppl and ECG recording (Figure 9:2) in which systole occurs during, (A) peak inspiration (MIN Ppl Insp. = -6 mm Hg) or (B) peak expiration (MAX Ppl Exp. = + 10 mm Hg), shows a pressure difference



Pulmonary artery pressure (PAP), Intrapleural pressure (PpL) and electrocardiograph (ECG) recordings from a symptomatic COPD affected horse, in which the PpL changes are mainly negative (PpL - 12 to + 3 mm Hg). Maximum PpL = 15 mm Hg).

Figure 9:1.



Simultaneous PAP, Ppl, and ECG from a symptomatic COPD affected horse. A is systole at peak inspiration, B is systole at peak expiration.

Figure 9:2.

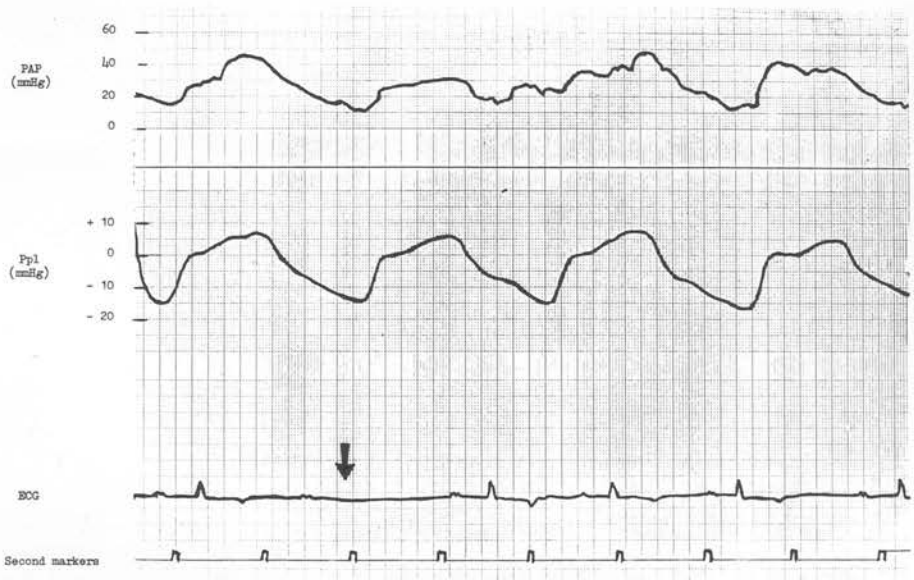
of 16 mm Hg (58-42) in systolic PAP associated with identical Ppl changes (MAX $\triangle$ Ppl = 16 mm Hg).

A recording (PAP, Ppl and ECG) obtained from a COPD affected horse also affected with a 2nd degree partial atrio-ventricular conduction defect (Figure 9:3) also provides a means of examining the effects of Ppl changes on PAP. A dropped beat in this recording (see arrow) indicates absence of ventricular activity and consequently PAP changes recorded during this beat, are due to Ppl changes. In this recording PAP is shown to increase by 21 mm Hg during the dropped beat and this was associated with an increase of 22 mm Hg in Ppl.

It can be seen from all three recordings (Figures 9:1 - 9:3) that the normal pulmonary arterial pulse contour is completely distorted by the large Ppl changes in these horses and in general the PAP contour closely resembles the Ppl contour.

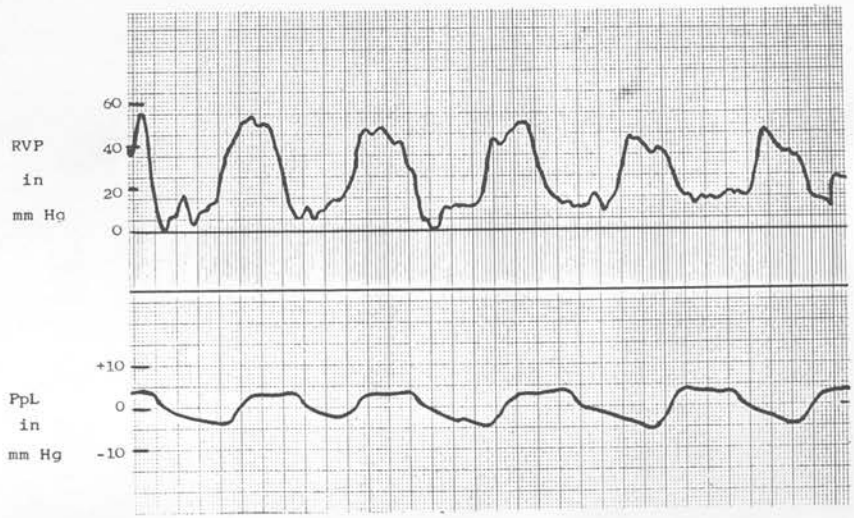
Right ventricle

There was also a very marked respiratory influence on RV pressures and pulse contours see figures 9:4 and 9:5. Although RVP levels were influenced by Ppl changes, maximum RVP levels were always recorded during systole and conversely minimum RVP was always recorded during diastole. In Figure 9:5 examination of the first two RVP pulses shows a difference of 8 mm Hg between their systolic RVP values (39 mm Hg and 31 mm Hg) associated with a Ppl difference of 29 mm Hg (24 mm Hg, - 5 mm Hg).



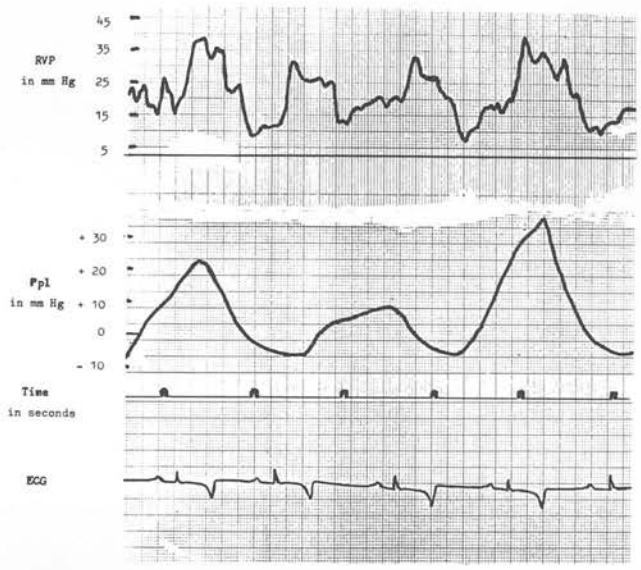
Simultaneous pulmonary artery pressure (PAP), intrapleural pressure (Ppl) and ECG recordings from a symptomatic COPD-affected horse with a partial atrioventricular heart block. The arrow indicates a dropped beat and at this stage the PAP continues to increase due to a positive Ppl change.

Figure 9:3.



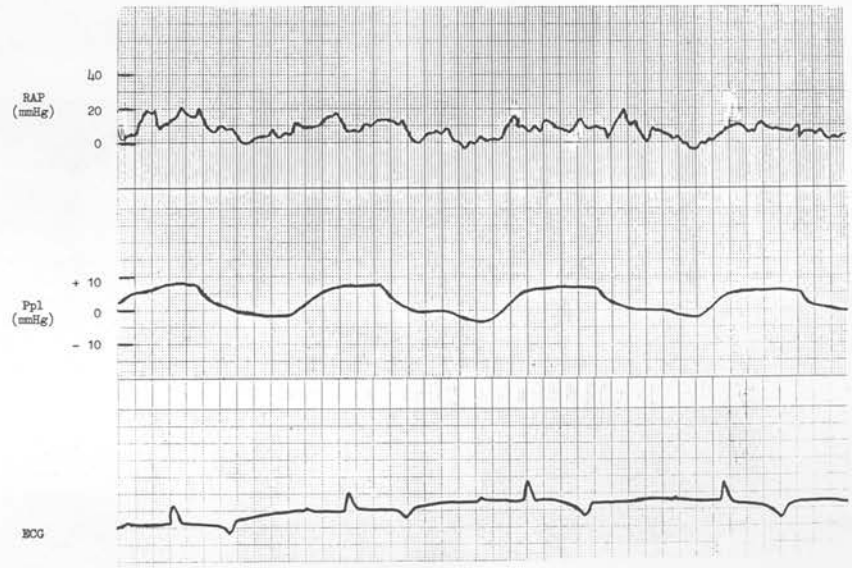
Simultaneous right ventricular pressure (RVP) and intrapleural pressure (PpL) recordings from a symptomatic COPD affected horse. Despite PpL related changes in RV pulse contour and pressure, maximum and minimum RVP still occur at systole and diastole respectively.

Figure 9:4.



Simultaneous right ventricular pressure (RVP), intrapleural pressure (Ppl) and ECG recordings from a symptomatic COPD affected horse. The large Ppl changes (ΔPpl > 43 mm Hg) greatly affects the RV pressure level and pulse contour.

Figure 9:5.



Simultaneous right atrial pressure (RAP), intrapleural pressure (Ppl) and ECG recordings from a symptomatic COPD-affected horse. The normal RAP contour is distorted because of the increased Ppl changes and its component waves cannot be identified.

Figure 9:6.

Although the RVP pulse contour was also altered by the increased Ppl changes, it always retained its rectangular like shape (Figures 9:4 and 9:5).

Right atrium

The normal low pressure and irregular RA pulse was greatly influenced by the increased Ppl changes that occur in COPD, see Figure 9:6. In this recording, the component atrial waves cannot be identified without referring to the concurrent ECG recording, because of respiratory relative alterations to the RA pulse contour and pressure. It was observed that Ppl changes caused pressure changes of similar magnitude at the right atrial site.

DISCUSSION

Blood pressure levels

Because peak blood pressures in COPD affected horses did not necessarily coincide with systole, it was decided to describe the peak blood pressures recorded as maximum pressures rather than as systolic pressures and conversely to describe the lowest blood pressure recorded as minimum pressures rather than as diastolic pressures.

The results showed that whilst PAP and maximal RVP levels were significantly increased in symptomatic COPD affected horses, minimal RVP or minimal RAP levels were not significantly changed. These results indicate that in the COPD affected horses, the RV had compensated for the increased workload caused by the pulmonary hypertension, i.e. by increasing its maximal pressure without the

development of any increased minimal RVP. This RV compensation prevented subsequent increases in minimal RVP and consequently in minimal right atrial pressure, which would then lead to general peripheral venous congestion and peripheral oedema, neither of which clinical signs had been observed in the 10 COPD affected horses.

An unexpected small but significant increase in maximal right atrial pressure was recorded in the COPD affected horses (Table 9:2) and it could be argued that its presence is evidence of right heart failure, but because the atrium had no increased workload, i.e. minimal RVP levels were not raised (Table 9:2), it would appear that the increase in maximal RAP was due to some other cause. A more rational explanation for the raised maximum RAP in the COPD affected animals is that they were caused by the increased positive Ppl changes, as the affected animals had a mean MAX Ppl Exp. of + 9.1 mm Hg which could readily explain the mean increase of 5.2 mm Hg recorded in these animals.

The presence of this severe pulmonary hypertension in horses clinically affected with COPD, indicates that an increased right ventricular workload is present in these animals and this could be a contributory factor to the poor performance usually observed in these animals. The mean PAP recorded from these COPD affected horses (55.7/26.6 mean 40.6 mm Hg) is similar to PAP recorded from COPD horses by other authors e.g. a mean PAP of 45.9 mm Hg recorded by Eberly et al. (1966) and PAP of 60/28 with a mean of 44.0 mm Hg recorded by

Bergsten 1974. Likewise the recorded systolic RVP of 66.5 mm Hg is similar to RVPs recorded in COPD horses by previous authors including values of 73.0 mm Hg obtained by Sporri and Schlatter (1959), 65.1 mm Hg obtained by Eberly et al. (1966) and 63.0 mm Hg obtained by Bergsten (1974).

The mean diastolic RVP of 8.7 mm Hg recorded in the present experiment differs from the value of - 6.0 mm Hg obtained by Sporri and Schlatter (1959) and of 15 mm Hg found by Eberly et al. (1966) but is close to the value of 11 mm Hg obtained by Bergsten (1974). It is likely that the differences between diastolic RVPs in the different studies is attributable to the different hydrostatic base-lines used when measuring RVP. This would have a greater overall effect on the low pressure diastolic RVP than on systolic RVP.

The recorded RAP in the present experiment of 15.8/ 2.6 mm Hg is comparable with the mean RAP of 10.4 mm Hg obtained by Bergsten (1974) in COPD affected horses.

Respiratory related variations

It is not surprising that respiratory related effects on pressure level and a pulse contour were much greater on the pulmonary artery and the right atrium as compared with the right ventricle. This is because the thin walled PA and RA chambers would respond more passively to Ppl changes than the thicker walled RV which additionally develops its own pressure.

It was initially thought that the simultaneous ECG recording, along with Ppl and right heart blood pressure recordings was superfluous, but as was quickly realised particularly with PA and RA recordings, the pulse contours and pressure levels were so distorted by Ppl changes, that systole or diastole could not be appreciated without use of an ECG recording. These Ppl related right heart blood pressure fluctuations in COPD affected horses are an excellent demonstration of the age old concept that the heart is a pump within a pump.

Because no evidence of RV failure was found, it was consequently decided that further right heart pressure measurements in symptomatic COPD affected horses should be concentrated solely on PAP measurements, unless some clinical evidence such as oedema, peripheral venous congestion or auscultatory evidence of pulmonary or tricuspid incompetance indicated that diastolic RVP or RAP value might be high, suggesting the presence of RV decompensation.

This seemed particularly advantageous for the envisaged longer term right heart pressure monitoring experiments, because it was likely that a continuous recording from the single PA site would be more useful than interrupted recordings from the RA, RV and PA sites. Recording from a single site would also prevent any possible hydrostatic errors caused by slight differences in the catheter tip position within chambers, due to constant catheter repositioning. Another advantage of recording from a single site is that it would reduce the possibility of animal disturbances with

consequent hypertension, which could be induced by constant catheter manipulation.

CONCLUSIONS

Horses symptomatically affected with COPD have pulmonary and systolic right ventricular hypertension, but no evidence of RV failure was observed. Nevertheless the marked pulmonary hypertension indicates that significant right ventricular strain is present in these horses.

Massive respiratory related changes occur in the right heart pressures and pulse contours, particularly in the pulmonary artery and the right atrium, because of large Ppl changes. These respiratory related changes were not as great on the right ventricular pulse.

CHAPTER 10.

STUDIES OF RIGHT HEART BLOOD PRESSURES IN ASYMPTOMATIC COPD AFFECTED HORSES

INTRODUCTION

As indicated in the review of the literature, equine COPD was believed to be irreversible until recently and consequently cardiovascular studies have not been recorded from asymptomatic COPD affected horses. Because large numbers of confirmed COPD cases, which were in various remission stages of the disease were available to the author, this offered an opportunity to ascertain whether the cardiovascular changes associated with this disease were reversible as has been shown to be the case in respect of the clinical and the respiratory function parameters.

Materials and Methods

Six of the 10 horses used in this experiment (Table 10:1) had previously been catheterised while symptomatic (Nos. B3, B4, B6, B7, B8, B9, in Table 9:1). The remaining 4 horses were also classified as being COPD affected using the previously described clinical and respiratory function examinations. For the present experiment, all horses were in a remission stage of the disease which was induced by removing the horses from the contact with the aetiological agents.

This was achieved by bedding the horses on peat moss and feeding them a complete cubed diet (Horse and pony cubes, Spillers, Liverpool). In most instances a minimum period of 1-2 weeks is necessary to allow the clinical signs of COPD to abate. Because of pressure of hospital space, right heart blood pressure measurements were normally performed on

asymptomatic animals as soon as possible in the remission period.

On the day of the catheterisation all horses had a MAX $\triangle$ Ppl of $<$ 6 mm Hg and a PaO_2 of $>$ 82 mm Hg, in addition to the absence of clinical signs of COPD. PA, RV and RA pressure recordings were obtained using previously described methods (Chapter 6).

RESULTS

A mean heart rate of 38.6/minute was recorded during the blood pressure measurements. The blood pressure measurements recorded are shown in Table 10:1. These values (mean $\pm$ S.D.) were compared with values obtained from the 10 asymptomatic horses (Chapter 9) by Student's 't' test in Table 10:2. They were also similarly compared with values obtained from the 12 control horses (Chapter 8) in Table 10:3.

The results (Table 10:2) show that maximum PAP, mean PAP and maximum RVP values of symptomatic COPD affected horses decrease significantly ($P < .01$) during remission stages of the disease thus showing that the pulmonary hypertension is reversible. However, during this remission period, their maximum and mean PAP values still differed significantly from those of normal horses (Table 10:3). There were no significant differences in minimum RVP or in RAP values between the asymptomatic COPD affected animals and the other two groups ($P > .05$) (Tables 10:2 10:3).

TABLE 10:1

Pulmonary arterial pressure (PAP), right ventricular pressure (RVP) and right atrial pressure (RAP) values obtained from 10 asymptomatic COPD affected horses.

Animal number	Breed	Age	Sex	PAP MAX/MIN	Mean	RVP MAX/MIN	RAP MAX/MIN
B 3	Pony	8y	Mn	34/24	30	35/11	-
B 4	Hunter	Aged	Mn	40/22	29	47/10	12/4
B 6	Polo Pony	6y	F	40/27	30	48/9	-
B 7	Hunter	9y	Mn	32/16	29	34/9	11/3
B 8	Draught	12y	Mn	42/16	29	42/8	11/12
B 9	Draught	15y	Mn	37/19	25	35/9	12/3
B 11	Hunter	8y	F	37/18	29	41/5	15/0
B 12	Hunter	13y	Mn	34/18	28	42/9	10/4
B 14	T.B.	7y	F	38/26	30	46/9	16/2
B 15	Hunter	6y	F	26/13	18	30/11	14/7
Mean				36.0/19.9	27.7	40.0/9.0	12.6/3.1
S.D.				4.69/4.65	3.71	6.18/1.70	2.13/2.03

TABLE 10:2

Comparison of pulmonary arterial pressure (PAP), right ventricular pressure (RVP) and right atrial pressure (RAP) values, (mean ± S.D.) obtained from the 10 asymptomatic COPD affected horses, with values obtained from the 10 symptomatic COPD affected horses in Chapter 9.

Blood Pressure in mm Hg			
	Asymptomatic COPD Vs.	Symptomatic COPD	SIGNIFICANCE
MAXIMUM PAP	36.0 ± 4.7	55.7 ± 18.9	**
MINIMUM PAP	19.9 ± 4.7	26.6 ± 13.9	NS
MEAN PAP	27.7 ± 3.7	40.6 ± 12.8	**
MAXIMUM RVP	40.0 ± 6.2	66.5 ± 18.9	***
MINIMUM RVP	9.0 ± 1.7	8.7 ± 3.2	NS
MAXIMUM RAP	12.6 ± 2.1	15.8 ± 4.0	NS
MINIMUM RAP	3.1 ± 2.0	2.6 ± 2.3	NS

NS = $P > .05$, * = $P < .05$, ** = $p < .01$, *** = $p < .001$.

TABLE 10.3.

Comparison of pulmonary arterial pressure (PAP), right ventricular pressure (RVP) and right atrial pressure (RAP) values (mean ± S.D.) obtained from the 10 asymptomatic COPD affected horses with values obtained from the 12 control horses in Chapter 8.

Blood pressures in mm Hg			
	Asymptomatic COPD Vs	Controls	Significance
MAXIMUM PAP	36.0 ± 4.7	32.0 ± 2.7	*
MINIMUM PAP	19.9 ± 4.7	13.8 ± 3.1	**
MEAN PAP	27.7 ± 3.7	22.5 ± 2.8	**
MAXIMUM RVP	40.0 ± 6.2	38.6 ± 3.2	NS
MINIMUM RVP	9.0 ± 1.7	10.2 ± 2.6	NS
MAXIMUM RAP	12.6 ± 2.1	10.6 ± 1.7	NS
MINIMUM RAP	3.1 ± 2.0	2.7 ± 1.9	NS

N.S. = $P > .05$, * = $P < .05$, ** = $P < .01$, *** = $P < .001$

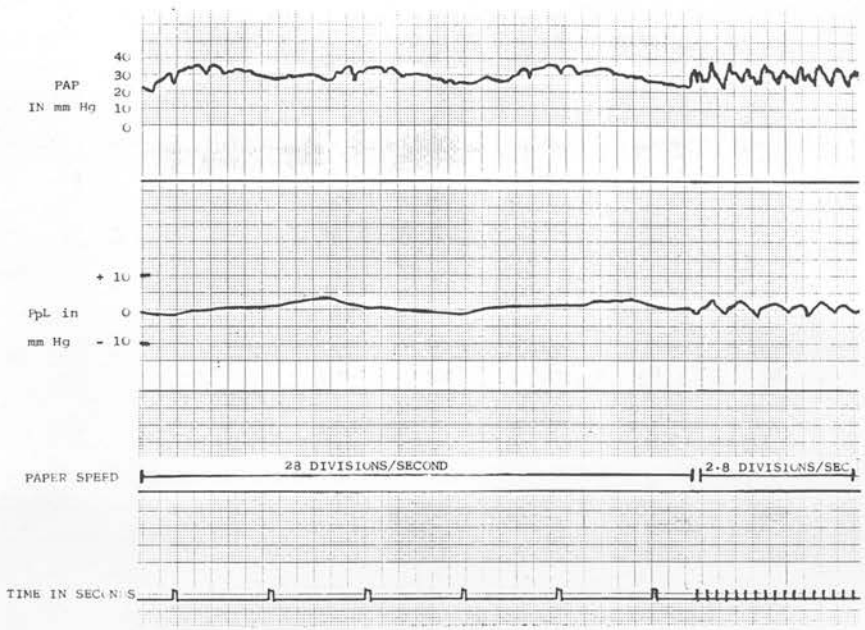
Right heart blood pressure recordings from asymptomatic COPD affected horses show pulse contours which are frequently of greater magnitude than those of normal horses, but the pulse contours and levels show little respiratory related variations as compared to symptomatic animals. An example of a PAP recording obtained from an asymptomatic COPD affected horse is given in Figure 10:1 and this is very similar to a normal PAP recording e.g. Figure 8:4, except for slightly higher pressure values.

Discussion

The reversibility of pulmonary arterial or right ventricular hypertension in horses with pulmonary disease has not been previously recorded. This reversibility suggests that the hypertension is due more to functional than to structural pulmonary cardiovascular changes.

Even though the PAP and maximal RVP levels significantly decrease during clinical remission of the disease, values from asymptomatic horses still differed significantly from control values suggesting that the pulmonary hypertension reversal was only partial.

Irreversible anatomical pulmonary vascular changes including sclerosis and fibrosis frequently occur in humans suffering from pulmonary hypertension especially if prolonged or severe (World Health Organisation 1963). Whilst some veterinary authors including Dahme (1960) and Gillespie and Tyler (1967) have also described similar pathological vascular changes in COPD affected horses, Nicholls (1978) found no evidence of such vascular disease in proven COPD affected



Pulmonary Artery Pressure (PAP) and intrapleural pressure (PpL) recordings from an asymptomatic COPD affected horse.

Figure 10:1.

horses, including many of the same horses used in this present experiment. Consequently the residual pulmonary hypertension in asymptomatic COPD affected horses cannot be attributed to anatomical vascular alterations. Most of the horses were examined early in the remission period. It appears likely that the spasm of the airways would be relieved but it is possible the anatomical pathological changes of COPD i.e. an infiltrative bronchiolitis, in these horses' lungs would not be fully reversed at the time of the right heart blood pressure measurements. Thus the horses may only have been in a partial remission stage and consequently the secondary cardiovascular changes would only be partially reversed. This aspect will be more fully discussed in the following chapter where right heart blood pressures alterations of COPD horses are correlated with some of their respiratory function parameters.

CONCLUSIONS

The pulmonary hypertension previously demonstrated in horses clinically affected with COPD was shown to be nearly fully reversible during remission stages of this disease. This finding indicates that the hypertension is mainly due to functional cardiovascular alterations.

CHAPTER 11.

STUDIES OF PULMONARY ARTERIAL PRESSURE AND CAROTID ARTERIAL BLOOD GASES AND pH IN NORMAL HORSES AND IN HORSES SUFFERING FROM COPD

INTRODUCTION

In human chronic obstructive lung disease (COLD) patients, a relationship between systemic arterial blood gases and pH alterations and pulmonary hypertension is well established, the hypertension usually being related to a combination of hypoxaemia, hypercapnia and acidosis (Thurlbeck, 1976). Gillespie et al. (1964), Beltran (1973) and Bergsten (1974) have recorded pulmonary hypertension in COPD horses which they found to be hypoxaemic with no evidence of hypercapnia or acidosis, but they have not attempted to correlate the hypoxaemia to the pulmonary hypertension. However their findings suggest that the pulmonary hypertension in COPD affected horses is related to hypoxaemia. However, none of the above authors have performed any PAP or arterial blood gases and pH studies on animals which were in remission stages of the disease.

Eyre (1972) found that in vitro, pulmonary vascular strips obtained from horses affected with COPD contracted when placed in contact with the aetiological agents of COPD, as also did their bronchial muscles. It is also possible that the pulmonary hypertension in symptomatic COPD affected horses could also be due to increased pulmonary vascular resistance caused by this mechanism.

In this study it was planned to measure PAP, P_aO_2, P_aCO_2 and arterial pH levels in normal, symptomatic and asymptomatic COPD affected horses and to examine for a relationship between these parameters.

Materials and Methods

Horses

The 39 control horses used (Appendix 11:1) were mainly experimental animals acquired for various other studies including cryosurgery, skin grafting, drug trials and as control horses for COPD studies. Fifty horses affected with COPD and currently symptomatic were used in this study (Appendix 11:2). Twentyone of these horses were also used while asymptomatic (Appendix 11:3). Remission of COPD signs was induced using previously described methods.

Techniques

PAP, P_aO_2, P_aCO_2 and pH levels were measured using previously described techniques (Chapter 6). The horses were classified as normal or COPD affected using the criteria outlined in Chapter 5 and 6. Animals shown to be COPD affected were classified as being asymptomatic if their P_aO_2 and MAX Δ Ppl values were within the normal range. The PAP values obtained from control, symptomatic and asymptomatic COPD affected horses which were previously presented in Tables 8.1, 9.1 and 10.1 are included with the present results.

Two COPD affected horses (B7, B12) had their PAP and P_aO_2, P_aCO_2 and arterial pH levels repeatedly measured over a 15-20 month period, during which time they were maintained under a variety of environmental conditions.

Statistical Analysis

P_aO_2, P_aCO_2, arterial pH and mean pulmonary arterial pressure values obtained from the three groups were compared in

pairs by the Student's 't' test.

Results

PAP, P_aO_2, P_aCO_2 and carotid blood pH results obtained from the control, symptomatic and asymptomatic COPD affected horses are presented in Appendices 11.1, 11.2 and 11.3 respectively and a summary of these results is presented in Table 11.1 and the results of statistical comparisons of these values are shown in Table 11.2. The results of the long term PAP and blood gas studies on animals B7 and B12 are presented in Figures 11.1 and 11.2. These show an inverse relationship between P_aO_2 and PAP levels in these 2 horses.

The results show that symptomatic COPD affected horses have significantly decreased P_aO_2 levels and significantly increased PAP levels as compared to the control horses. During remission of clinical signs of COPD in asymptomatic horses, the P_aO_2 levels increase significantly and the PAP levels decrease significantly. However, PAP and P_aO_2 values in these asymptomatic horses still differed significantly from control values. No significant change was observed in P_aCO_2 or arterial pH level between any of the three groups.

Discussion

Comparisons of PAP, P_aO_2, P_aCO_2 and carotid arterial pH values between control and symptomatic COPD affected horses indicated that the COPD horses were hypoxaemic but no evidence of hypercapnia or acidosis was found. This suggests that

TABLE 11.1.

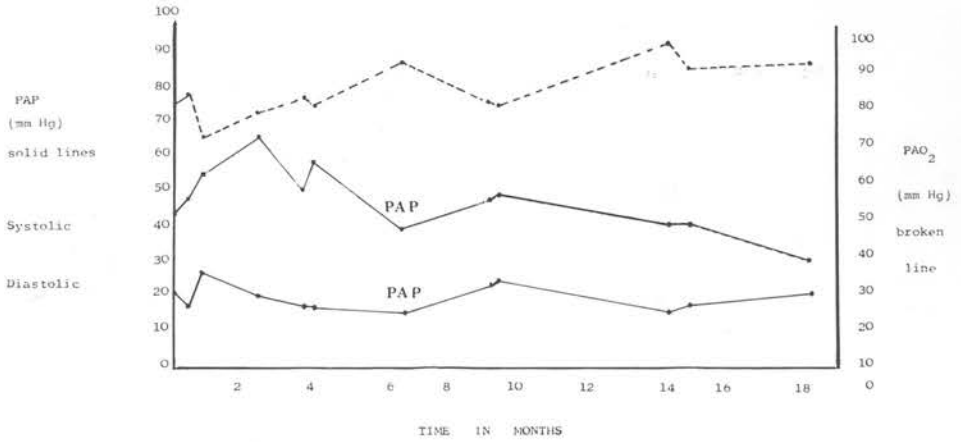
Pulmonary artery pressures, P_aO_2, P_aCO_2 and pH values (mean $\pm$ S.D.) obtained from normal, symptomatic COPD and asymptomatic COPD affected horses.

	Control horses	COPD affected horses	
		Symptomatic	Asymptomatic
PAP (mm Hg)			
Maximum	32.2 $\pm$ 3.42	56.1 $\pm$ 14.72	37.6 $\pm$ 5.31
Minimum	16.8 $\pm$ 3.52	25.3 $\pm$ 10.79	20.1 $\pm$ 3.80
Mean	23.8 $\pm$ 2.70	39.8 $\pm$ 10.83	28.2 $\pm$ 3.82
Carotid arterial			
P_aO_2 (mm Hg)	92.0 $\pm$ 5.06	70.0 $\pm$ 7.41	87.2 $\pm$ 5.10
P_aCO_2 (mm Hg)	37.5 $\pm$ 2.84	38.9 $\pm$ 4.22	36.1 $\pm$ 3.21
pH	7.403 $\pm$ 0.036	7.408 $\pm$ 0.029	7.398 $\pm$ 0.038

Table 11:2 RESULTS OF STATISTICAL COMPARISONS BY STUDENT'S T TEST OF PULMONARY ARTERY PRESSURES, P_aO_2, P_aCO_2 AND pH VALUES OF NORMAL, SYMPTOMATIC AND ASYMPTOMATIC COPD AFFECTED HORSES

Maximum PAP	Controls	vs	Symptomatic COPD	***
	Controls	vs	Asymptomatic COPD	***
	Symptomatic COPD	vs	Asymptomatic COPD	***
Minimum PAP	Controls	vs	Symptomatic COPD	***
	Controls	vs	Asymptomatic COPD	***
	Symptomatic COPD	vs	Asymptomatic COPD	*
Mean PAP	Controls	vs	Symptomatic COPD	***
	Controls	vs	Asymptomatic COPD	***
	Symptomatic COPD	vs	Asymptomatic COPD	***
P_aO_2	Controls	vs	Symptomatic COPD	***
	Controls	vs	Asymptomatic COPD	***
	Symptomatic COPD	vs	Asymptomatic COPD	***
P_aCO_2	Controls	vs	Symptomatic COPD	NS
	Controls	vs	Asymptomatic COPD	NS
	Symptomatic COPD	vs	Asymptomatic COPD	*
pH	Controls	vs	Symptomatic COPD	NS
	Controls	vs	Asymptomatic COPD	NS
	Symptomatic COPD	vs	Asymptomatic COPD	NS

*** $P < 0.001$ ** $P < 0.01$ * $P < 0.05 > 0.01$ NS $P > 0.05$



Pulmonary artery pressure (PAP) and PaO_2 recordings from a COPD-affected horse (87) taken over a 21-month period. During this time the horse was maintained under a variety of environmental conditions, thus causing fluctuation in the clinical severity of the disease with subsequent changes in PaO_2 and PAP. The inverse relationship between PaO_2 and PAP is evident in this recording.

Figure 11:1.

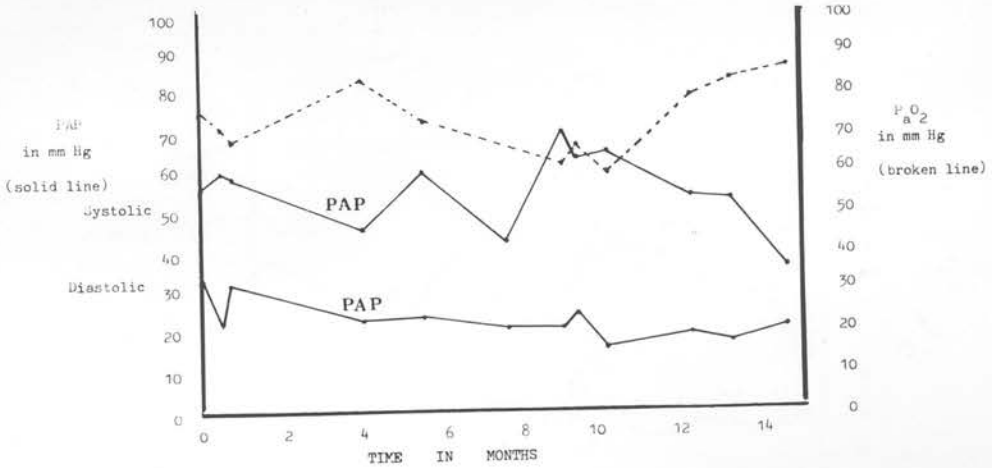


Fig. Pulmonary artery pressure (PAP) and $P_{a}O_2$ recordings from a COPD affected horse (B12), taken over a 15 month period. During this time the horse was maintained under a variety of environmental conditions thus causing fluctuations in the clinical severity of the disease with subsequent changes in $P_{a}O_2$ and PAP. The inverse relationship between $P_{a}O_2$ and PAP is evident in this recording.

Figure 11:2.

the pulmonary dysfunction in equine COPD is a perfusion: ventilation disorder rather than a generalised alveolar hypoventilation, where the hypoxaemia would be accompanied by hypercapnia and possibly by respiratory acidosis (World Health Organisation, 1963).

In pulmonary perfusion - ventilation disturbances, blood passing through the alveoli which are still normal can eliminate extra CO_2 because of the speed of CO_2 diffusion, but due to the nature of the O_2 dissociation curve, hypoxaemic blood passing through these normal alveoli cannot take up significant extra amounts of O_2 (World Health Organisation, 1963; Sasse, 1971; Clark et al., 1977). Even if hyperventilation occurs in the remaining normal alveoli, P_aO_2 will still remain lowered with ventilation - perfusion disturbances because of this non-linearity of oxyhaemoglobin dissociation (Youmans and Siebens, 1973).

The results show that there is a close inverse relationship between P_aO_2 and PAP levels in horses. This tends to indicate that hypoxia, as adjudged by carotid arterial hypoxaemia, might cause the pulmonary hypertension in COPD affected horses. As no evidence of hypercapnia or acidosis was observed in symptomatic COPD affected horses, the pulmonary hypertension cannot be related to either of these factors. It is possible that the previously noted allergic pulmonary vasoconstriction also plays some role in the aetiology of pulmonary hypertension in COPD affected horses.

Complete remission of the hypoxaemia (i.e. to levels

of control horses) was not observed in most COPD affected horses during remission stages (Appendix 11.3, Table 11.1). It appears possible that the residual pulmonary hypertension observed in these horses is related to their P_aO_2 levels (mean 87.2 mm Hg), although above the arbitrarily decided 'normal' level of 82 mm Hg, was still below the mean P_aO_2 levels (92.0 mm Hg) found in normal horses. Some of the asymptomatic COPD affected horses (animals B8, B14, B22, B58 in Appendix 11:3) however, had P_aO_2 levels similar to values of the control horses indicating that complete remission of the hypoxaemia can occur at least in some animals, yet their PAP levels remained above normal levels.

There are many reasons why P_aO_2 levels still remained low and consequently why the PAP levels remained elevated in most of the asymptomatic horses, the most likely being a time factor between removal from contact with the aetiological agents and the PAP and P_aO_2 measurements as noted in Chapter 10.

It is also possible that complete remission was not obtained in all horses because the animals were not completely removed from contact with the aetiological agents, i.e. small amounts of airborne moulds from adjacent stalls and yards could still have affected COPD horses which were maintained on peat bedding and fed a completely cubed diet.

CONCLUSIONS

A close inverse relationship between P_aO_2 and PAP levels occurs in COPD affected horses. No relationship was observed between PAP and P_aCO_2 or carotid arterial pH levels in these horses.

CHAPTER 12.

THE EFFECTS OF ADMINISTRATION OF NITROGEN ENRICHED AIR ON PULMONARY ARTERY PRESSURE, CAROTID BLOOD GASES AND pH IN NORMAL AND COPD AFFECTED HORSES

INTRODUCTION

While it is now generally recognised that hypoxia causes an increase in pulmonary vascular tone and consequently an increase in PAP (Fishman et al., 1960A; Fowler, 1960; Lloyd 1964; Harvey 1965; Kazemi et al., 1972; Malik and Kidd, 1973A; Bisgard, 1977), there still remains some confusion in the literature regarding hypoxic pulmonary vasoconstriction. This is due to experimental findings where a small PAP increase recorded during acute hypoxia production, has been accompanied by increased cardiac output, thus causing difficulties in establishing whether the limited PAP increase was due to pulmonary vasoconstriction, or to the increased cardiac output (Rudolph and Yuan, 1966). Some confusion also exists because many reports on oxygen therapy in hypoxaemic patients showed the hypoxaemia to be relieved, without reducing the existing pulmonary hypertension. However, in these patients the oxygen therapy frequently decreased the patients' respiratory drive to such an extent, that significant hypercapnia and acidosis developed which also affected the pulmonary vasculature (Harvey, 1965).

Most experimental studies on the hypoxic pulmonary vascular reflex have been performed on adult humans and anaesthetised dogs. Both species appear to have poor pulmonary pressor response, which causes difficulties in subjectively assessing this reflex (Rudolph and Yuan, 1966). Additionally

many of the above experiments have been performed using very low levels of hypoxia (Rudolph and Yuan, 1966).

The previous studies (Chapter II) have indicated that in horses affected with COPD,a relationship exists between arterial hypoxaemia and pulmonary hypertension. Additionally Bisgard et al. (1975) have shown that severe pulmonary hypertension (mean PAP 56.3 mm Hg) was induced in ponies of the small grade breed (adult wt. <200 kg),when moved to high altitudes (from 250 m to 3,400 m). These authors ha e also induced pulmonary hypertension in normal grade ponies by causing acute hypoxaemia through inhalation of nitrogen enriched air. There appear to be no reports on the cardio-pulmonary effects of acute hypoxaemia on horses of other breeds or on horses suffering from pulmonary disease.

The effects of acute hypoxia at low altitudes (200 m) on some cardiac and respiratory parameters,both in normal horses and in horses affected with COPD,were therefore examined.

MATERIALS AND METHODS

Eight normal and eight symptomatic COPD affected horses were used in this experiment (Appendices 12:1 and 12:2). Some details of these horses have been given previously in Tables (11:1) and (11:2) respectively. ECG, Ppl, PAP, blood gases and pH were recorded using methods previously described (Chapter 6). Compressed nitrogen was passed through a reducing valve and fed via rubber tubing to an open plastic facemask. The facemask was constructed

from a rigid conical plastic cylinder extended proximally by a flexible polythene sleeve. This mask was fitted to horse's face to enclose both the mouth and the nose and was loosely sealed to the upper part of the horse's face with a self-adhesive foam strap. This type of facemask had been used successfully in this institution for inhalation challenge of suspect COPD cases with nebulised fungal antigens. It was hoped that it could cause a high proportion of the added nitrogen to be inhaled,along with atmospheric air drawn into the facemask.

After applying the facemask the horse was given time to become accustomed to it and then the resting PAP Ppl levels were measured. A carotid blood sample for gases and pH analyses was also obtained. The N_2 flow was then started slowly initially (< 5 l/minute) to prevent excitement caused by the sounds of the gas release. The nitrogen flow was then gradually increased over a 30 - 120 second period to maximum levels of between 20-50 l/minute according to the size of horse, the degree of dyspnoea already present in the COPD affected horses and the degree of dyspnoea induced by the nitrogen administration.

Once the maximal flow rate was achieved,it was kept at this level for up to 10 minutes until the PAP and heart rate achieved a steady state. The PAP and Ppl were then noted and a further carotid arterial blood sample was obtained for P_aO_2, P_aCO_2 and pH analyses. During the peak N_2 flow, a mid inspiratory tracheal air sample was collected

using a 20 cc plastic syringe and a 4 cm, 16 g needle which was inserted into the trachea. The nitrogen flow was then discontinued. The mean PAP and carotid blood gases and pH levels obtained before and during the N_2 administration were compared by Student's 't' test as applied to paired observations.

RESULTS

The PAP, P_aO_2, P_aCO_2 and arterial pH results are presented in Appendices 12:1 and 12:2 and these results are summarised in Tables 12:1 and 12:2. Statistical analysis of the results showed that highly significant ($P < 0.001$) decreases in P_aO_2 and increases in mean PAP, occurred in both groups during acute hypoxaemia. A decrease in P_aCO_2 was also recorded which was significant in both groups. An increase in arterial blood pH recorded in both groups, was not significant ($P > 0.01$) in either group.

The heart rate, respiratory rate and Ppl results are presented in Table 12:3. These show that the N_2 inhalation caused greater increases in heart and respiratory rates in the control horses than in the COPD affected horses. In both groups, MAX $\triangle$ Ppl values doubled during the treatment and this was mainly due to deeper inspiration i.e. to increased MIN Ppl Insp. A simultaneous mean PAP and Ppl recording obtained from a symptomatic COPD affected horse during N_2 administration (Figure 12:1) shows an increasing PAP associated with limited increases in the depth and rate of respiration. The increased depth of respiration is shown to be due to increased depth of inspiration (i.e. increased MIN Ppl Insp.).

Analysis of tracheal air obtained during mid inspiration

TABLE 12:1

P_aO_2, P_aCO_2, arterial pH and mean pulmonary arterial pressure values (mean $\pm$ S.D.) obtained from 8 normal horses before and during the inhalation of nitrogen enriched air.

	Before treatment	After treatment	Significance of change
P_aO_2 mm Hg	91.9 $\pm$ 7.33	50.5 $\pm$ 7.75	$P < .001$
P_aCO_2 mm Hg	36.5 $\pm$ 3.50	29.1 $\pm$ 2.50	$P < .001$
pH mm Hg	7.392 $\pm$ 0.032	7.474 $\pm$ 0.060	$P > .01$
mean PAP mm Hg	24.1 $\pm$ 2.42	33.7 $\pm$ 4.75	$P < .001$

TABLE 12:2

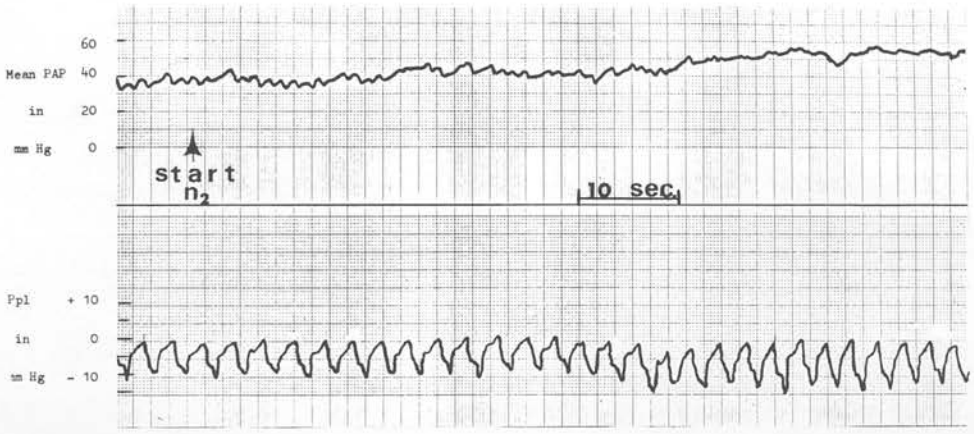
P_aO_2, P_aCO_2, arterial pH and mean pulmonary arterial pressure values (mean $\pm$ S.D.) obtained from 8 symptomatic COPD affected horses before and during inhalation of nitrogen enriched air.

	Before treatment	After treatment	Significance of change
P_aO_2 mm Hg	71.5 $\pm$ 8.07	48.3 $\pm$ 6.37	$P < .001$
P_aCO_2 mm Hg	37.8 $\pm$ 3.86	34.0 $\pm$ 3.08	$P < .01$
pH	7.411 $\pm$ 0.041	7.442 $\pm$ 0.065	$P > .01$
mean PAP mm Hg	32.5 $\pm$ 2.20	46.6 $\pm$ 4.60	$P < .001$

TABLE 12:3

Heart rate, respiratory rate and intrapleural pressure values in normal and COPD affected horses, at rest and during inhalation of nitrogen enriched air.

	Control Horses		COPD affected horses	
	Rest	Hypoxaemic	Rest	Hypoxaemic
Heart rate/min. Mean $\pm$ S.D.	31.2 $\pm$ 7.64	57.2 $\pm$ 7.4	41.4 $\pm$ 5.5	44.4 $\pm$ 8.6
Mean resp. rate/min.	16	24	11	13
Ppl changes (mm Hg)				
MIN Ppl Insp.	-5	-9	-6	-13
MAX Ppl Exp.	-1	-1	+2	- 1
MAX $\triangle$ Ppl	4	8	8	12



Simultaneous mean pulmonary artery pressure (PAP) and intrapleural pressure (Ppl) recordings from a symptomatic COPD affected horse during inhalation of an N_2 rich air (beginning at arrow). The acute hypoxaemia production causes a large increase in PAP but has little effect on respiratory rate or depth as judged by the Ppl recording.

Figure 12:1.

in the 4 acutely hypoxaemic horses showed O_2 and CO_2 contents respectively of 6.3% and 0.8%, 8.7% and 1.0%, 14.2% and 0.7%, 7.9% and 2.0%. These results show that the nitrogen content of the inspired air had been increased from the normal 79% of atmospheric air to between 85-95%.

DISCUSSION

The results indicate that acute hypoxaemia in normal and COPD affected horses causes a sudden and significant increase in PAP. Because no facilities for cardiac output measurements were available and consequently no pulmonary vascular resistance estimations were performed in these horses, it cannot be conslusively stated that the PAP increase was due to pulmonary vasoconstriction. Bergsten (1974) has shown that increases in cardiac output in horses is almost entirely due to increases in heart rate, increases in stroke volume playing a much less significant role. Heart rate is therefore a reliable indicator of cardiac output in horses. Little heart rate increase was recorded during hypoxaemia in the COPD affected horses (Table 12:3) and it can be deduced that in this group at least, that the PAP increase during hypoxaemia was not simply due to increased cardiac output.

Although MAX Δ Ppl was increased during hypoxia, this was accomplished by increased MIN Ppl Insp. changes (Table 12:3) which would tend to decrease PAP. The induced Ppl changes are therefore not responsible for the PAP increase associated with the acute hypoxaemia. Similarly in experi-

mental dogs a hypoxaemic PAP increase has been recorded, even in open chest preparations, thus indicating that Ppl changes are not an important factor in raising the PAP. It is most likely therefore that the PAP increases recorded were mainly due to pulmonary vasoconstriction. It appears that the equine pulmonary circulation is much more sensitive to hypoxaemia than the human or canine pulmonary circulation.

Although an increase in the rate and depth of respiration was recorded during the hypoxaemia, which induced significant hypocapnia, the respiratory rates or depths never came close to the maximal levels which we have recorded from severely affected COPD horses. It thus appears that induced hypocapnic hypoxaemia (Figure 12:1) does not stimulate maximal respiratory effort in horses, even if the hypoxaemia is marked.

As expected it was observed that lower N_2 flows were required to cause dyspnoea and increased PAP levels in COPD affected horses. These horses were already hypoxaemic and had pre-existing pulmonary hypertension and it was found that a smaller P_aO_2 decrease caused a more marked PAP increase in COPD affected animals as compared to the control horses. This suggests that the pulmonary vasculature of horses which are already hypoxaemic, is more responsive to further induced acute hypoxaemia than that of normal horses. A similar increased sensitivity to induced acute hypoxaemia has been observed by Bisgard et al. (1975) in ponies with pre-existing high altitude induced hypoxaemia and pulmonary hypertension.

CONCLUSIONS

Short term hypoxaemia production in normal or COPD affected horses is associated with significant pulmonary arterial pressure increases in both groups.

CHAPTER 13.

THE EFFECTS OF INHALATION OF OXYGEN ENRICHED AIR ON PULMONARY ARTERY PRESSURE, CAROTID BLOOD GASES AND pH IN ORMAL AND COPD AFFECTED HORSES.

INTRODUCTION

Inhalation of oxygen enriched air in normal man has been shown to have little effect on PAP (Barrat-Boyes and Wood, 1958), but in man affected with chronic obstructive lung disease (COLD), with concurrent pulmonary hypertension, it frequently causes large decreases in PAP (Harvey, 1965). Similarly in cattle with high altitude pulmonary hypertension (Grover et al., 1963) or with surgically created pulmonary hypertension (Vogel et al., 1963), oxygen inhalation has been shown to induce partial remission of the pulmonary hypertension.

Bisgard et al. (1975) found that induction of hyperoxaemia in grade ponies suffering from high altitude pulmonary hypertension, caused partial remission of the pulmonary hypertension, but they did not record the concurrent $PaCO_2$ or arterial pH changes. Muir et al. (1975) while studying ventilatory alterations caused by hyperoxaemia in normal horses, found that the hyperoxaemia was accompanied by a slight decrease in respiratory rate and small increases in tidal and minute volume.

There appear to be no further reports concerning the effects of administration of O_2 enriched air to conscious normal horses or any regarding the effects of O_2 administration on horses suffering from pulmonary disease. Studies were therefore carried out on the effects of administering O_2 enriched air to normal horses and symptomatic COPD affected horses and in particular its effect on PAP, carotid blood gases and pH.

Materials and Methods

Five normal horses and twelve symptomatic COPD affected horses (see Appendices 13:I, 13:2) were used in this experiment. PAP, Ppl and carotid blood gas and pH measurements were made using previously described methods (Chapter 6). In four horses mid-inspiratory tracheal air samples were obtained and analysed during peak O_2 administration using the technique described in Chapter 12. The O_2 was administered from a compressed O_2 cylinder by the technique described for N_2 administration (Chapter 12). PAP, arterial blood gas and pH measurements were made in all horses and Ppl and respiratory rates were recorded in two normal and in two COPD affected horses.

After allowing the animal to become accustomed to the face mask, resting PAP, Ppl, respiratory rate and carotid blood gases and pH values were obtained. O_2 administration was then started gradually, allowing the animal to become accustomed to the noise of the escaping gas and thereafter, the O_2 flow rate was increased to a maximum of 20-50 l/minute, depending on animal size. The flow rate increase was individually adjusted according to the animal's response as judged by appearance, heart rate and PAP.

Once the optimal O_2 flow rate was achieved, it was maintained at this level for 4-12 minutes until heart rate and PAP levels stabilised. At this stage a further carotid sample was obtained for blood gases and pH analyses and the PAP, Ppl and respiratory rate were noted. The O_2 administration was then stopped and PAP and Ppl measurements were continued until

their values returned to pre-treatment levels.

Individual resting PAP, PaO_2, $PaCO_2$ and pH values were compared with levels obtained during the O_2 administration, by Student's 't' test as applied to paired observations.

Results

Analysis of mid-inspiratory tracheal air during maximal O_2 flow revealed O_2 levels of 58.7%, 61.7%, 78.3% and 82.0%, showing that the O_2 contents of the inspired air had been increased from the normal 20% of atmospheric air to between 59-82%. In the control horses, the mean respiratory rate and max Ppl changes were 18/minute and 4 mm Hg respectively at rest and 19/minute and 2.5 mm Hg after hyperoxaemia production. In the COPD affected horses those values were 17/minute and 9 mm Hg respectively at rest and 18/minute and 8 mm Hg after the induction of hyperoxaemia.

PAP, carotid blood gas and pH results are presented in Appendices 13:I and 13:2 and are summarised in Tables 13:I and 13:2. These show that a highly significant increase in PaO_2 levels, to above physiological levels occurred in both groups, with the larger PaO_2 increase occurring in the normal horses. Both groups also showed evidence of slight CO_2 retention during the period of hyperoxaemia but this $PaCO_2$ increase was significant in the control group only. Both groups showed a small but non-significant decrease in arterial pH during the hyperoxaemia.

The COPD group showed a highly significant mean PAP decrease while they were hyperoxaemic whereas the controls showed a non-significant PAP change. An increase in PAP in the COPD

TABLE 13:I

PaO_2, $PaCO_2$, arterial pH and mean pulmonary arterial pressure values (mean $\pm$ S.D.) obtained from 5 normal horses before and during the inhalation of oxygen enriched air.

	before treatment	during treatment	Significance of change
PaO_2 mm Hg	92.2 $\pm$ 3.49	167.3 $\pm$ 16.09	$P < .001$
$PaCO_2$ mm Hg	38.3 $\pm$ 0.49	42.0 $\pm$ 1.01	$P < .002$
pH	7.385 $\pm$ 0.035	7.335 $\pm$ 0.042	$P > .05$
mean PAP mm Hg	25.8 $\pm$ 1.64	24.8 $\pm$ 2.05	$P > .05$

TABLE 13:2

PaO_2, $PaCO_2$, arterial pH and mean pulmonary arterial pressure values (mean $\pm$ S.D.) obtained from 12 horses symptomatically affected with chronic obstructive pulmonary disease before and during inhalation of an oxygen enriched air mixture.

	before treatment	during treatment	Significance of change
PaO_2 mm Hg	71.6 $\pm$ 8.86	124.0 $\pm$ 40.54	$P < .001$
$PaCO_2$ mm Hg	38.7 $\pm$ 4.15	40.67 $\pm$ 3.53	$P > .05$
pH	7.417 $\pm$ 0.039	7.405 $\pm$ 0.047	$P > .05$
mean PAP mm Hg	35.6 $\pm$ 7.60	31.4 $\pm$ 5.99	$P < .001$

affected horses began within one minute of cessation of O_2 administration and their PAP reached pre-treatment levels within 3-7 minutes.

Discussion

A very marked increase in PaO_2 levels was achieved even after 10-12 minutes of O_2 administration and as expected, the largest PaO_2 increase occurred in normal horses because their respiratory system was unimpaired. In man, administration of even 100 % O_2 seldom produces PaO_2 levels of 150 mm Hg and to achieve higher PaO_2 levels, O_2 must be administered at greater than atmospheric pressure, i.e. hyperbaric oxygenation (Nunn, 1971). Bisgard et al. (1975), administering a 60% O_2 air mixture at an altitude of 3,400 m which they stated was equivalent to 40% O_2 at sea level, recorded mean PaO_2 levels of 150 mm Hg in ponies. It thus appears that there is a difference in PaO_2 response to oxygen inhalation between man and horses.

Nunn (1971) noted that during hyperoxaemia in man, lung collapse can occur, because at the very high alveolar O_2 content required to achieve such PaO_2 levels in man, the diffusion of oxygen from the alveoli into the alveolar capillaries may be so fast that alveoli collapse occurs. Prolonged inhalation of 60% or greater O_2 mixtures in animals has also been shown to cause a fatal illness known as oxygen toxicity in which pulmonary congestion, oedema and even necrosis occurs (Aviado, 1965). In the present experiment, no clinical evidence of such adverse changes was observed in any horses after the hyperoxaemic period. The hypercapnia recorded in the normal horses

during the hyperoxaemia was possibly due to a reduction in respiratory stimulus caused by the O_2 administration (Harvey 1965).

The COPD group showed a significant ($P < 0.001$) decrease in PAP associated with the increased PaO_2 levels but even though PaO_2 was increased to above the normal range (Table II:1), a full remission of the pulmonary hypertension was not obtained. The PAP reducing effect of the hypoxaemia relief may have been partly offset by the small but non-significant $PaCO_2$ increase and arterial pH decrease which also occurred during the period of hyperoxaemia.

In no instance was the overall ventilatory drive so reduced by the O_2 treatment that severe hypercapnia and respiratory acidosis developed as frequently has been recorded during O_2 therapy of humans suffering from pulmonary disease. In many of these patients the PAP increasing influences of the hypercapnia and the respiratory acidosis completely offset any PAP reducing effect of the hypoxaemia relief (Harvey, 1965).

The absence of complete remission of pulmonary hypertension during the period of acute hyperoxaemia does not necessarily imply that the pulmonary hypertension in COPD affected horses is not solely due to hypoxia. Grover et al. (1963) however, came to such a conclusion when hyperoxaemia production failed to fully reverse high altitude pulmonary hypertension in cattle. They surmised that the residual degree of pulmonary hypertension was due to anatomical pulmonary vascular changes. Bisgard et al. (1975) also found that

short term induced hyperoxaemia only partially relieved high altitude pulmonary hypertension in ponies yet found that within one week of moving the ponies back to sea level the hypertension fully reversed. This indicates that although the pulmonary hypertension was entirely attributable to hypoxia, it was not possible to quickly reverse it by O_2 administration. A similar situation may occur in horses with raised PAP levels caused by COPD, and it is possible that if the O_2 had been administered for longer than 10-12 minutes, a greater PAP decrease may have occurred.

The slight, non-significant PAP decrease observed in normal horses after hyperoxaemia induction is similar to the results obtained by Bisgard et al. (1975).

CONCLUSIONS

Short term administration of oxygen rich air to symptomatic COPD affected horses caused a partial temporary relief of pulmonary hypertension associated with hypernormal PaO_2 levels, increased $PaCO_2$ and decreased arterial pH levels. This finding provides further evidence that the pulmonary hypertension in symptomatic COPD affected horses is related to hypoxia in these animals. Hyperoxaemia production in normal horses was found to have no significant effect on their PAP.

CHAPTER 14.

THE EFFECTS OF ADMINISTRATION OF CARBON DIOXIDE ENRICHED AIR ON PULMONARY ARTERY PRESSURE, ARTERIAL BLOOD GASES AND pH IN NORMAL HORSES AND IN HORSES AFFECTED WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

INTRODUCTION

The blood gas alterations in equine COPD do not include hypercapnia and a similar situation has been shown to exist in dogs with a variety of chronic pulmonary diseases (Clark et al., 1977). In many human chronic obstructive lung disease(COLD)patients, however, hypercapnia does occur, along with the hypoxaemia. Many authors including Fowler (1960), Harvey (1965) and Malik and Kidd (1973B) have suggested that hypercapnia can cause pulmonary hypertension and so increase the pulmonary hypertension already present due to the hypoxia, but some experimental work in man and in dogs has failed to verify this (Fishman et al., 1960B; Enson et al., 1964).

There appears to be no information available regarding the effects of hypercapnia production on the PAP or arterial blood gases and pH in normal horses or in horses with respiratory disease. Muir et al. (1975) investigated the effects of acute hypercapnia production on the respiratory rate and tidal volume in 6 normal horses and found that hypercapnia caused little change in respiratory rate but that it caused large increases in tidal volume.

MATERIALS AND METHODS

Eight symptomatic COPD affected horses (appendix 14:1) and 6 normal horses (appendix 14:2) were used in this experiment. PAP, heart rate and carotid arterial blood gases and pH measurements were made in all horses. Ppl and respiratory rate measurements were made in two normal and in two COPD affected horses. All measurements were made using previously described techniques (Chapter 6). CO_2 was administered from a compressed CO_2 cylinder using the technique previously used to administer N_2 (Chapter 12).

Resting PAP, Ppl, heart rate, respiratory rate and arterial blood gases and pH values were obtained after the horses had become accustomed to the facemask. The CO_2 flow was then started. It had been observed in pilot experiments that inhalation of a CO_2 enriched mixture could occasionally cause distress to the horses unless initially slowly administered, consequently particular care was taken on humane grounds to administer the CO_2 gradually to prevent such distress, particularly in the COPD affected horses which had some degree of pre-existing respiratory distress.

Maximum CO_2 flow rates of 5-7 l/minute were used. When a steady state was reached during optimal CO_2 flow, PAP, heart rate, respiratory rate and Ppl values were noted and a further carotid blood sample for P_aO_2, P_aCO_2 and pH analyses was obtained. The CO_2 flow was discontinued and

PAP and Ppl were monitored until they returned to pre-treatment levels. The individual PAP, P_aO_2, P_aCO_2 and arterial pH values obtained at rest and after hypercapnia production were statistically compared by Students' 't' test as applied to paired observations.

RESULTS

The PAP and blood gases and pH results are given in appendices 14:1 and 14:2 and a summary of these results are given in Tables 14:1 and 14:2. The results show that a significant P_aCO_2 increase occurred only in the control horses but that significant PAP increases occurred in both groups. The CO_2 inhalation also caused significantly increased P_aO_2 and significantly decreased arterial pH changes in both groups.

TABLE 14:1

P_aO_2, P_aCO_2, arterial pH and mean pulmonary arterial pressure values (mean $\pm$ S.D.) obtained from 6 normal horses before and during the inhalation of a carbon dioxide enriched air mixture.

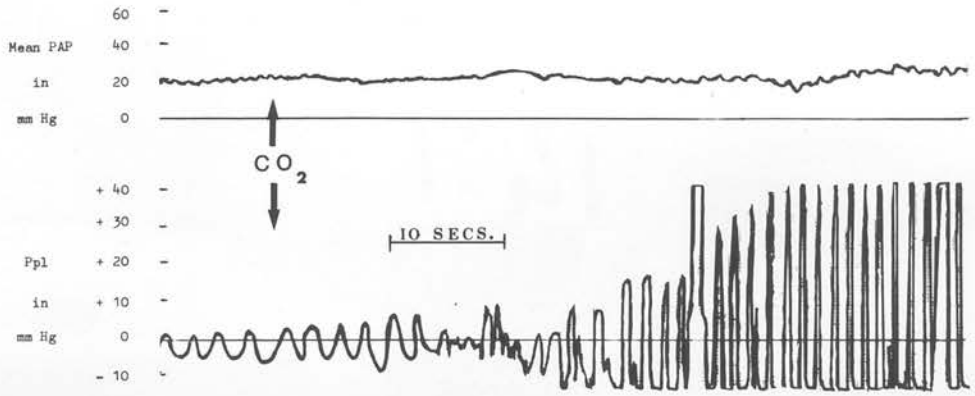
	Before treatment	during treatment	Significance of change
P_aO_2 mm Hg	90.2 $\pm$ 3.32	104.2 $\pm$ 8.14	$P < .01$
P_aCO_2 mm Hg	37.1 $\pm$ 3.24	52.7 $\pm$ 8.31	$P < .001$
Arterial pH	7.398 $\pm$ 0.018	7.274 $\pm$ 0.033	$P > .001$
Mean PAP mm Hg	24.0 $\pm$ 2.53	35.2 $\pm$ 7.63	$P < .001$

TABLE 14:2

P_aO_2, P_aCO_2, arterial pH and mean pulmonary arterial pressure values (mean $\pm$ S.D.) obtained from 8 horses symptomatically affected with chronic obstructive pulmonary disease before and during inhalation of a carbon dioxide enriched air mixture.

	Before treatment	during treatment	Significance of change
P_aO_2 mm Hg	72.4 $\pm$ 5.53	104.6 $\pm$ 6.98	$P < .001$
P_aCO_2 mm Hg	40.0 $\pm$ 0.99	43.7 $\pm$ 4.69	$P > .05$
Arterial pH	7.389 $\pm$ 0.039	7.332 $\pm$ 0.037	$P < .05$
Mean PAP in mm Hg	30. 8 $\pm$ 2.29	40.9 $\pm$ 6.56	$P < .01$

Analysis of tracheal inspiratory air during peak hypercapnia production revealed CO_2 levels of 3.4% and 3.8% in the COPD affected horses and 5.3% and 6.7% in the control horses. Carbon dioxide inhalation caused very obvious clinical changes in the respiratory patterns in both groups of horses, including a very obvious increase in both the rate and depth of respirations (Figure 14:1). The mean respiratory rate and MAX Δ Ppl in the two COPD horses before treatment were 19/minute and 9 mm Hg respectively and after treatment were 23/minute and 26 mm Hg. In the control horses these parameters were 18/minute and 5 mm Hg respectively before treatment and 46/minute and 30 mm Hg after treatment. Mean heart rates before and after treatment were 33/minute and 36/minute



The effects of inhalation of CO_2 enriched air (beginning at arrow) on the mean pulmonary artery pressure (PAP) and intrapleural pressure (Ppl) of a normal horse. This shows a large CO_2 induced increase in respiratory rate and depth associated with a gradual and limited PAP increase.

Figure 14:1.

in the COPD affected horses and 47/minute and 60/minute in the control horses.

A simultaneous mean PAP and Ppl recording obtained from a normal horse during CO_2 inhalation (Figure 14:1) shows large increases in the depth and rate of respiration associated with a gradual and moderate PAP increase. The Ppl changes after CO_2 administration are greater than the range of the recording i.e. 50 mm Hg.

It was observed that in spite of the slow and gradual introduction of CO_2 into the facemask, distress occurred on two occasions during hypercapnia production in COPD affected horses. This distress was manifested mainly as excited expression, snorting, laboured respirations and even shivering and sweating. In these instances the CO_2 flow was stopped and re-introduced at such a rate that distress did not occur.

DISCUSSION

The marked respiratory stimulation induced by inhalation of the CO_2 rich air, contrasted with the relatively mild increase in respiratory effort which was observed during experimental acute hypoxaemia (Chapter 12 Figure 12:1). This CO_2 stimulated respiratory increase was of such magnitude that it prevented a significant P_aCO_2 increase from occurring in the COPD group and it markedly increased P_aO_2 levels in both groups. A larger and more significant P_aCO_2 increase occurred in the control group, although the Ppl and respiratory

rate results indicated that they had a greater increase in respiratory drive induced by the hypercapnia. There thus appears to be some difference in P_aCO_2 response to hypercapnia production between the normal and COPD affected horses. Because of the very raised respiratory rate in the control horses while hypercapnic (< 60/minute), when inspiration took just approximately 0.5 second it is likely that the tracheal sample even when aspirated as fast as possible, contained some expiratory air with a raised CO_2 content of metabolic origin.

The large rise in respiratory rate observed was in contrast to the findings of Muir et al. (1975) who found that in horses, acute hypercapnia production caused an increase in respiratory depth but no change in rate. Fishman et al. (1960B) observed that inhalation of a 5% CO_2 air mixture caused a greater increase in respiratory drive in normal man than in COLD affected subjects. He also found a greater P_aCO_2 increase in the COLD affected patients, presumably because of their lesser respiratory stimulation. A major difference between Fishman's COLD human patients and the present COPD affected horses was that his patients were hypercapnic at rest and so had some respiratory tolerance to increased P_aCO_2 levels. Cherniak (1965) has noted that humans affected with COLD have a diminished respiratory response to CO_2 inhalation and suggested that this was because their medullary respiratory centre had become acclimatised to their chronically elevated P_aCO_2 levels.

The marked respiratory stimulation observed in the present experiment caused significant P_aO_2 increases in both groups. This shows that the COPD affected horses, whose hypoxaemia was fully relieved by the CO_2 administration, have the capacity to maintain normal P_aO_2 levels, but this occurs only with great energy expenditure by the respiratory muscles.

Significant PAP increases were recorded in both groups during hypercapnia production, but in the COPD group, the induced blood gas changes included a reversal of hypoxaemia which would be expected to cause a reduction in PAP. Non-significant P_aCO_2 and arterial pH changes also occurred and so theoretically an overall decrease in PAP would be expected. Similarly these blood gas and arterial pH levels obtained after CO_2 administration would not be expected to cause such an increase in the respiratory drive.

The PAP increase could possibly be explained by the increased MAX Ppl changes associated with inhalation of CO_2 enriched air, but examination of the 4 Ppl records showed that the increase in MAX Ppl was mainly due to an increase in the depth of inspiration i.e. to increased min. Ppl Insp., which would be estimated to reduce PAP. The limited cardiac output increase recorded during the CO_2 inhalation, as estimated from heart rates, was not big enough to account for the full PAP increases observed either.

It appears likely, then, that CO_2 induced pulmonary vasoconstriction occurred thus causing the recorded PAP rise.

The stimulus for this PAP increase and indeed for the increased respiratory drive appeared to have originated in the respiratory system. It is believed that receptors for the hypoxic pulmonary reflex are in the alveoli and it is possible that raised alveolar CO_2 levels stimulate similar pulmonary vasoconstriction in the horse. Whatever its mechanism, it appears that during CO_2 inhalation, a more marked PAP response occurs in the horse than has been recorded in man or the dog.

CONCLUSIONS

Inhalation of a CO_2 enriched air mixture caused a significant increase in the PAP of normal and COPD affected horses. P_aCO_2 levels were not significantly changed in the COPD group due to a marked increase in respiratory drive associated with the CO_2 inhalation. It was concluded that the stimulus for the increased PAP and the increased respiratory drive occurred in the respiratory system.

CHAPTER 15.

I THE EFFECTS OF ARTERIAL BLOOD pH ALTERATIONS ON PULMONARY ARTERIAL PRESSURES IN HORSES

INTRODUCTION

Respiratory acidosis frequently occurs in human chronic obstructive lung disease (COLD) patients and it is believed to be an additional pulmonary hypertensive stimulus in these subjects along with hypoxia (Thurlbeck 1976). Experimental acidosis by intravenous infusions of acetic, hydrochloric or lactic acids have also been shown to cause pulmonary hypertension in man and in dogs (Enson et al. 1964, Harvey 1965, Rudolph and Yuan 1966, Malik and Kidd 1973B). Acidosis has also been shown to potentiate the hypoxic pulmonary arterial reflex (Harvey 1965, Rudolph and Yuan, 1966).

Aviado (1965) and Malik and Kidd (1973B) have suggested that alkali infusions such as bicarbonate, could partially relieve the pulmonary hypertension in COLD patients suffering from respiratory acidosis, but Enson et al. (1964) and Harvey (1965) found that alkali infusions caused no significant PAP changes in human COLD patients and experimental dogs respectively. Harthoorn and Young (1976) found that wild zebras and wildebeest developed severe acidosis (arterial blood pH 6.77) and pulmonary hypertension (Systolic PAP 98 mm Hg) after forced exercise and showed that intravenous bicarbonate infusion would rapidly reverse both.

There appears to be no information available concerning the relationship between arterial blood pH and PAP in the horse. Because no alteration of the acid-base state have been found in

COPD affected horses (Chapter II), no differentiation was made between normal and COPD affected horses in this present experiment. In this experiment it was planned to decrease arterial blood pH in horses by I/V infusion of an acidic buffer or a fixed acid and to increase arterial blood pH by bicarbonate infusion. Because of the effective buffering power of blood particularly by the bicarbonate-carbon dioxide buffer system and by compensatory respiratory P_aCO_2 changes, blood pH measurements do not always totally reflect the acid-base state of the blood (Varley 1963, Sasse 1971). Consequently it was planned to measure two further blood parameters before and after infusion of the pH altering solutions namely standard bicarbonate (St. Bic.) and base excess (B.E.).

Standard bicarbonate refers to the bicarbonate levels of whole blood at 38°C after it has been fully oxygenated and has had its P_aCO_2 content standardised to 40 mm Hg. Base excess refers to whole blood total base concentration, as measured by titration against a strong acid to a pH of 7.40 at 38°C after standardising its P_aCO_2 content to 40 mm Hg (Varley 1963, Sasse 1971).

MATERIALS AND METHODS

The concentration and volumes of infusions used in this experiment were selected from the results of preliminary trials which had shown these concentrations and dosage to have no adverse effect on the horses. In this experiment, treatments 1 - 3 are further pilot experiments using single animals.

In these experiments, heart rate, PAP, P_aO_2, P_aCO_2 and arterial blood pH measurements were recorded using methods previously described (Chapter 6). Standard bicarbonate and base excess were estimated by the techniques of Varley (1963). The solutions were intravenously infused by gravity through 12 cm long 16 gauge intravenous catheters. (Intranule, 112-23, Vygon U.K. Ltd.). After the infusion was finished the catheter was flushed with normal saline prior to its withdrawal.

Treatment I

Horse C32 was infused with 350 cc of 0.05 Molar (M) Tris-(Hydroxy Methyl)-Aminomethane, (THAM Buffer), pH 7.3 at 37°C, (Trizma T4253, Sigma London Chemical Company Ltd., Dorset) over a 2 minute period and its P_aO_2, P_aCO_2, pH, Std. Bic., B.E., heart rate and PAP levels were measured before, immediately after and at 1, 2 and 3 minutes after the infusion.

Treatment 2

Horse B19 was infused with 500 cc of 0.05 M THAM buffer, pH 7.12 at 37°C (Trizma 4003, Sigma Chemical Company Ltd., Dorset) over a $3\frac{1}{2}$ minute period and had the same parameters measured before, immediately after and 2 minutes after the infusion.

Treatment 3

Horse (C34) had 0.1M HCl infused at a dosage rate of 100 cc/50 Kg body weight, over a 5 minute period and had the above mentioned parameters measured before, immediately after and at 2 minutes after the infusion.

Treatment 4

6 horses including 4 control and two COPD affected animals (see Appendix 15:1) had the above mentioned parameters measured before and immediately after the infusion of 0.2M HCl at a dose rate of 100 cc/50 kg body weight infused over a 5 - 7 minute period.

Treatment 5

Seven horses (see Appendix 15.2) including 5 controls and 2 COPD affected horses were monitored for these same parameters, before and immediately after I/V infusion of sodium bicarbonate solution 1,000 mM/l at a dose of 100 cc/50 kg body weight over a 5 - 7 minute period.

The results obtained from treatments 4 and 5 were statistically analysed by Student's 't' test as applied to paired observations.

RESULTS

Treatments 1 and 2

The PAP and carotid blood gas and pH results obtained in treatments 1 and 2 are shown in Table 15:1. These show that infusion of the acidic THAM buffer caused minor changes in all of the parameters measured.

Treatment 3

The results obtained during treatment 3 are given in Table 15:1. These show that intravenous infusion of 0.1M HCl caused minor arterial pH and Std. Bic. changes but caused a decrease in B.E. and an increase in PAP.

Treatment 4

The results obtained during treatment 4 (0.2 M HCl infusion) are shown in Appendix 15:1 and a summary of these results including statistical comparisons are shown in Table 15:2. These show that a very limited pH decrease occurred during the treatment (mean value 7.400 before treatment and of pH 7.336 after treatment). However more significant changes were recorded in Std. Bic. and B.E. (Table 15:2). Associated with these limited arterial pH changes a sudden and massive mean PAP increase from a mean value of 26.0 mm Hg at rest to 56.7 mm Hg immediately after acid infusion was recorded. PAP recordings obtained from two animals during this treatment are shown in Figures 15:1 and 15:2, which illustrate the speed and magnitude of the PAP response as well as its temporary nature.

TABLE 15.1

The effects of infusion of pH decreasing solutions on the mean pulmonary arterial pressure (PAP), P_aO_2, P_aCO_2, arterial pH, standard bicarbonate and base excess values in horses.

TREATMENT I (THAM pH 7.3)	P_aO_2 (mm Hg)	P_aCO_2 (mm Hg)	pH	Std.Bic. m mols/L.	B.E. m/mls.	MEAN PAP (mm Hg)
Before treatment	90.4	35.2	7.450	25.2	+ 1.0	20
Immediately post treatment	85.0	36.6	7.441	25.0	+ 0.5	22
1 Minute post treatment	91.4	34.2	7.462	25.0	+ 1.0	21
2 Minutes post treatment	86.6	37.2	7.449	26.5	+ 2.0	22
3 Minute post treatment	86.2	42.0	7.442	28.5	+ 4.5	20
TREATMENT II (THAM pH 7.12)						
Before treatment	74.3	39.6	7.334	21.0	- 2.0	34
Immediately post treatment	72.4	42.7	7.401	19.2	- 2.5	34
2 Minutes post treatment	68.4	37.4	7.399	18.8	- 2.9	34
TREATMENT III (0.1M HCl)						
Before treatment	84.1	36.6	7.388	22.5	- 2.5	24
Immediately post treatment	91.6	35.0	7.318	18.5	- 7.5	32
2 Minutes post treatment	84.1	34.3	7.342	19.0	- 6.5	33

Treatment 5

The results obtained during treatment 5 (sodium bicarbonate infusion) are presented in Appendix 15:2.

TABLE 15:2

P_aO_2, P_aCO_2, arterial pH, standard bicarbonate, base excess, heart rate and mean pulmonary arterial pressure values (mean $\pm$ S.D.) from 6 horses before and immediately after intravenous infusion of 0.2 molar HCl at a dosage of 100 cc per 50 kg body weight over a 5 - 7 minute period.

	Before Treatment	After treatment	Significance of change
P_aO_2 mm Hg	86.7 $\pm$ 11.6	95.9 $\pm$ 10.3	$P > .05$
P_aCO_2 mm Hg	36.0 $\pm$ 2.3	27.6 $\pm$ 4.6	$P < .001$
pH	7.400 $\pm$ 0.029	7.336 $\pm$ 0.0416	$P < .05$
Std.Bic. m mols/L	20.9 $\pm$ 3.7	14.2 $\pm$ 2.5	$P < .01$
Base excess m mols/L	-2.1 $\pm$ 1.9	-11.3 $\pm$ 3.7	$P < .001$
Heart rate/minute	40.1 $\pm$ 4.5	64.7 $\pm$ 15.5	$P < .01$
mean PAP	26.0 $\pm$ 3.74	56.7 $\pm$ 17.3	$P < .01$

A summary of these results with statistical comparisons are shown in Table 15:3. These show that infusion of sodium bicarbonate solution caused a highly significant increase in arterial pH associated with large P_aCO_2, Std. Bic. and B.E. changes but no significant mean PAP change was recorded i.e. mean value of 22.9 $\pm$ 2.27 mm Hg before treatment to 25.9 $\pm$ 4.69 mm Hg after treatment.

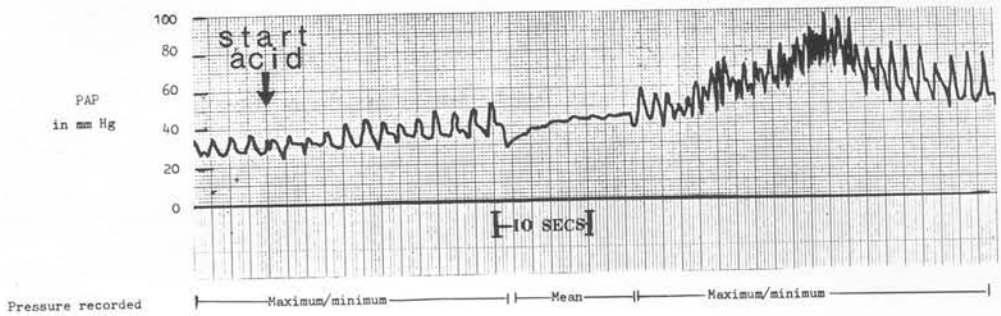
TABLE 15:3

P_aO_2, P_aCO_2, arterial pH, standard bicarbonate, base excess and mean pulmonary arterial pressure values (mean ± S.D.) from 7 horses before and immediately after intravenous infusion of sodium bicarbonate solution at a dose of 100 meq/50 kg body-weight over a period of 5 - 7 minutes.

	Before treatment	After treatment	Significance of change
P_aO_2 mm Hg	91.7 ± 5.91	82.7 ± 6.73	$P < .05$
P_aCO_2 mm Hg	36.7 ± 2.19	39.5 ± 3.91	$P < .05$
pH	7.402 ± 0.047	7.526 ± 0.070	$P < .001$
Std. Bic. m mols/L	22.8 ± 2.31	32.5 ± 7.40	$P < .01$
B.E. m mols/L	-2.6 ± 2.05	11.2 ± 6.67	$P < .01$
mean PAP mm Hg	22.9 ± 2.27	25.9 ± 4.69	$P > .05$

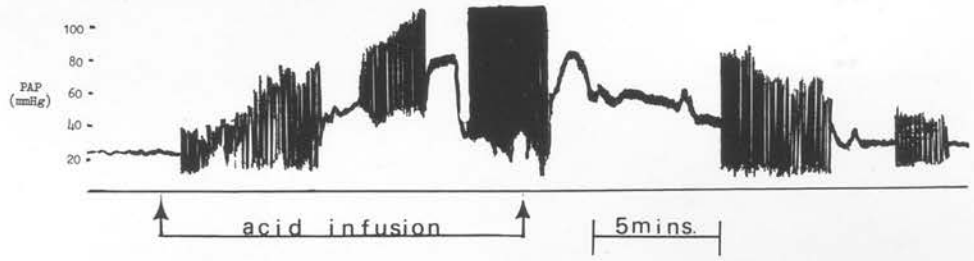
The PAP results obtained from all 5 treatments are summarised in Figure 15:3. The observed PAP changes after all treatments were transient (see Figure 15:2) with values returning to normal levels within minutes after the infusions had finished. During HCl infusion, a slight increase in the rate and depth of respiration was clinically observed but Ppl recordings were not made.

In two horses, slight muscle fasiculations were observed particularly in the shoulder muscles, during infusion of 0.2 M HCl (Treatment number 4) and in one of these animals a marked jugular pulse also developed. Both of these changes were



Simultaneous pulmonary arterial pressure (PAP), alternate maximum/minimum and mean pressure recordings from a control horse before and during intravenous administration of 0.2 ml HCl, which causes a rapid and large increase in PAP.

Figure 15:1.



Pulmonary artery pressure (PAP): alternate maximum/minimum and mean values recorded from a normal horse during and after intravenous infusion of 0.2 m HCl at a dose rate of 2 ml/kg. At peak PAP response, maximum PAP levels are greater than the range of the recording equipment, i.e. > 110 mmHg.

Figure 15:2.

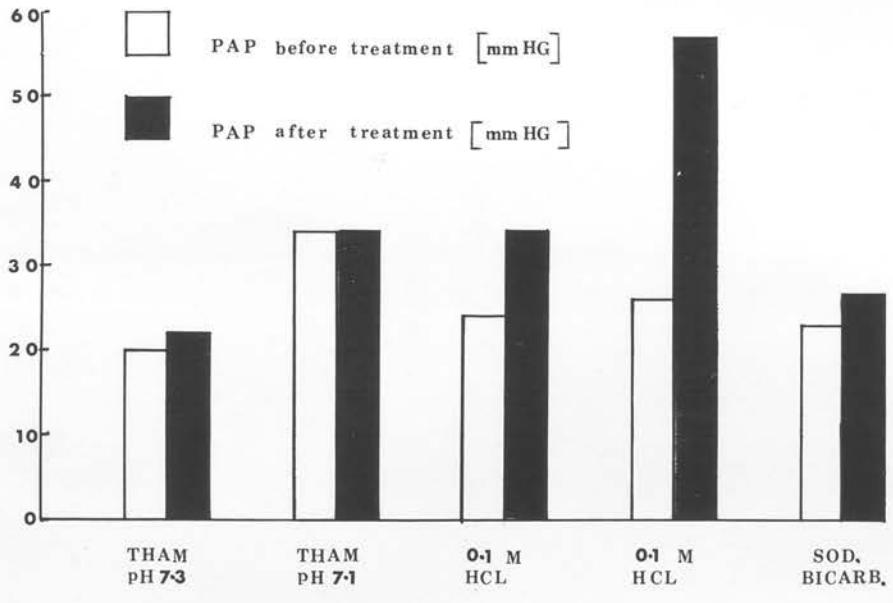

60
50
40
30
20
10
0
PAP before treatment [mm HG]
PAP after treatment [mm HG]
THAM pH 7·3
THAM pH 7·1
0·1 M HCL
0·1 M HCL
SOD. BICARB.

Figure 15:3.

transitory, disappearing within minutes after the infusion finished. No local or systemic side effects were observed in any animals after any of the treatments.

DISCUSSION

Treatments 1 and 2

The very limited change induced in any parameter after the THAM infusions was surprising as this buffer has been successfully used to alter blood pH in man by Aber et al. (1963) who used a total dose of 300-450 cc of 0.3M THAM in adults over a 1-1½ hour period. Although a smaller dose rate was used in this experiment the infusion time was much shorter (2 and 3½ minutes) and consequently some transitory pH alteration of the blood would have been expected. This buffer has also been successfully used to alter arterial pH in man by Enson et al. (1964) and in calves by Rudolph and Yuan (1966) but neither author gave full details about their dosage and infusion rates.

Treatment 3

Infusion of 0.1 M HCl (Treatment 3) had surprisingly little effect on any of the parameters measured except on B.E. and P.A.P.

Treatment 4

It was found that infusion of 0.2 M HCl caused significant alterations to the arterial acid base state, without causing any permanent untoward effects on the horses. 0.3M HCl has previously been shown by Harvey (1965) to cause pulmonary vasoconstriction with subsequent increased pulmonary

hypertension in humans suffering from COLD. In the present experiment the HCl infusion induced a large and sudden PAP increase to more than double resting levels, accompanied by approximately a 50% increase in heart rate, consequently it is very unlikely that the full PAP increase recorded was due to increased cardiac output as adjudged by heart rate. It appears therefore that a major part of the PAP increase was due to pulmonary vasoconstriction induced by the acid infusion.

The 0.2M HCl infusion caused very limited arterial pH decrease,which attests to the great buffering power of equine blood. That all these changes were temporary, further demonstrates its strong buffering capacity.

It is difficult to correlate the very limited arterial pH decrease with the large PAP and heart rate increase recorded. Indeed some normal resting horses previously examined (Appendix 11:1) had lower arterial pH levels than had this current group after the acid infusion. It is possible that the infused acid directly acted on the pulmonary vasculature and so the measurement of pH from the carotid artery did not accurately reflect right heart blood pH changes because passage through the lungs and left heart allowed a more thorough mixing of the acid with blood and also allowed extra time for buffering of the acid by the blood.

It is also possible that the significant B.E. and/or Std. Bic. changes recorded were the stimuli for the cardiovascular changes, acting at central or at local levels.

Treatment 5

The bicarbonate infusion was found to cause significant alterations to the arterial acid-base state including arterial blood pH changes but caused no significant PAP changes. The pH increase of 0.12 recorded is similar to the pH changes of 7.40 to 7.51 observed by Enson et al. (1964) after bicarbonate infusion in man, although these authors recorded a significant P_aCO_2 increase of 9 mm Hg in their subjects, which they suggested was due to an alkalosis induced decrease in respiratory drive.

CONCLUSIONS

Although arterial acidosis has not been shown to occur in horses suffering from respiratory disease, it was shown that experimental intravenous acid infusion caused large, rapid and transient PAP increases, associated with relatively small arterial pH decreases, but with significant P_aCO_2, standard bicarbonate and base excess changes. It thus appears that acid infusion is a powerful pulmonary hypertensive stimulus in horses. In contrast the results suggest that alkali infusion has little influence on PAP in horses.

CHAPTER 16.

I THE EFFECTS OF INTRAVENOUS FUROSEMIDE ADMINISTRATION ON THE PULMONARY ARTERIAL PRESSURES OF NORMAL AND COPD AFFECTED HORSES

INTRODUCTION

Epistaxis is a widespread problem amongst racehorses. Its causes can be divided into two main groups, firstly where the epistaxis is due to an upper respiratory or head lesion such as guttural pouch mycosis, ethmoid haematoma, nasal trauma, tumours and ulcerative upper respiratory infections (Cook, 1974). Epistaxis caused by these upper respiratory lesions are frequently very severe and usually occur at rest.

The second type of epistaxis occurs in horses during or shortly after exercise, is usually a limited haemorrhage, and no head or upper respiratory lesion is demonstrable. It was previously widely believed that this type was caused by nasal haemorrhage but recent studies, particularly those of Cook (1965, 1974) have conclusively shown that it is caused by haemorrhage of pulmonary origin. It will be referred to as pulmonary epistaxis.

Cook (1974) and Gertson and Dawson (1977) also discovered that some horses which unexpectedly slowed down during races had pulmonary haemorrhages without epistaxis. It is therefore likely that exercise related pulmonary haemorrhage is more widespread than is commonly recognised.

In Britain Cook (1974) observed that 90% of horses which suffer from pulmonary haemorrhage have evidence of low grade chronic pulmonary disease, but Pfaff (1976) in South

Africa and Fregin et al. (1977) in the United States have not noted the presence of concurrent pulmonary disease in horses with pulmonary haemorrhage which they have examined.

The cause(s) or mechanism(s) of pulmonary haemorrhage is unknown, as very few pathological studies have been performed on horses with pulmonary haemorrhage and in particular on those which had recently haemorrhaged. In a horse which had recently suffered from pulmonary haemorrhage, Mahaffey (1962) observed ruptured alveolar blood vessels without noting the presence of any pre-existing blood vessel pathology.

Some limited pathological studies of this condition have also been performed by Rooney (1970) and Johnson et al. (1973). It can be concluded from the literature that pulmonary haemorrhage is due to rupture of apparently normal pulmonary blood vessels, possibly induced by an exercise related increase in blood pressure. It is unclear whether the haemorrhage occurs from pulmonary arterioles or venules, but as much higher blood pressure occurs in the arterioles and in horses this is known to significantly increase with exercise (Bergsten 1974), it appears more likely that pulmonary haemorrhage is due to pulmonary arteriolar haemorrhage. Because increased pulmonary arterial pressure occurs in horses with chronic respiratory disease and this pulmonary artery hypertension increases proportionally with exercise (Bergsten, 1974), it may be that horses with chronic pulmonary disease would theoretically be more at risk to pulmonary haemorrhage as in fact Cook (1974) suggested.

To date very many prophylactic treatments have been unsuccessfully advocated for this disease, varying from quack remedies like a copper wire around the horse's tail or rectal saline administration, to parenteral vitamin and oestrogen injections (O'Connor, 1941; Johnson et al., 1973; Hamlin, 1975).

The diuretic Furosemide (Frusamide) is currently widely used for pulmonary haemorrhage prophylaxis, particularly in the U.S. where the racing authorities of most states permit its use prior to racing, for this purpose only (Johnson et al., 1973; Hamlin, 1975). However, in some states between 50 - 70% of all racehorses receive furosemide prior to racing (Hamlin 1975; Fregin et al., 1977) allegedly for pulmonary haemorrhage prevention in all cases! Furosemide, an anthranilic acid derivative is a very potent diuretic, acting by decreasing sodium resorption in the renal tubules (Girdwood, 1976). It is very effective for this purpose in the horse, the peak diuretic effect occurring 20 minutes after I/V administration and most of the diuretic effect occurring within 2 hours (Gabel et al., 1977). The direct effects of furosemide are restricted to the kidney (Girdwood 1976), but it does have some haemodynamic effects secondary to its diuretic effect of decreasing plasma volume.

Recently the haemodynamic effects of furosemide in horses have been studied by Muir et al. (1976), Gabel et al. (1977) and Milne et al. (1977B) who all found that furosemide causes

slight but significant decreases in right heart blood pressures. It has been proposed by Muir et al. (1976) and Milne et al. (1977B), that the haemodynamic effects of furosemide could explain its alleged mode of action in pulmonary haemorrhage prevention.

In this experiment it was planned to study the effects of furosemide on the PAP of normal horses and of horses suffering from COPD which had pre-existing pulmonary hypertension and to examine for PAP changes in either of these groups, which could explain a possible mode of action for furosemide in pulmonary haemorrhage prevention.

MATERIALS AND METHODS

The twenty horses used in this study, were mainly adult hunters and ponies (Appendix 16:1). Eight animals which showed no evidence of respiratory disease were used as controls. Twelve horses which were confirmed as COPD cases by the methods outlined in Chapter 5 and 6 were also used and these animals were in various remission stages of this disease.

The pulmonary artery trunk was catheterised and its pressure recorded using methods previously described (Chapter 6). Resting mean PAP values were obtained over a 5-10 minute period, ensuring that basal PAP values were obtained. Furosemide (Lasix 50 mg/ml Hoecht Pharmaceuticals, Hounslow, Middlesex) was then administered intravenously at a dose of 1 mg/kg body weight and particular care was taken to avoid disturbing the horses during this procedure. The 12 COPD affected horses were randomly divided into a group of 8

horses (group B) and one of 4 horses (group C). The controls (group A) and group B had their PAP continuously monitored for 30 minutes after the furosemide administration and group C had their PAP similarly monitored but over a $2\frac{1}{2}$ hours period. Blood samples for blood gas and pH analyses were obtained from group A and group B at rest, and at 30 minutes after furosemide administration. Similar samples were obtained from group C at rest, at 1 hour and at $2\frac{1}{2}$ hours post administration.

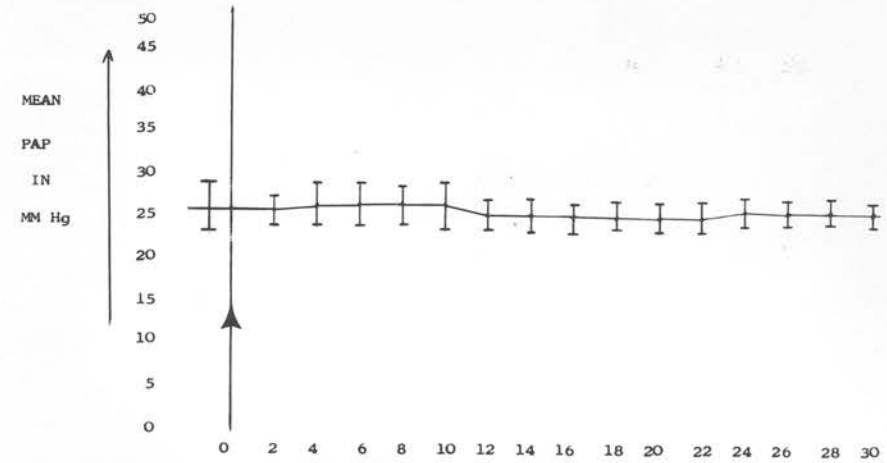
Statistical Analysis of Results

In the three groups, differences between resting PAP values and values obtained at two minute intervals after furosemide administration throughout the monitoring period, were compared by Student's 't' test as applied to paired observations. Resting and post treatment blood gas and pH levels were similarly compared.

RESULTS

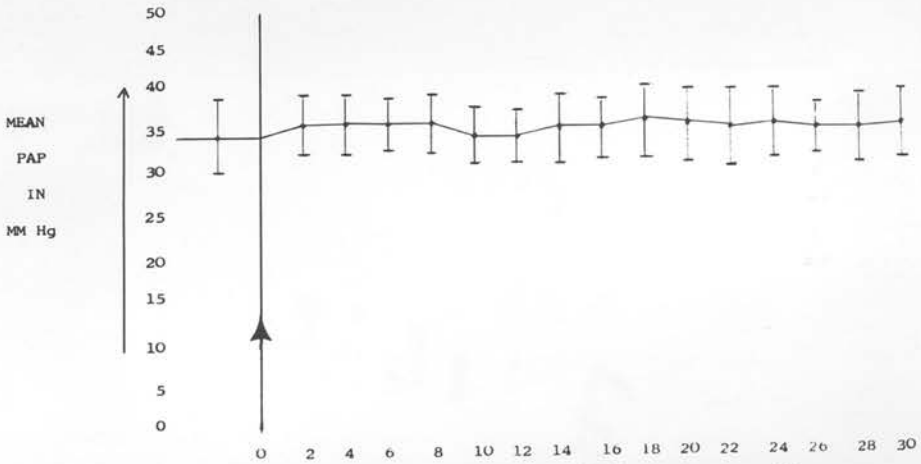
Although chosen at random, the COPD affected horses in group C were found to have higher P_aO_2 and lower PAP levels than those in group B (Table 16:1).

The results of the PAP studies for the 3 groups are shown in Figures 16:1 - 16:3 and these show no significant changes in PAP after furosemide administration in any of the three groups. However, a small but non-significant ($P > 0.05$) decrease in PAP occurred in the control group (A) approximately 12 minutes after furosemide administration and a small but non-significant increase in PAP occurred in



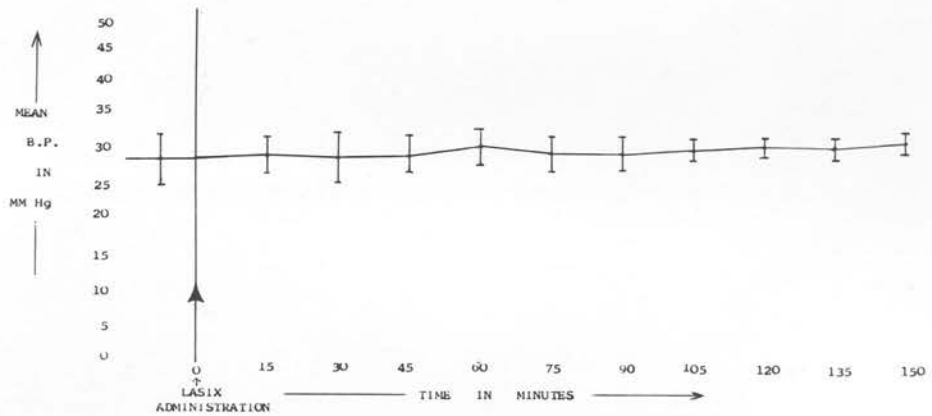
Mean pulmonary artery pressure (mean ± S.D.) of eight normal horses given 1 mg Furosemide / Kg body weight intravenously at ▲

Figure 16:1.



Mean pulmonary artery pressure (mean ± S.D.) of eight horses affected with chronic obstructive pulmonary disease (COPD) given 1 mg. Furosemide/Kg body weight intravenously at ▲

Figure 16:2.



Mean pulmonary artery pressure (mean ± S.D.) of four horses affected with chronic obstructive pulmonary disease given 1 mg. Furosemide/Kg body weight intravenously

Figure 16:3

b1.

	CONTROL VALUES			POST LASIX ADMINISTRATION								
				30 MINUTES			60 MINUTES			150 MINUTES		
	P_AO_2	P_ACO_2	pH	P_AO_2	P_ACO_2	pH	P_AO_2	P_ACO_2	pH	P_AO_2	P_ACO_2	pH
CONTROL HORSES	88.2 ± 3.04	38.3 ± 2.22	7.43 ± 0.024	84.7 ± 6.74	37.2 ± 1.93	7.45 ± 0.055	-	-	-	-	-	-
COPD AFFECTED HORSES (A)	72.7 ± 7.04	40.1 ± 3.72	7.42 ± 0.016	70.5 ± 7.09	39.2 ± 3.21	7.43 ± 0.025	-	-	-	-	-	-
COPD AFFECTED HORSES (B)	83.1 ± 6.80	35.7 ± 2.40	7.41 ± 0.007	-	-	-	82.0 ± 3.90	34.2 ± 3.2	7.43 ± 0.024	85.6 ± 7.40	34.8 ± 4.60	7.43 ± 0.029

Carotid blood gas and pH values (mean ± S.D.) of normal horses and of horses affected with chronic obstructive pulmonary disease before and after intravenous furosemide administration.

Table 16:1

both groups of COPD affected animals after furosemide administration. No significant blood gas or pH changes were observed in any group (see Table 16:1).

DISCUSSION

The small and transient PAP decrease obtained in the control animals after furosemide administration while non-significant in this case is similar in magnitude to the changes observed by Muir et al. (1976), Gabel et al. (1977) and Milne et al. (1977B). It is difficult to envisage how such a relatively small PAP decrease could have a major influence on pulmonary haemodynamics.

The haemodynamic effects of furosemide on horses suffering from respiratory disease does not appear to have been reported previously. Gabel et al. (1977) have advocated the use of this drug prior to racing in horses with chronic pulmonary disease which did not suffer from epistaxis and they suggested that this drug would increase their performance. The COPD affected horses used in these experiments were in varying degrees of remission of the disease but most were nearly asymptomatic and consequently these group's PAP and blood gas levels particularly of COPD group B, are closer to asymptomatic than to clinically affected levels (Chapter II). The COPD affected horses were selected for the experiment at near remission stages for the sake of reality, because horses severely affected with COPD would not normally be expected to exercise.

After furosemide administration the COPD affected horses had small but non-significant increases in their PAP which was associated with small but non-significant decreases in their $P_{a}O_{2}$ levels. Authors who previously studied the haemodynamic effects of furosemide in horses have also observed that these changes were transient and began to disappear within 30 minutes of intravenous administration of furosemide and had completely disappeared by 2 hours 10 minutes (Muir et al., 1976; Gabel et al., 1977; Milne and Gabel, 1977; Milne et al., 1977B). Furosemide is normally administered by the intravenous or intramuscular route 4 hours before racing. If given intravenously its haemodynamic effects would not be detectable by the time of racing and as no extrarenal effects are known, it is difficult to envisage a mode of action for its alleged efficacy in the control of pulmonary haemorrhage. If given intramuscularly, its plasma half life is prolonged but the highest plasma concentration is only a fraction of that obtained by I/V administration (Roberts et al., 1978) and consequently its diuretic and secondary haemodynamic effects would be much less, than after intravenous administration.

Recently Gabel et al. (1977) has suggested that its alleged mode of action in epistaxis control is by preventing pulmonary oedema, but it has not been shown that pulmonary oedema does in fact occur in normal horses or in horses with pulmonary disease. Consequently the

efficacy of furosemide against pulmonary oedema in the horse is unproven. The findings of Beltran (1974) that horses with COPD had normal pulmonary arterial wedge pressures and consequently normal pulmonary venous pressures suggests that pulmonary oedema does not occur in horses with chronic pulmonary disease even in those with severe pulmonary hypertension. Pulmonary oedema is invariably due to increased back pressure on the alveolar circulation caused by pulmonary venous hypertension rather than by pulmonary arterial hypertension (Bisgard 1977).

Although these experiments suggest that furosemide would not prevent pulmonary haemorrhage, this finding cannot be regarded as conclusive until the pathological mechanisms of pulmonary haemorrhage are better understood.

It has been speculated by Gabel et al. (1977) that furosemide could also prevent pulmonary haemorrhage by increasing pulmonary venous capacitance. It is also possible that plasma electrolyte changes induced by furosemide could alter the vascular reactivity of the pulmonary blood vessels and so prevent pulmonary haemorrhage. This could be a more rational hypothesis as Muir et al. (1978) have shown that furosemide induced plasma electrolyte changes can persist in horses well after the haemodynamic effects have worn off.

CONCLUSIONS

Intravenous furosemide administration had no significant

effect on pulmonary arterial pressures of normal or COPD affected horses.

CHAPTER 17.

I THE EFFECTS OF INTRAVENOUS ATROPINE ADMINISTRATION ON PULMONARY ARTERY PRESSURES OF NORMAL AND COPD AFFECTED HORSES

INTRODUCTION

Atropine (a racemic mixture of D and L Hyoscyamine) has been reported to cause temporary relief of dyspnoea in COPD affected horses (Obel and Schmiterlow" 1948, Udall 1954). Obel and Schmiterlow" (1948) have shown that I/V administration of 10-20 mg atropine causes a temporary reduction (30 minutes) of the existing increased Ppl changes in COPD affected horses. Muylle and Oyaert (1973) have also shown that intravenous atropine sulphate reduced the functional pulmonary abnormalities in COPD horses within 15 minutes of its administration. There appears to be no information available regarding the effect of atropine on the PAP of normal or COPD affected horses.

MATERIALS AND METHODS

Eight normal horses (C4, C5, C6, C7, C8, C9, C10, C11) Appendix 11:1 and 8 COPD affected horses (B7, B8, B9, B19, B21, B31, B32, B33) Appendix 11:2 were used. The resting PAP, heart rate, arterial blood gases and pH levels were measured using previously described methods (Chapter 6). While monitoring PAP and heart rate atropine (atropine sulphate, Bimeda Chemicals, Liverpool) was administered intravenously over a one minute period at a dose of 0.02 mg/kg.

The PAP and heart rate were recorded for 25-30 minutes

continuously after the atropine administration. A second carotid sample for blood gas and pH analyses was obtained 20 minutes after atropine administration.

Statistical Analyses of Results

PAP values obtained at rest were compared by Students' 't' test as applied to paired observations with PAP values obtained at two minute intervals throughout the full monitoring period after the atropine administration. The resting P_aO_2, P_aCO_2 and arterial pH values were compared by the same method with the values obtained 20 minutes after the atropine administration.

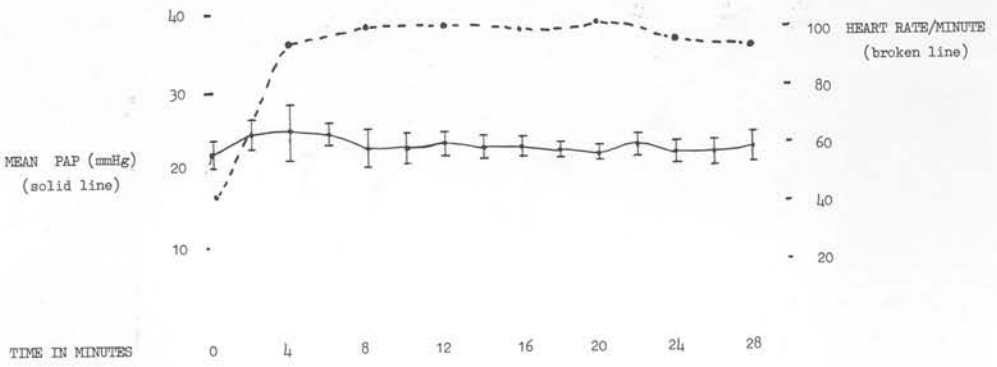
RESULTS

The PAP and heart rate values recorded (mean $\pm$ S.D.) from normal and COPD affected horses are presented in Figures 16.1 and 16.2 respectively. Statistical analysis showed a significant increase in heart rate in both groups within minutes after atropine administration ($P < .001$) but no significant PAP changes were obtained at any stage ($P > .05$). The arterial blood gas and pH values are presented below in Table 17:1.

TABLE 17:1

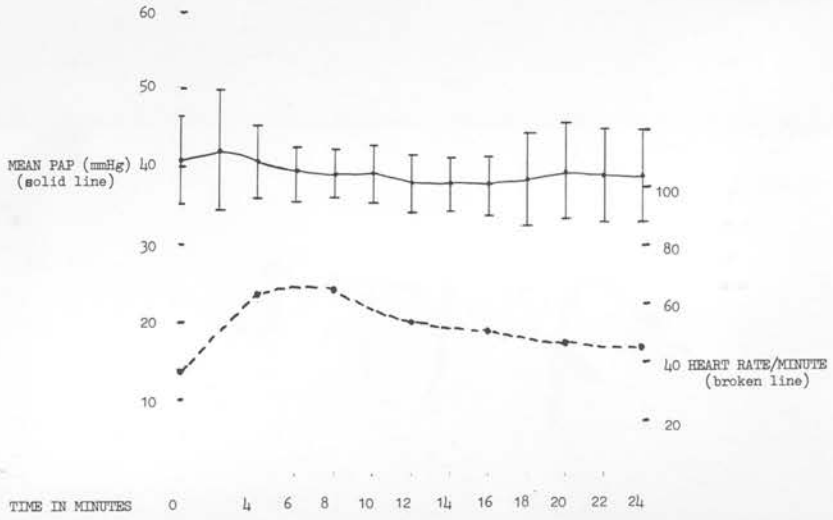
		P_aO_2 mm Hg	P_aCO_2 mm Hg	pH
Control Horses	Rest	88.3 ± 3.50	36.2 ± 2.95	7.403 ± 0.030
	20 Minutes Post atropine	88.6 ± 5.69	34.4 ± 6.03	7.371 ± 0.056
COPD Horses	Rest	70.3 ± 12.50	36.8 ± 4.16	7.402 ± 0.048
	20 Minutes Post atropine	68.5 ± 11.68	35.4 ± 4.03	7.409 ± 0.047

$P > .05$ for all comparisons.



Mean pulmonary artery pressure (PAP) and heart rate recordings from 6 control horses obtained immediately after intravenous injection of atropine sulphate at a dose rate of 0.2 mg/kg body weight.

Figure 17:1.



Mean pulmonary artery pressure (PAP) and heart rate recordings from 6 symptomatic COPD-affected horses obtained immediately after intravenous injection of atropine sulphate at a dose rate of 0.2 mg/kg body weight.

Figure 17:2.

DISCUSSION

The results indicate that I/V atropine administration has no acute effect on the PAP of normal or COPD affected horses. After atropine administration the PAP levels are influenced by many factors including a large increase in cardiac output and possible direct vasodilating effect of atropine on the pulmonary vasculature. The tachycardia recorded after atropine administration is as a result of the reduced vagal tone on the heart, consequently improving conduction in the bundle of His. Surprisingly a much greater increase in heart rate was recorded in control horses (see Figures 17.1 and 17.2) and this could possibly be explained by the fact that the control group contained a greater number of ponies. These had slightly higher resting heart rates and the possibility of an interbreed difference in heart rate response to atropine exists.

Obel and Schmiterlow" (1948) and Muylle and Oyaert (1973) observed large and sudden decreases in the work of respiration following atropine administration which shows that atropine induces bronchodilation which relieves the dyspnoea, but the present study indicates that this is not accompanied by an increase in $P_{a}O_{2}$ or relief of the pulmonary hypertension, within 20 minutes after treatment.

CONCLUSIONS

Atropine administration has no significant acute effects on PAP or $P_{a}O_{2}$ levels of normal or COPD affected horses.

CHAPTER 18.

ANATOMICAL STUDY OF HEARTS IN NORMAL HORSES AND IN HORSES AFFECTED WITH CHRONIC PULMONARY DISEASE

INTRODUCTION

The literature survey indicated that right ventricular (RV) hypertrophy is not a well documented finding in horses suffering from chronic pulmonary disease. RV hypertrophy occurs very frequently in humans with chronic pulmonary disease (WHO, 1963), it is therefore surprising that in similarly diseased horses where marked pulmonary hypertension occurs, that RV hypertrophy has not been more frequently recorded.

Alexander (1959) and Salutini (1959) have both stated that RV hypertrophy occurs in horses with long-standing COPD, but neither author makes it clear whether this was a personal observation. Sporri and Schlatter (1959) recorded that on post mortem examination of two horses affected with COPD, both showed RV hypertrophy, but they did not give any heart or body weights nor right or left ventricular weights or thicknesses. None of the following authors who have examined horses with COPD have noted the presence of RV hypertrophy on post mortem examinations. (Eberly et al. 1966; Sasse, 1971; Beltran, 1973; Bergsten, 1974).

A review of the literature also showed an apparent scarcity of normal values of cardiac parameters such as relative heart weight: body weights (HW/BW %), RV and LV weights or RV and LV wall thicknesses. Crocker (1918) reported an 'average' value of 1 for HW/BW % in horses but

did not give the breeds or number of observations from which his figure is derived. Hermann (1929) reported that he found a mean HW/BW % of 0.93 in 16 thoroughbreds which he noted was well above the then accepted 'normal' HW/BW % value of 0.68 for this breed. A further anatomical report by Quiring and Baker (1953) on 56 horses including 40 thoroughbreds, 3 draught horses and 13 ponies showed no interbreed differences between HW/BW % or relative ventricular thickness (LV/RV thicknesses) in these horses. These authors do not specify the sites at which they measured RV or LV thicknesses, nor the time after death at which these measurements were made. Kubo et al. (1974) examined (HW/BW %) and LV/RV thickness in trained compared with untrained thoroughbreds. They found differences in HW/BW % between trained (1.1 ± 0.14) and untrained horses (0.94 ± 0.16) but found no differences between LV/RV thicknesses (1.95 in both groups), indicating that the exercise related cardiac hypertrophy was equal in both ventricles. In this study the authors measured ventricular thicknesses after fixing the hearts in formalin for 72 hours and they did not state the sites at which ventricular thicknesses were measured.

It was not clear from the literature whether the low incidence of RV hypertrophy recorded in horses with chronic pulmonary disease and in particular with COPD, was due to an actual low incidence of this condition or because the condition has not been carefully looked for. Because of the shortage of information on HW/BW % and relative ventricular

sizes in normal horses, particularly in the non-thoroughbred breeds and also in horses with chronic pulmonary disease, it was also decided to examine and compare these parameters in normal horses and in horses with respiratory disease.

This report is in two parts, firstly an anatomical survey of relative heart and ventricular sizes amongst the general horse population and secondly the results of ventricular measurements from proven COPD cases made by a colleague who has studied the pathology of equine COPD.

I ANATOMICAL SURVEY OF HEARTS AMONGST THE GENERAL HORSE POPULATION

MATERIALS AND METHODS

The survey was performed in a horse abbatoir which slaughtered approximately 180 horses per week for human consumption, for the Continental trade (North Kilkenny Meat Exporters, Freshford, Co. Kilkenny, Ireland). Before slaughter the horses were restrained, for weighing (to the nearest kg) for mane and tail clipping and for the required antemortem veterinary inspection. The horses were also clinically examined by the author at this stage. As most horses were purchased from dealers, usually no reliable clinical history was available. For this survey each horse was given a general clinical examination with particular emphasis placed on cardiac and respiratory examinations. Horses were classified into four breed types: 1. thoroughbreds, 2. thoroughbred cross draught, which are called hunters or halfbreds 3. draught horses, 4. ponies. The animals' age was also recorded.

The horses were divided into three groups following the clinical examination (A) normal horses showing no evidence of cardiac or respiratory disease, (B) animals with evidence of chronic pulmonary disease, (C) horses which showed clinical evidence of cardiac disease other than cor pulmonale, using the criteria of Littlewort (1962), Glendinning (1972) and Hamlin and Fregin (1975) for this cardiological examination. Horses showing evidence of acute or upper respiratory diseases were also included in group C.

The horses were slaughtered by stunning with a captive bolt pistol, followed immediately by exsanguination from the anterior vena cava. The carcasses were then coded to allow them to be identified through the production line.

The thoracic contents were removed between 15-20 minutes after slaughter. The pericardium was examined and removed and the heart was then examined for colour, shape, size and rigidity. The great blood vessels were cut off at atrial level. Blood clots were removed from the RV and the atria through atrial incisions and the heart was washed. Pericardial fat was not trimmed. The hearts were then weighed to the nearest gram and were then examined for any gross pathological lesions by methods outlined by Rooney (1970).

As the thickness of the ventricular walls varies greatly at different sites, it was decided to measure ventricular wall thicknesses at fixed points. The RV wall was measured midway between the insertion of the large anterior papillary muscle and the tricuspid valve immediately dorsal to it. LV wall thickness was measured midway between the insertions

of the anterior and the posterior papillary muscles.

The lungs and trachea were examined by visual inspection, palpation and incision, using standard pathological techniques and interpretations (Nicholls, 1978). The split skulls were also inspected for evidence of upper respiratory disease. On the basis of the post mortem findings, the horses were divided into three groups: (A) normal horses - no evidence of cardiac or respiratory disease, (B) horses with evidence of pulmonary disease, (C) horses with evidence of upper respiratory disease or of gross cardiac disease.

As the purpose of the study was to examine anatomical cardiac parameters in normal horses and in horses with chronic pulmonary disease, results obtained from horses showing clinical or post mortem evidence of other types of respiratory or cardiac disease (group C) were omitted from the survey.

The results obtained from each breed were divided into two groups: I. normal horses, i.e. showing no clinical or pathological evidence of cardiac or respiratory disease, II. abnormal horses, i.e. showing clinical or post mortem evidence of chronic pulmonary disease.

For each horse, HW/BW % and LV/RV wall thickness was determined. The mean HW/BW % and mean LV/RV wall thicknesses were compared by analysis of variance (Snedecor and Cochran, 1971) both between normal and abnormal animals within breeds and also between breeds (including normal and abnormal horses).

RESULTS

All animals slaughtered during the survey were adults. No clinical evidence of infectious respiratory disease was

observed. Most of the horses classified as having chronic pulmonary disease were so designated on clinical grounds. The results are presented in Tables 18:1 and 18:2.

TABLE 18:1

Heart weight/body weight (HW/BW %) values obtained from normal horses and from horses suffering from chronic pulmonary disease.

		HW/BW %			
		Pony	Draught	Hunter	Thoroughbred
NORMAL	N	170	75	42	29
	X	0.5943	0.5544	0.6595	0.7779
	SD	0.1166	0.0862	0.1058	0.1187
	SE	0.008943	0.00953	0.016325	0.02204
ABNORMAL	N	16	8	3	2
	X	0.6381	0.555	0.7333	0.6650
	SD	0.1224	0.0475	0.0387	0.1625
	SE	0.03060	0.01696	0.02234	0.11491

N = Number, X = Mean Value, SD = Standard Deviation, SE = Standard Error.

Relative Heart Weight (HW/BW%)

Comparison of HW/BW% differences between breeds (including both normal and abnormal horses) by an analyses of variance showed the presence of highly significant interbreed difference in this parameter ($F_{312}^{3} = 33.45$; $P < .001$). Further analyses by Duncan's multiple range test indicated that each breed formed a significant subset.

The results of interbreed HW/BW comparison by Student's 't' test is as follows:

Pony	v	draught	$P < 0.01$
Pony	v	hunter	$P < 0.01$
Pony	v	TB	$P < 0.001$
Draught	v	hunter	$P < 0.001$
Draught	v	TB	$P < 0.001$
Hunter	v	TB	$P < 0.001$

Within each breed type no difference was obtained between normal and abnormal horses and individual comparisons by Student's 't' test gave the following results.

Normal	vs	abnormal pony	$P > 0.1$
Normal	vs	abnormal draught	$P > 0.9$
Normal	vs	abnormal hunter	$P > 0.2$
Normal	vs	abnormal T.B.	$P > 0.2$

Relative ventricular size

LV/RV/ wall thickness of the four breeds (Table 18:2) were compared by an analyses of variance and significant differences were found between the breeds ($F_{312}^{3} = 3.77$; $P < .05$). Further

analysis of Duncan's multiple range test indicated that the breeds fell into two significant but overlapping subsets i.e. /Pony + Draught/ and /Draught + T.B.X + T.B./, but within each subset the differences between normal and abnormal horses were non significant ($F_{267} = 1.211$, $F_{157} = 0.018$ respectively).

TABLE 18:2

Left ventricular/right ventricular (LV/RV) wall thickness values obtained from normal horses and from horses with chronic pulmonary disease.

		LV/RV Wall Thickness			
		Pony	Draught	Hunter	Thoroughbred
NORMAL	N	170	75	42	29
	X	2.4435	2.368	2.1971	2.1421
	SD	0.5962	0.6093	0.4223	0.4848
	SE	0.04573	0.07036	0.06516	0.09002
ABNORMAL	N	16	8	3	2
	X	2.1344	2.511	2.0433	1.685
	SD	0.4996	1.112	0.1459	0.3606
	SE	0.1249	0.39321	0.68423	0.25499

N = Number, X = Mean Value, SD = Standard Deviation, SE = Standard Error.

DISCUSSION

Relative Heart Weight

The survey indicated that very significant differences in HW/BW % occur between the different breeds of horses studied. No previous studies have apparently indicated the significance of this interbreed difference. Because of this finding, it is advisable that ventricular size comparisons between normal horses and horses with respiratory disease are performed within breeds.

However, no significant difference in HW/BW % was observed between normal and abnormal horses in any breed, indicating that general cardiac hypertrophy did not occur with pulmonary disease.

Relative Ventricular Size

The survey indicated that there also was some interbreed difference between LV/RV wall thickness, but more significantly it showed that there was no significant difference between LV/RV wall thicknesses of normal and diseased horses in any breed, indicating the absence of RV hypertrophy in the horses with chronic pulmonary disease.

It is accepted that the classification of the horses into the two groups, *i.e.* normal or those with clinical or gross pathological evidence of chronic pulmonary disease was not completely satisfactory. As the survey was carried out in August when most horses would be outdoors on unsupplemented grazing, it is possible that some horses affected with COPD may have been asymptomatic because of lack of exposure to the aetiological agents. Consequently these animals might have

been classified as normal horses on clinical examination. Unless they had detectable pulmonary changes on post mortem they might also have been classified as normal on this examination. It is therefore possible that some COPD affected horses which might be expected to have RV hypertrophy, were included in the normal group, thereby elevating the mean LV/RV wall thickness of the normal group.

Conversely it is possible that some horses which were classified as having chronic pulmonary disease might have been suffering from relatively short term pulmonary disease such as viral pneumonia. Animals suffering from such conditions would not be expected to develop RV hypertrophy. However, it was hoped that the inclusion of such horses in the survey was minimised by the exclusion of horses that had clinical or gross pathological evidence of viral or bacterial infections, or of upper respiratory disease. As noted, no clinical evidence of infectious respiratory disease was observed in the survey and this was in keeping with a general low incidence of such infectious respiratory diseases in Ireland in the summer of 1976.

Further, no gross pathological evidence of generalised infectious pulmonary disease or of pulmonary abscessation was observed throughout the entire survey. It is likely, therefore, that most horses classified as being affected with chronic pulmonary disease were in fact accurately classified. It would not be possible, however, to state what % of these horses with chronic pulmonary disease were actually suffering from COPD, because as previously noted, McPherson et al. (1978)

have shown that it is not possible to accurately diagnose COPD on clinical grounds only.

Because the survey was carried out under field conditions it was not possible to perform any respiratory function or allergen inhalation tests to more accurately identify the chronic pulmonary disease present. Serum precipitin examination of all horses was considered, but was not carried out because it is believed that the isolated examination for serum precipitins against M. faeni and A. fumigatus without pulmonary function and inhalation challenge testing is of very limited value (Lawson 1976 pers. comms.).

Pathologists agree that the most accurate method of assessing RV hypertrophy is to dissect free the RV and compare its weight with that of the LV + Septum (Thurlbeck, 1976). Cardiac dissection could not be performed in this survey because EEC regulations on intercommunity horse meat movement prevents the export for human consumption of any viscera which is not intact, this measure being thought necessary to prevent the sale of damaged viscera which might be trimmed.

Consequently ventricular wall thickness measurements were used to assess RV hypertrophy.

One of the main arguments against this form of ventricular hypertrophy assessment is that ventricular thicknesses can be influenced by rigor mortis myocardial contractions. In horses the LV contracts fully at death and remains fully in systole, the RV contracts within a few minutes of death and remains in systole for a few hours and then relaxes (Rooney, 1970). As all ventricular thickness measurements in this survey were performed within 15-30 minutes of death, both LV

and RV thicknesses were measured while both ventricles were fully contracted.

Another argument against ventricular thickness assessment is that ventricular wall thickness varies from site to site and this prevents objective ventricular thickness assessment. This variation in thickness was very evident to the observer and for this reason the measurements were made at two representative ventricular sites which could be definitely identified.

Bove and Scott (1966) used ventricular measurements at fixed sites to assess RV hypertrophy in man and they noted that the RV thickness (6.2 mm) in patients with pulmonary hypertension was 63% greater than that of the normal RV (3.8 mm). Overall it was felt that because of the uniform state of contraction of the ventricles and the identical measurement sites used, the form of ventricular hypertrophy assessment used was satisfactory. The presence of RV dilation could also interfere with relative ventricular thickness assessment but no evidence of cardiac dilation was observed in this survey.

2. ANATOMICAL HEART MEASUREMENTS IN HORSES AFFECTED WITH COPD

As previously noted a pathological study into COPD was simultaneously undertaken by the Glasgow school using many COPD cases referred by the Edinburgh workers. Consequently pathological examinations of the cardiovascular

system were necessarily undertaken by these workers and some of their findings have recently been published by Nicholls (1978).

The COPD affected horses examined by Nicholls included some cases which had histories of severe clinical COPD for more than five years and all referred cases had been shown by the author to have pulmonary hypertension while symptomatic. Nicholls dissected free the right ventricle and compared its weight with that of the left ventricle and septum. He found conclusive evidence of RV hypertrophy in only 2 out of 17 horses affected with COPD. Nicholls noted that this surprisingly low incidence of RV hypertrophy she recorded was in contrast to the severity of the clinical signs and the pathological pulmonary findings.

Nicholls did not note the breeds or the body weights of the horses she examined. As previously noted Nicholls found no evidence of pulmonary vascular disease in these horses.

GENERAL DISCUSSION

The low incidence of right ventricular hypertrophy found in both studies is in complete contrast to the findings in man where right ventricular hypertrophy is a very common finding with an incidence up to 40% in patients with chronic pulmonary disease, (W.H.O. 1963).

A possible reason why RV hypertrophy does not commonly occur in COPD affected horses may be the reactivity of the equine pulmonary vascular bed, which allows the pulmonary

hypertension to be readily reversed when the hypoxaemic stimulus dissappears. This reversibility of the pulmonary hypertension would prevent constant right heart strain. The absence of pulmonary vascular changes in COPD affected horses would also prevent continuous RV strain and thus decrease the possibility of RV hypertrophy developing.

GENERAL CONCLUSIONS

Because significant interbreed differences in cardiac anatomy occurs in horses it is advisable that comparative anatomical studies between normal and diseased should be performed within breeds. The findings indicated that right ventricular hypertrophy is an infrequent finding in horses with chronic pulmonary disease.

RIGHT HEART BLOOD PRESSURE MEASUREMENTS

GENERAL DISCUSSION AND CONCLUSIONS

Right heart blood pressures were readily measured in horses, using flow directed catheters and normal right heart blood pressures were shown to have small respiratory, pressure and pulse variations. Horses affected with chronic obstructive pulmonary disease were shown to have severe pulmonary hypertension, indicating that right ventricular strain is present in these animals.

This pulmonary hypertension in clinically affected horses was shown to be related to hypoxaemia and no evidence of hypercapnia or respiratory acidosis was found. During remission phases of COPD, the pulmonary and right ventricular hypertension almost disappeared, associated with a return of P_aO_2 values to within the normal range. This relationship between pulmonary hypertension and arterial hypoxaemia in COPD affected horses was further supported by the observation that experimental induction or relief of hypoxaemia in horses, was associated with increases or decreases of PAP respectively.

Previous authors who have studied cardiac output and pulmonary vascular resistance in COPD affected horses have found that increased pulmonary vascular resistance caused the pulmonary hypertension. In the work here reported, no increases in heart rate and consequently in cardiac output was observed in COPD affected horses and so it appears that the pulmonary hypertension in equine COPD must therefore be attributed to increased pulmonary vascular resistance. The

finding that the pulmonary hypertension and consequently the increased pulmonary vascular resistance of COPD can be reversed, shows that the increased pulmonary vascular resistance is caused by functional pulmonary vasoconstriction, which appears to be induced by hypoxia as adjudged by the presence of decreased carotid arterial O_2 partial pressure.

Although neither hypercapnia nor acidosis were observed in the COPD affected horses, experimental hypercapnia production or intravenous acid infusion were also shown to cause marked pulmonary hypertension. Intravenous bicarbonate, atropine or furosemide administration caused no changes in PAP levels in normal or COPD affected horses.

Despite the marked pulmonary hypertension in clinically affected COPD horses, no evidence of right heart failure was found in any animal. This observation was substantiated by the relative infrequency of RV hypertrophy observed on post mortem examination of horses affected with chronic pulmonary disease.

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APPENDIX 11.1. Pulmonary artery pressures, carotid blood gas and pH values obtained from normal horses.

Horse no.	Breed	Age	Sex	PAP (mm Hg)					
				Max	Min	Mean	P_AO_2	P_ACO_2	pH
C 1	Hunter	8	Mn	28	12	18	92.0	37.2	7.44
C 2	Pony	3	F	39	12	25	95.0	-	-
C 3	Hunter	7	F	34	19	18	84.2	41.2	7.408
C 4	Pony	4	F	32	19	24	91.3	40.1	-
C 5	Pony	4	Mn	32	18	24	93.9	38.7	7.430
C 6	Pony	Aged	F	34	15	25	96.3	34.1	7.376
C 7	Pony	5	F	29	13	18	96.0	35.8	7.366
C 8	TB	3	Mn	32	10	25	96.1	35.6	7.372
C 9	Pony	5	F	30	18	23	93.8	40.0	7.353
C 10	Pony	4	F	32	14	24	90.4	35.2	7.450
C 11	Pony	3	Mn	30	14	23	84.2	36.6	7.388
C 12	Hunter	3	Mn	32	12	24	96.2	38.2	7.440
C 13	Draught	5	Mn	34	20	26	94.8	38.5	7.378
C 14	Pony	3	Mn	29	23	26	85.9	33.8	7.427
C 15	Pony	4	F	-	-	24	83.7	37.9	7.406
C 16	Hunter	Aged	Mn	35	14	23	86.5	31.4	7.408

Table continued

APPENDIX 11.1 continued

Horse no.	Breed	Age	Sex	PAP (mm Hg)					
				Max	Min	Mean	P_AO_2	P_ACO_2	pH
C 17	Pony	8	F	29	14	22	88.2	36.9	7.375
C 18	Pony	5	F	38	18	29	89.3	37.3	7.40
C 19	Draught	7	Mn	36	14	24	92.1	34.4	7.320
C 20	Draught	4	Mn	32	18	24	100.9	34.2	7.327
C 21	TB	2	M	32	10	25	93.0	-	-
C 22	Pony	4	F	26	12	22	94.6	35.1	7.384
C 23	Pony	12	Mn	32	20	24	94.5	36.8	-
C 24	Pony	4	F	31	19	22	89.6	35.6	7.395
C 25	Pony	2	M	30	18	22	104.5	40.7	7.398
C 26	Pony	5	Mn	32	20	26	98.0	39.4	7.417
C 27	Hunter	5	F	30	17	24	91.6	38.8	7.450
C 28	Pony	4	F	26	14	19	93.1	38.8	7.543
C 29	Hunter	6	Mn	-	-	24	89.1	35.5	-
C 30	Pony	3	F	34	18	25	91.8	36.5	-
C 31	Pony	7	F	36	16	24	89.5	37.8	7.366
C 32	Pony	9	F	33	17	20	84.2	37.5	7.399

Table continued

APPENDIX 11.1 continued

Horse no.	Breed	Age	Sex	PAP (mm Hg)					
				Max	Min	Mean	P_AO_2	P_ACO_2	pH
C 33	Hunter	4	Mn	42	21	29	82.7	35.0	7.426
C 34	TB	5	F	35	23	29	94.5	36.8	-
C 35	TB	4	F	29	19	26	102.1	37.1	7.408
C 36	Pony	3	Mn	28	19	23	93.8	37.5	7.472
C 37	Pony	4	Mn	30	19	23	86.7	41.0	7.440
C 38	Pony	5	Mn	32	22	26	89.9	47.2	7.412
C 39	Pony	5	F	35	19	27	92.6	41.9	7.411
Mean				32.2	16.8	23.8	92.0	37.5	7.403
± S.D.				3.42	3.52	2.70	5.06	2.84	0.036
N = 39				37	37	39	39	37	32

Mean heart rate 47.2 ± 8.2

APPENDIX 11.2. Pulmonary artery pressures, carotid blood gas and pH values obtained from symptomatic COPD affected horses.

Horse no.	Breed	Age	Sex	PAP			P_AO_2	P_ACO_2	pH
				Syst.	Diast.	Mean			
B 1	Hunter	Aged	F	43	23	30	80.4	-	-
B 2	Pony	10	F	59	22	38	69.0	-	-
B 3	Pony	8	Mn	60	40	46	74.0	-	-
B 4	Hunter	Aged	Mn	44	26	38	78.0	-	-
B 5	Hunter	8	F	46	22	34	63.8	-	-
B 6	Polo pony	6	F	64	15	40	58.7	-	-
B 7	Hunter	9	Mn	52	18	36	77.9	-	-
B 8	Draught	12	Mn	45	22	34	82.0	-	-
B 9	Draught	15	Mn	40	17	35	66.7	-	-
B 10	Hunter	12	F	104	61	75	62.0	-	-
B 13	½ Bred	9	F	59	29	37	63	-	-
B 16	Hunter	Aged	F	67	22	42	63	-	-
B 17	Hunter	6	F	94	70	80	62	-	-
B 18	Hunter	10	Mn	58	31	43	68	-	-
B 19	Pony	5½	F	68	30	46	60	-	-
B 20	Hunter	Aged	F	62	18	40	-	-	-

Table continued

APPENDIX 11.2 continued

Horse no.	Breed	Age	Sex	PAP					
				Syst.	Diast.	Mean	P_AO_2	P_ACO_2	pH
B 21	Draught	6	Mn	59	19	39	74	-	-
B 22	Draught	Aged	Mn	45	25	38	-	-	-
B 23	TB	9	Mn	42	17	29	66.4	42.9	7.42
B 24	Pony	7	Mn	36	27	31	80	34.5	7.377
B 25	Hunter	Aged	Mn	59	22	32	71.5	40.7	7.420
B 26	TB	6 yo	F	65	30	48	61.2	47.2	7.431
B 27	Hunter	Aged	F	50	28	33	65.7	33.2	7.363
B 28	TB	7 yo	F	57	34	45	74.5	-	-
B 29	Draught	6 yo	Mn	59	22	38	66.1	39.4	7.390
B 30	½ Bred	5	F	52	18	36	77.9	41.7	7.340
B 31	Pony	4½	Mn	42	20	29	77.1	35.9	7.398
B 32	Draught	Aged	Mn	48	18	32	63.9	39.2	7.398
B 33	Draught	Aged	Mn	48	14	35	66.1	36.1	7.480
B 34	Draught	9	Mn	40	18	30	80.4	34.1	7.390
B 35	Draught	10	Mn	58	22	42	64.7	36.5	7.400
B 36	Draught	Aged	Mn	48	30	37	76.9	36.8	-

Table continued

APPENDIX 11.2. Continued

Horse no.	Breed	Age	Sex	PAP					
				Syst.	Diast.	Mean	P_AO_2	P_ACO_2	pH
B 37	Draught	6	Mn	48	22	34	66.2	35.8	7.435
B 38	TB	7	Mn	41	24	31	66.7	39.6	7.414
B 39	Polo pony	10	Mn	38	26	31	82.0	35.4	-
B 40	½ Bred	7	F	73	18	45	64.4	47.6	-
B 41	Hunter	7	F	50	18	34	63.9	44.2	7.411
B 42	Hunter	Aged	F	58	22	42	65.8	42.2	7.420
B 43	Draught	Aged	Mn	39	18	28	76.4	35.4	-
B 44	Hunter	7	Mn	52	22	33	66.0	39.4	7.415
B 45	Pony	7	M	45	22	39	74.3	43.8	7.450
B 46	Hunter	7	M	42	22	34	82.0	39.4	7.399
B 47	Hunter	5	F	45	28	36	-	-	-
B 48	½ Bred	7	Mn	58	26	43	71.3	43.4	7.412
B 49	TB	5	F	54	26	38	74.8	35.8	7.425
B 50	Hunter	9	Mn	56	18	33	80.3	32.3	7.402
B 53	Hunter	8	F	87	49	61	75.0	-	-

Table continued

APPENDIX 11.2. Continued

Horse no.	Breed	Age	Sex	PAP					
				Syst.	Diast.	Mean	P_AO_2	P_ACO_2	pH
B 54	Hunter	8	F	91	44	66	51.0	-	-
B 55	Hunter	9	Mn	56	21	39	69.0	-	-
B 56	TB	13	F	79	20	53	66.0	-	-
Mean				56.10	25.3	39.8	70.0	38.9	7.418
± S.D.				14.72	10.79	10.83	7.41	4.22	0.029
N				50	50	50	48	26	22

Mean heart rate 39.0 ± 8.6

APPENDIX 11.3. Pulmonary artery pressures, carotid blood gas and pH values obtained from asymptomatic COPD affected horses.

Horse no.	Breed	Age	Sex	PAP Max	PAP Min	PAP Mean	P_AO_2	P_ACO_2	pH
B 3	Pony	8	Mn	34	24	30	88.2	-	-
B 4	Hunter	Aged	Mn	40	22	29	83.0	-	-
B 6	Polo pony	6	F	40	27	30	86.5	-	-
B 7	Hunter	9	Mn	32	16	29	84.0	-	7.311
B 8	Draught	12	Mn	42	16	29	93.0	33.0	7.395
B 9	Draught	15	Mn	37	19	25	86.0	34.5	-
B 11	Hunter	8	F	39	18	27	92.6	38.2	-
B 12	Hunter	13	Mn	34	18	28	87.4	32.2	7.390
B 14	TB	7	F	38	26	30	101.4	36.6	7.385
B 15	Hunter	6	F	26	13	18	93.0	33.1	7.372
B 22	Draught	Aged	Mn	41	21	34	92.7	38.5	7.406
B 25	Hunter	Aged	Mn	36	20	28	83.9	43.2	7.415
B 27	Hunter	Aged	F	-	-	22	86.8	30.7	7.390
B 28	TB	7	F	34	17	22	82.1	34.9	7.451

Table continued

APPENDIX 11.3 continued

Horse no.	Breed	Age	Sex	PAP			P_AO_2	P_ACO_2	pH
				Max	Min	Mean			
B 31	Pony	4½	Mn	52	16	31	82.6	38.6	7.360
B 32	Draught	Aged	Mn	40	18	30.0	82.4	34.1	7.390
B 38	TB	7	Mn	40	22	33	82.9	38.8	-
B 39	Polo pony	10	Mn	38	26	31	82.0	35.4	7.4000
B 44	Hunter	7	Mn	42	20	30	82.5	39.4	7.399
B 57	TB	9	F	32	23	26	86.5	38.1	7.440
B 58	TB	7	F	34	19	30	90.7	34.1	7.467
Mean				37.6	20.1	28.2	87.2	36.1	7.398
± S.D.				5.31	3.80	3.82	5.16	3.21	0.038
N				20	20	21	21	17	15

Mean heart rate 38.3 ± 6.4

MEAN PULMONARY ARTERIAL PRESSURE, ARTERIAL BLOOD GASES AND pH VALUES FROM 8 NORMAL HORSES AT REST AND DURING ACUTE HYPOXAEMIA PRODUCTION

Appendix 12:1

	Rest				After N_2 administration			
Horse no.	P_aO_2 (mm Hg)	P_aCO_2 (mm Hg)	pH	Mean PAP (mm Hg)	P_aO_2 (mm Hg)	P_aCO_2 (mm Hg)	pH	Mean PAP (mm Hg)
1 C5	93.9	38.7	7.430	24	39.6	26.5	7.52	29
2 C24	87.9	39.1	7.400	26	44.0	28.5	7.54	29
3 C15	83.7	37.4	7.406	24	60.7	31.3	7.52	35
4 C20	100.9	31.2	7.432	22	48.1	31.3	7.40	43
5 C18	89.3	37.3	7.400	29	47	30.4	7.498	
6 C17	88.2	36.9	7.375	22	60.2	31.3	7.395	34
7 C16	86.5	31.4	7.408	24	56.4	24.6	7.443	34
8 C20	104.5	40.7	7.398	22	47.6	28.7		32
Mean	91.9	36.65	7.392	24.1	50.5	29.1	7.474	33.7
± S.D.	7.33	3.50	0.032	2.42	7.75	2.50	0.060	4.75

MEAN PULMONARY ARTERIAL PRESSURES, ARTERIAL BLOOD GASES AND pH VALUES FROM 8 COPD AFFECTED HORSES AT REST AND DURING ACUTE HYPOXAEMIA PRODUCTION

Appendix 12:2

	Rest				After N_2 administration			
Horse no.	P_aO_2 (mm Hg)	P_aCO_2 (mm Hg)	pH	Mean PAP (mm Hg)	P_aO_2 (mm Hg)	P_aCO_2 (mm Hg)	pH	Mean PAP (mm Hg)
1 B37	63.8	40.6	7.368	34	52.3	35.2	7.362	55
2 B33	66.7	32.7	7.475	35	43.2	31.1	7.525	48
3 B24	81.6	38.6	7.36	31	40.8	37.0	7.403	42
4 B31	77.9	41.0	7.42	29	37.6	29.2	7.510	45
5 B34	80.4	34.1	7.39	30	59.9	32.8	7.40	46
6 B44	66.2	35.8	7.435	34	45.2	34.9	7.450	40
7 B50	-	-	-	33	6	-	-	48
8 B25	63.9	42.6	7.431	34	49.0	37.0	-	49
Mean	71.5	37.8	7.411	32.5	48.3	34.0	7.442	46.6
± S.D.	8.07	3.86	0.041	2.20	6.37	3.08	0.065	4.60

Appendix 13:1

Pulmonary artery pressure (PAP), and arterial blood gases and pH levels in 5 normal horses before and during inhalation of oxygen enriched air.

	Before Treatment				During Treatment			
Animal No.	P_aO_2 (mm Hg)	P_aCO_2 (mm Hg)	pH	Mean PAP (mm Hg)	P_aO_2 (mm Hg)	P_aCO_2 (mm Hg)	pH	Mean PAP (mm Hg)
C 25	96.6	37.9	7.400	26.0	179.9	42.4	7.321	24
C 26	92.7	38.5	7.324	27.0	187.4	41.4	7.271	23
C 27	87.9	39.1	7.400	26	164	42.4	7.341	27
C 28	94.2	38.1	7.392	23	149	40.6	7.361	23
C 29	89.6	38.0	7.411	27	156	43.2	7.382	27
Mean	92.2	38.3	7.385	25.8	167.3	42.0	7.335	24.8
$\pm$ S.D.	3.49	0.49	0.035	1.64	16.09	1.01	0.042	2.05

Appendix 13:2

Pulmonary artery pressure (PAP), and arterial blood gases and pH levels in 12 symptomatically affected COPD horses before and during inhalation of oxygen enriched air.

	Before Treatment				During Treatment			
Animal No.	P_aO_2 (mm Hg)	P_aCO_2 (mm Hg)	pH	Mean PAP (mm Hg)	P_aO_2 (mm Hg)	P_aCO_2 (mm Hg)	pH	Mean PAP (mm Hg)
B31	81.2	41.2	7.408	28	152.2	42.0	7.338	27
B34	80.1	40.1	7.396	28	226.1	43.1	7.364	27
B39	82.0	35.4	-	31	142.9	37.2	-	28
B50	81.6	38.6	7.360	31	102.9	39.3	7.356	31
B48	73.8	40.5	-	32	99.2	37.1	-	28
B23	66.2	47.7	7.481	45	98.6	48.8	7.469	30
B29	66.7	32.7	7.475	48	106	39.9	7.449	43
B35	63.4	34.2	7.406	46	101.7	41.2	7.450	39
B32	56.6	-	-	43	114.5	-	-	39
B30	77.9	41.0	7.426	29	163.7	39.3	7.430	24
B41	63.9	39.2	7.412	32	94.4	36.6	7.412	27
B38	66.7	40.3	7.387	34	86.1	42.9	7.379	34
Mean	71.6	38.7	7.417	35.6	124.0	40.67	7.405	31.4
$\pm$ S.D.	8.86	4.15	0.039	7.60	40.54	5.53	0.047	5.99

Appendix 14:1

The effects of inhalation of carbon dioxide enriched air on the mean pulmonary artery pressure (PAP) and arterial blood gases and pH of 6 normal horses.

	Before Treatment				During Treatment			
Animal No.	P_aO_2 (mm Hg)	P_aCO_2 (mm Hg)	pH	Mean PAP (mm Hg)	P_aO_2 (mm Hg)	P_aCO_2 (mm Hg)	pH	Mean PAP (mm Hg)
C 39	92.6	37.9	7.380	27	90.0	55.4	7.265	49
C 30	93.0	38.5	7.387	27	114.6	50.4	7.303	27
C 33	94.0	38.7	7.430	24	106.5	47.9	7.306	37
C 34	87.9	39.6	7.406	21	103.0	66.8	7.217	34
C 28	87.0	37.3	7.392	23	103	53.6	7.269	34
C 26	86.8	30.7	7.390	22	107.8	42.2	7.284	30
Mean	90.2	37.1	7.398	24.0	104.2	52.7	7.274	35.2
$\pm$ S.D.	3.32	3.24	0.018	2.53	8.14	8.31	0.033	7.63

Appendix 14:2

The effects of inhalation of carbon dioxide enriched air on the mean pulmonary artery pressure (PAP) and arterial blood gases and pH of 8 horses symptomatically affected with chronic obstructive pulmonary disease.

Horse no.	Before Treatment				During Treatment			
	P_aO_2 (mm Hg)	P_aCO_2 (mm Hg)	pH	Mean PAP (mm Hg)	P_aO_2 (mm Hg)	P_aCO_2 (mm Hg)	pH	Mean PAP (mm Hg)
B25	71.5	40.7	7.414	32	102	42.7	7.370	35
B14	72.8	40.0	7.392	31	106.3	39.7	7.372	36
B19	81.2	41.2	7.408	28	115.7	51.7	7.303	36
B24	67.2	39.1	7.411	28	101.4	43.4	7.371	40
B27	69.4	38.9	7.321	29	97.4	41.1	7.291	41
B30	-	-	-	32	-	-	-	38
B31	-	-	-	34	-	-	-	54
B36	-	-	-	32	-	-	-	47
Mean	72.4	40.0	7.389	30.8	104.6	43.7	7.332	40.9
$\pm$ S.D.	5.35	0.99	$\pm$ 0.039	2.29	6.98	4.69	0.037	6.56

APPENDIX 15:1

P_aO_2, P_aCO_2, arterial pH, standard bicarbonate (Std. Bic.) base excess (B.E.), heart rate and mean pulmonary artery pressure (PAP) values from 6 horses before and immediately after intravenous infusion of 0.2 molar HCl at a dosage of 100 cc/50 Kg bodyweight over a 5-7 minute period.

	Horse no.	C27	C25	C14	B57	B27	C30	Mean ± S.D.
Before Acid Infusion	P_aO_2 mm Hg	96.2	94.8	85.9	88.2	65.7	89.6	86.7 ± 11.0
	P_aCO_2 mm Hg	38.2	38.5	33.8	35.9	33.2	35.6	36.0 ± 2.3
	pH	7.440	7.378	7.427	7.398	7.363	7.395	7.400 ± 0.029
	Std. Bic. m.mols/L	23.0	22.5	25.0	22	15	18.0	20.9 ± 3.7
	Base excess m.mols/L	-2.0	-2.0	0	-1	-5.5	-2.1	-2.1 ± 1.9
	Heart rate/min.	45	38	44	33	42	42	40.1 ± 4.5
	Mean PAP mm Hg	25	26	26	24	33	22	26.0 ± 3.74
	Horse No.	C27	C25	C14	B57	B27	C30	Mean ± S.D.
After Acid Infusion	P_aO_2 mm Hg	98.5	98.3	97.9	99.7	105.2	75.5	95.9 ± 10.3
	P_aCO_2 mm Hg	31.9	31.9	25.6	23.0	21.9	31.1	27.6 ± 4.6
	pH	7.361	7.304	7.295	7.299	7.368	7.390	7.336 ± .0416
	Std. Bic. m.mols/L	18.5	15.5	12	13	11.9	14	14.2 ± 2.5
	Base excess m.mols/L	-6.5	-10	-11	-9.6	-17.5	-13	-11.3 ± 3.7
	Heart rate/min.	56	62	78	52	51	89	64.7 ± 15.5
	Mean PAP mm Hg	30	45	76	72	55	62	56.7 ± 17.3

APPENDIX 15:2

P_aO_2, P_aCO_2, arterial pH, standard bicarbonate (Std. Bic.) base excess (B.E.) and mean pulmonary arterial pressure (PAP) values from 6 horses before and immediately after intravenous infusion of sodium bicarbonate solution at a dose of 100 ml/50Kg bodyweight over a 5-7 minute period.

	Horse no.	C6	B28	C7	C8	C9	C34	B25	Mean ± S.D.
Before Bicarbonate Infusion	P_aO_2 mm Hg	96.3	82.4	96.0	96.1	93.8	93.1	84.1	91.6 ± 5.91
	P_aCO_2 mm Hg	34.1	37.9	35.8	35.6	40.0	38.8	34.9	36.7 ± 2.19
	pH	7.376	7.460	7.366	7.272	7.353	7.453	7.450	7.402 ± .047
	St. Bic. m.mols/L	21.0	27.0	21.0	22.0	25.0	22.0	21.5	22.8 ± 2.31
	Base excess m.mols/L	-4.0	+3.0	-4.5	-4.0	-4.0	-3.0	+1.0	-2.6 ± 2.05
	Mean PAP mm Hg	25	25	21	24	24	19	22	22.9 ± 2.27
	Horse no.	C6	B28	C7	C8	C9	C34	B25	Mean ± S.D.
After Bicarbonate Infusion	P_aO_2 mm Hg	82.2	84.5	89.2	74.9	90.8	72.9	84.5	82.7 ± 6.73
	P_aCO_2 mm Hg	40.5	43.5	36.1	43.9	39.9	40.0	32.9	39.5 ± 3.91
	pH	7.449	7.620	7.441	7.562	7.580	7.554	7.478	7.526 ± .070
	St. Bic. m.mols/L	25.0	45.0	36.5	37.5	26.0	29.7	27.5	32.5 ± 7.40
	Base excess m.mols/L	+3.5	+20.0	+1.0	+15.0	+14.0	+13.2	+11.5	11.2 ± 6.67
	Mean PAP mm Hg	25	25	23	25.5	32	19	32	25.9 ± 4.69

Appendix 16:1

Details of 8 normal and 12 COPD affected horses used in Chapter 16.

Control horses (Group A)

No.	Age	Breed	Sex
1	4 years	Arab	Mn
2	3 years	Hunter	F
3	10 years	Hunter	F
4	14 years	Light Draught	Mn
5	7 years	Hunter	Mn
6	1 year	T.B.	F
7	4 years	Welsh Pony	Mn
8	4 years	Welsh Pony	Mn

COPD affected horses (Group B)

No.	Age	Breed	Sex
1	15 years	Draught	Mn
2	7 years	Hunter	Mn
3	8 years	Hunter	F
4	10 years	Hunter	Mn
5	12 years	Hunter	F
6	7 years	Hunter	F
7	9 years	T.B.	Mn
8	7 years	Hunter	Mn

COPD affected horses (Group C)

No.	Age	Breed	Sex
1	13 years	Hunter	Mn
2	12 years	Pony	Mn
3	10 years	Hunter	Mn
4	7 years	T.B.	F

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LETTER

THE EFFECT OF SUBMAXIMAL EXERCISE ON THE PERIPHERAL BLOOD PRESSURE OF UNTRAINED PONIES

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ABSTRACT

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A significant increase in systolic and diastolic peripheral blood pressure was recorded after 8 minutes submaximal exercise in untrained ponies. Blood pressure was recorded by a modified auscultatory method from the coccygeal artery.

INTRODUCTION

Although there is widespread use of exercise tests in horses in veterinary medicine, only recently has there been any real interest in the physiological and biochemical effects of exercise in this species. Increased peripheral blood pressure (BP) due to exercise has been recorded in man by many authors, including Korner (1952), and in the dog by Vatner et al. (1970). Although it has also been recorded in the horse (Gehring, 1939; Laskov et al., 1960; Hornicke et al., 1971), the comprehensive, recent study of the effect of exercise on BP in the untrained horse by Bergsten (1974) showed no such BP increase during exercise.

The present experiment was designed to examine the effect of submaximal exercise on the indirectly measured BP of untrained ponies.

MATERIALS AND METHODS

The animals used were three Shetland (two geldings and one mare) and one Welsh (gelding) ponies, between 2·5 and 3 years old. These animals had been fully confined in pairs, in looseboxes, 5 m by 5 m, for 2 years. Two weeks before the start of the experiments, the ponies were walked

30 metres to the laboratory and made accustomed to the BP measurement procedures, to reduce the possibility of hypertension induced by exci ment. All measurements were performed in a quiet laboratory, with minimal external influences on the animals.

During each experiment, BP was first measured for a period of 5 to minutes with the animal at rest. The animal was then lunged for 8 minutes in an indoor riding school, at approximately 2·5 metres/secon as calculated from time of circuit. BP was measured immediately pos exercise for a period of 20 minutes. The first measurement was usua recorded within 30 seconds post-exercise, this being the time require to affix and inflate the tail cuff and to attach its pneumatic and electrical connections. No more than one experiment was performed o each animal daily and all experiments were at least 4 hours after the last feed to prevent any postprandial cardiovascular changes (Beverga and Shepherd, 1967).

BP was measured from the coccygeal artery by the modified auscultat method described by Dear (1968) and Ellis (1975), using the latter's criteria to establish systole and diastole. A standard 23 cm by 13 self-adhesive sphygmomanometer cuff[1] was used. The piezocrystal[2] within the cuff was attached to a phonocardiograph receiver[3]. The c was pneumatically connected to a strain gauge manometer[4] and pressure transducer[3]. Both results were recorded on a multichannel recording system[3].

Many of the experiments had to be repeated due to faulty positionin of the microphone over the artery, which resulted in poor recording o the Korotkoff sounds, and also because of breakage of the piezocrysta or its delicate electrical attachments, due to tail movement. Eight satisfactory recordings were obtained from each pony.

BP levels were measured at approximately 30-second intervals throug out the monitoring period. As this is an intermittent measuring method, the times of each reading varied due to slight differences in the BP levels. For each experiment, BP and heart rate were plotted (against time) and the mean and standard deviation (SD) for each pony calculated. While in situ, the mid-point of the tail cuff was 18 cm and 20 cm above the level of the point of the shoulder (tuberositas lateralis of the humerus) in the Shetland and Welsh ponies respective

1 A. & C. Cossar Ltd., London.
2 B.S.R. Ltd., Cradley Heath, Worcs.
3 Devices Instruments Ltd., Welwyn Garden City, Herts.
4 Bell & Howell Ltd., Basingstoke.

RESULTS

The resting BP levels were relatively stable. For each pony, analysis of results by Student's "t" test, as applied to paired observations (Snedecor and Cochran, 1971), on the significance of mean differences between the systolic and diastolic BP before and at 30 seconds after exercise, showed that the post-exercise BP was significantly raised (Table 1).

The fall in BP occurred in two stages. A rapid initial fall for approximately 3 minutes was followed by a slower decrease to near resting levels about 15 minutes post-exercise. The recorded Korotkoff sounds post-exercise were much increased in amplitude as well as in frequency, compared with those at rest.

TABLE 1

Mean diastolic and systolic blood pressure (mmHg) in 4 ponies before and after 8 minutes of exercise

Pony	Diastolic blood pressure		Systolic blood pressure	
	Pre-exercise	Post-exercise	Pre-exercise	Post-exercise
1	65·6 ± 7·80	98·40 ± 14·80***	125·1 ± 5·44	175·4 ± 19·83***
2	59·5 ± 5·59	98·90 ± 21·58***	120·7 ± 5·57	167·9 ± 6·71***
3	67·4 ± 8·48	94·25 ± 17·38***	118·3 ± 11·79	150·8 ± 18·45**
4	64·6 ± 5·45	105·90 ± 10·78***	119·3 ± 8·14	165·8 ± 16·58***

** $P < 0.01$ *** $P < 0.001$

DISCUSSION

During exercise, increased cardiac output, which is proportional to tissue requirements (Herd, 1970), has been measured in horses by Bergsten (1974). Increased cardiac output would cause a proportional increase in BP, unless a simultaneous decrease in peripheral vascular resistance occurred. The latter is largely due to dilatation of the muscular vasculature (Astrand and Rodahl, 1970). The balance between these opposing forces is the basis on which the BP during exercise depends.

In exercising horses, marked splenic contraction occurs increasing the haematocrit (Swenson, 1977). Blood with increased viscosity requires greater pressure for perfusion (Herd, 1970). Thus, along

with the increased cardiac output, in horses haemoconcentration will further tend to raise the BP during exercise.

Increased BP due to emotional effects has been recorded in athletes just prior to exercise (Detweiler, 1973) and, also in man, excitement during exercise can potentiate the hypertensive effect of the latter (Barger et al., 1956). In thoroughbred horses, Hall et al. (1976) have recorded excitement-induced increases in heart rates to 300-400% of resting levels just prior to racing. The possibility that the increased BP recorded in the present experiments was due to excitement rather than to exercise, was considered. However, tachycardia was not recorded on any occasion prior to exercise, which indicated a lack of excitement at this stage.

The louder Korotkoff sounds recorded post-exercise are due to increased cardiac output (Ur and Gordon, 1970). There is no evidence that these sounds occur at an earlier stage during cuff deflation, thus giving apparently higher BP readings by auscultatory methods of measurement.

Of the authors who have recorded BP increases in the horse during exercise, Gehring (1939) used a tonoscillograph for BP measurement, a method which was subsequently shown to be unreliable for measurement of diastolic BP (Collins and Magora, 1963), Laskov et al. (1960) did not report the number of horses studied, the method used or the values obtained and Hornicke et al.(1971), using 3 horses, gave neither the method used nor the values obtained.

Bergsten (1974), using 20 Swedish standardbred riding horses on treadmill exercises at 4 metres/second and recording the BP directly by carotid catheterisation, found no statistical increase in integrated mean BP during exercise. It is possible that an increase in systolic pressure occurred without affecting the mean pressure, because with tachycardia the systole is often very peaked and, even if increased, it might not raise the mean BP to any significant extent. Direct BP recording methods are, in general, more accurate than indirect methods (Shirer, 1962). A possible reason why no BP increase was obtained by Bergsten may have been the relative fitness of his horses, due to their training for treadmill exercises with fixed short catheters. Another possible reason is that speeds of 4 metres/second would be very submaximal for this breed of horse, whose maximal speed is greater than 12 metres/second (Lindholm and Saltin, 1974). In well-trained human athletes, submaximal exercise may have little effect on BP (Detweiler, 1973).

Cardiovascular changes due to training have also been described in dogs (Vogel and Hannon, 1966) and in horses (Milne et al., 1977). Thus, the difference between Bergsten's results and those reported here may be partly due to the fitness of the animals.

Another possible reason for the differences between the present results and Bergsten's is a breed difference. It has been observed in this laboratory that ponies have higher resting heart rates and slightly lower BP than horses of the larger breeds and there may also be a difference in their physiological response to exercise.

CONCLUSION

Although this study was on a limited number of animals and the BP was measured after exercise, the results demonstrate a consistent hypertensive effect of submaximal exercise in untrained ponies. The variation between these findings and those of other authors may be due to differences in the fitness and breed of the animals used in the different studies.

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Pulmonary Artery Pressures in Normal Horses and in Horses affected with Chronic Obstructive Pulmonary Disease

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SUMMARY

Horses clinically affected with chronic obstructive pulmonary disease (COPD) were found to have pulmonary artery hypertension which was associated with systemic arterial hypoxia. The pulmonary hypertension in symptomatic COPD-affected horses was partially reversible upon remission of clinical signs or by oxygen administration. The induction of acute hypoxaemia caused an increase in pulmonary artery pressure in both normal and COPD-affected horses.

INTRODUCTION

PULMONARY artery hypertension secondary to chronic pulmonary disease is of major importance in human medicine (World Health Organisation, 1963). The horse's pulmonary anatomy and pulmonary vascular distribution are similar to those of man (McLaughlin, *et al.*, 1965; Tyler, Gillespie and Newell, 1971) so that a similar pulmonary hypertension might be expected to develop in chronic pulmonary disease in the horse. The pulmonary artery pressure of normal horses has been described by many authors. In some reports (Gall, 1967; Beltran, 1973; Bergsten, 1974; Milne, Muir and Skarda, 1975; Milne, Gabel, Muir and Skarda, 1977; Orr, *et al.*, 1975; Buss and Bisgard, 1977), the values recorded were obtained in circumstances which fulfil the presently accepted criteria for normal resting pulmonary artery pressure, namely, the animals were standing and untranquillised and a suitable baseline was established for a fluid-filled manometric system. Pulmonary artery hypertension has been demonstrated in horses with a variety of chronic pulmonary diseases (Alexander, 1959; Sporri and Schlatter, 1959; Eberly, Tyler and Gillespie, 1966; Beltran, 1973; Bergsten, 1974). The mean pulmonary artery pressure (PAP) value derived from the work of these authors is 44.95 mmHg. Bisgard, Orr and Will (1975) have shown that pulmonary artery hypertension also occurs in ponies moved to high altitudes. Previously, the occurrence of pulmonary hypertension due to hypoxia caused by residing at high altitudes had been well recorded in cattle (brisket disease) and in other species, including man.

This paper describes some studies on the measurements of PAP and carotid arterial blood gases and pH in normal horses and in horses affected with chronic obstructive pulmonary disease (COPD) during different stages of the disease. Observations are reported on the effect of oxygen administration and of acute hypoxaemia production in normal and COPD-affected horses.

MATERIALS AND METHODS

Horses were classified as COPD-affected, using the recently described criteria of McPherson, *et al.* (1978). The animals showed longstanding evidence of respiratory disease including many of the following clinical signs, coughing, dyspnoea, double expiratory effort, louder or wheezing chest sounds and in all cases a resting arterial oxygen partial pressure (PaO_2) of less than 82 mmHg and maximum intrapleural pressure changes of greater than 6 mmHg. The COPD cases referred to the veterinary hospital during a 3 year period, were all adults and consisted mainly of ponies and hunters with fewer Thoroughbred and draught horses. The controls included a higher proportion of ponies. COPD-affected animals were judged to be symptomatic or asymptomatic at the time of the recordings on the basis of clinical signs, their (PaO_2) and intrapleural pressures. Remission of clinical signs in COPD cases was obtained by using a peat bedding and feeding only a concentrated diet in cube form. These measures reduced exposure of the horses to the environmental aetiological agents. Clinical signs in COPD cases were induced by both natural and artificial exposure to the aetiological agents.

During all procedures, the animals were standing, untranquillised and were quietly handled to prevent pulmonary hypertension induced by excitement (Beltran, 1973). Prior to catheterisation, an area in the lower one-third of the jugular groove was anaesthetised with 1 ml lignocaine. A catheter was introduced into the jugular vein, passed through the right heart and advanced approximately 2 cm into the main trunk of the pulmonary

artery. Positioning was judged by the pulse contours and pressure values observed during manipulation of the catheter.

The catheter (Cardioflex 1150-09, Vygon U.K. Ltd.; Normocath 115-20, Vygon U.K. Ltd.) was connected by a tube (Lectocath 1150-20, Vygon U.K. Ltd.) to a strain gauge manometer (L-221-2-3, Bell & Howell, Basingstoke). This was attached to a pressure transducer (3552, Devices Instruments Ltd., Herts.). The manometer was positioned 2-3 cm above the point of the shoulder, at a site level with the right atrium (Beltran, 1973). The results were recorded on a multichannel recording system (M19, Devices Instruments Ltd., Herts.).

Intrapleural pressure measurements were made by the method of McPherson, *et al.* (1978) and standard lead 1 ECG tracings were also recorded.

Samples of carotid arterial blood were obtained as described by McPherson, *et al.* (1978). Acute hypoxaemia was produced by adding nitrogen to the inspired air through an open plastic face mask. Oxygen was similarly administered. The gases were administered at 20-50 l/min over a 3-10 min period until the heart rate and PAP reached a steady state.

Mid-inspiratory air samples were aspirated quickly into a 20 ml plastic syringe through a 14-gauge needle inserted interannularly into the trachea. The syringe was immediately sealed and the gas analysed within 5 min. Inspired air, blood gases and pH measurements were made using a gas analyser (Corning 161, Corning Ltd., Essex). The altitude of the hospital and laboratory is 200 m.

In the statistical analysis of results, the significance of differences between the means of groups was tested by Student's *t*-test. Paired data were analysed by Student's *t*-test as applied to paired observations.

RESULTS

Compared with the controls, horses showing clinical signs of COPD (Table I) had significantly raised PAP ($P < 0.001$) and significantly lowered PaO_2 ($P < 0.001$).

The arterial carbon dioxide partial pressures and pH values were within the normal range. During a remission (asymptomatic) phase, 10 of the COPD cases were again investigated; they had PaO_2 levels within the normal range. Their PAP in this phase was significantly below ($P < 0.001$) that of the symptomatic phase but was still significantly greater ($P < 0.01$) than that of the controls.

Increasing the oxygen content of inspired air to 60-80 per cent, as determined by mid-inspiratory tracheal air analysis, resulted in the clinically affected COPD group having a temporary partial remission of pulmonary hypertension until a few minutes after the oxygen administration was discontinued (Table II). This decrease in PAP was associated with PaO_2 levels, which were above normal.

Increasing the nitrogen content of the inspired air to 85-95 per cent in 8 normal and 8 COPD-affected horses caused a temporary hypoxaemia in all and, in addition, respiratory alkalosis in the control horses (Table III). In both groups a significant increase in PAP was induced. This was, however, more marked in the COPD-affected animals, although both groups showed a similar, induced reduction in PaO_2.

DISCUSSION

The findings indicate the relationship of hypoxaemia to the pulmonary hypertension observed in symptomatic COPD-affected horses. Humans, when clinically affected with COPD, are usually hypoxic, hypercapnic and acidotic and the associated pulmonary hypertension is related to all 3 factors (Thurlbeck, 1976). Neither hypercapnia nor acidosis appears to play a part in the aetiology of pulmonary hypertension in horses clinically affected with COPD. The COPD syndrome of Sasse (1971) and, to a lesser extent, of Beltran (1973) and the chronic alveolar emphysema of Bergsten (1974) appear to be functionally similar to the COPD syndrome of McPherson, *et al.* (1978) although they may differ aetiologically. The first 3 authors also found a normocapnic hypoxaemia in their affected horses. The

TABLE I

PULMONARY ARTERY PRESSURES AND CAROTID BLOOD GASES AND pH (MEAN VALUES AND S.D.) IN NORMAL AND COPD-AFFECTED HORSES

Group	No.	Pulmonary artery pressures (mm Hg)			Carotid arterial values		
		Maximum	Minimum	Mean	PaO_2 (mm Hg)	$PaCO_2$ (mm Hg)	pH
Control	20	33.77 ± 3.19	15.08 ± 4.91	23.54 ± 2.98	91.15 ± 5.23	36.28 ± 2.77	7.389 ± 0.038
COPD cases symptomatic	25	65.45 ± 19.85	31.01 ± 15.61	44.56 ± 13.84	66.13 ± 6.40	39.38 ± 5.98	7.423 ± 0.054
COPD cases asymptomatic	10	42.25 ± 4.60	19.25 ± 4.64	28.13 ± 4.37	86.51 ± 6.39	34.26 ± 2.75	7.412 ± 0.033

PaO_2: Arterial oxygen partial pressure $PaCO_2$: Arterial carbon dioxide partial pressure

TABLE II

EFFECT OF INHALATION OF AN OXYGEN-RICH MIXTURE ON CAROTID BLOOD GASES AND pH AND PULMONARY ARTERY PRESSURES (MEAN VALUES AND S.D.) IN 8 HORSES SYMPTOMATICALLY AFFECTED WITH COPD

Treatment	PaO_2 (mm Hg)	$PaCO_2$ (mm Hg)	pH	Mean PAP (mm Hg)
Pre-oxygenation	66.95 ± 6.22	38.54 ± 5.17	7.442 ± 0.040	38.8 ± 7.87
During oxygenation	108.03 ± 23.96***	40.77 ± 4.21	7.431 ± 0.032	33.4 ± 7.45**

*** P < 0.001 ** P < 0.01

bsence of hypercapnia in COPD-affected horses has een attributed by Sasse (1971) to the hypoxia-timulated hyperventilation of normally functioning lveoli. However, because of the sigmoid shape of the aemoglobin oxygen dissociation curve, blood is unable o carry appreciably more oxygen from the overventilated reas and so is unable to compensate similarly for nsaturated blood leaving underventilated areas (Clark, ones and Clark, 1977). The pathology of equine COPD s different from that of human COPD (Nicholls, 1978) nd this may be a possible reason for the differences in CO_2 retention between human and equine COPD cases.

Systemic acidosis is also associated with a pulmonary asoconstrictor response (Harvey, 1965; Rudolph and Yuan, 1966). There was no evidence of acidosis in the resent horses while they were clinically affected with COPD and this is probably related to the absence of ypercapnia.

Euler and Liljestrand (1946) first showed the pulmonary ypertensive effect of hypoxia. Later work showed that hat this was due, in part, to a direct pressor reflex by he capillary vessels (Lloyd, 1964) as well as to the more bvious hypoxia-induced increase in cardiac output aused by both tachycardia and increased myocardial ontractility (Aviado, 1965).

In this work, hypoxaemia was shown to be the main actor in the aetiology of pulmonary hypertension in quine COPD. However, since oxygen administration nly partially reversed the hypertension, the involvement f some factor or factors other than hypoxia is likely. Further support for this opinion is derived from the act that in some asymptomatic cases the PAP remained levated although PaO_2 was within the normal range. n some COPD horses the increased intrapleural pressure hanges are mainly due to positive pressure changes and in these cases the increased positive intrapleural pressure will cause an increase in the mean PAP. Likewise increased negative intrapleural pressure changes will tend to decrease the PAP. The reversibility, even partial, of the pulmonary hypertension of equine chronic respiratory disease does not appear to have been reported previously. That the hypertension can be reduced so readily implies that it is mainly due to a pulmonary vascular hypoxic response rather than to structural vascular changes.

A very wide variation in the degree of pulmonary hypertension in symptomatic COPD-affected horses was also observed (Tables I and II). This does not appear to be related to the degree of hypoxia as the symptomatic groups shown in the tables have similar PaO_2 values yet the group shown in Table I has a more marked pulmonary hypertension than the group shown in Table II. Acute hypoxaemia production caused a more pronounced pulmonary hypertensive response in the affected horses than in the control group. A similar marked pulmonary reaction to acute hypoxaemia was observed by Bisgard, *et al.* (1975) in ponies with existing high altitude-induced pulmonary hypertension.

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TABLE III

EFFECT OF INDUCED ACUTE HYPOXIA ON CAROTID ARTERIAL GASES AND pH AND ON PULMONARY ARTERY PRESSURE (MEAN VALUES AND S.D.) IN 8 NORMAL AND 8 COPD-AFFECTED HORSES

	PaO_2 (mm Hg)	$PaCO_2$ (mm Hg)	pH	Mean PAP (mm Hg)
Normal horses				
resting	91.9 ± 7.33	36.7 ± 3.5	7.392 ± 0.032	24.1 ± 2.42
acutely hypoxic	50.5 ± 7.75***	29.1 ± 2.5	7.474 ± 0.060	33.7 ± 4.75***
COPD cases				
resting	71.5 ± 8.07	37.8 ± 3.86	7.411 ± 0.041	32.5 ± 2.20
acutely hypoxic	48.3 ± 6.37***	34.0 ± 3.08	7.442 ± 0.065	46.6 ± 4.60***

*** P < 0.001

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RÉSUMÉ

Les chevaux atteints de maladie pulmonaire chroniq obstructive présentent une hypertension pulmonai artérielle associée avec une hypoxie artérielle systém tique. L'hypertension pulmonaire chez les chevau cliniquement atteints semble partiellement reversibl lorsqu'il y a rémission des signes cliniques ou adminis tration d'oxygène. L'hypoxie provoquée engendre un élévation de la pression pulmonaire artérielle tant chez les chevaux sains que chez les chevaux atteints de maladie respiratoire chronique obstructive.

ZUSAMMENFASSUNG

Pferde mit einer klinisch feststellbaren chronisch-obstruktiven Lungenkrankheit (COPD) wiesen eine Hypertension in der Pulmonalarterie auf zusammen mit einer systemischen, arteriellen Hypoxie. Der Lungen-überdruck bei kranken Pferden erwies sich als teilweise reversibel während der Remission von klinischen Krank-heitszeichen oder nach O_2-Zufuhr. Die Provokation einer akuten Hypoxie erhöhte den Pulmonaldruck bei normalen und COPD-kranken Pferden.

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