ACROMEGALIC-GIGANTISM:

A

HYPOTHESIS

by

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VOL. III.

CHAPTER XX.

THE POST-MORTEM EXAMINATION OF THE BODY OF A VICTIM OF ACROMEGALY.

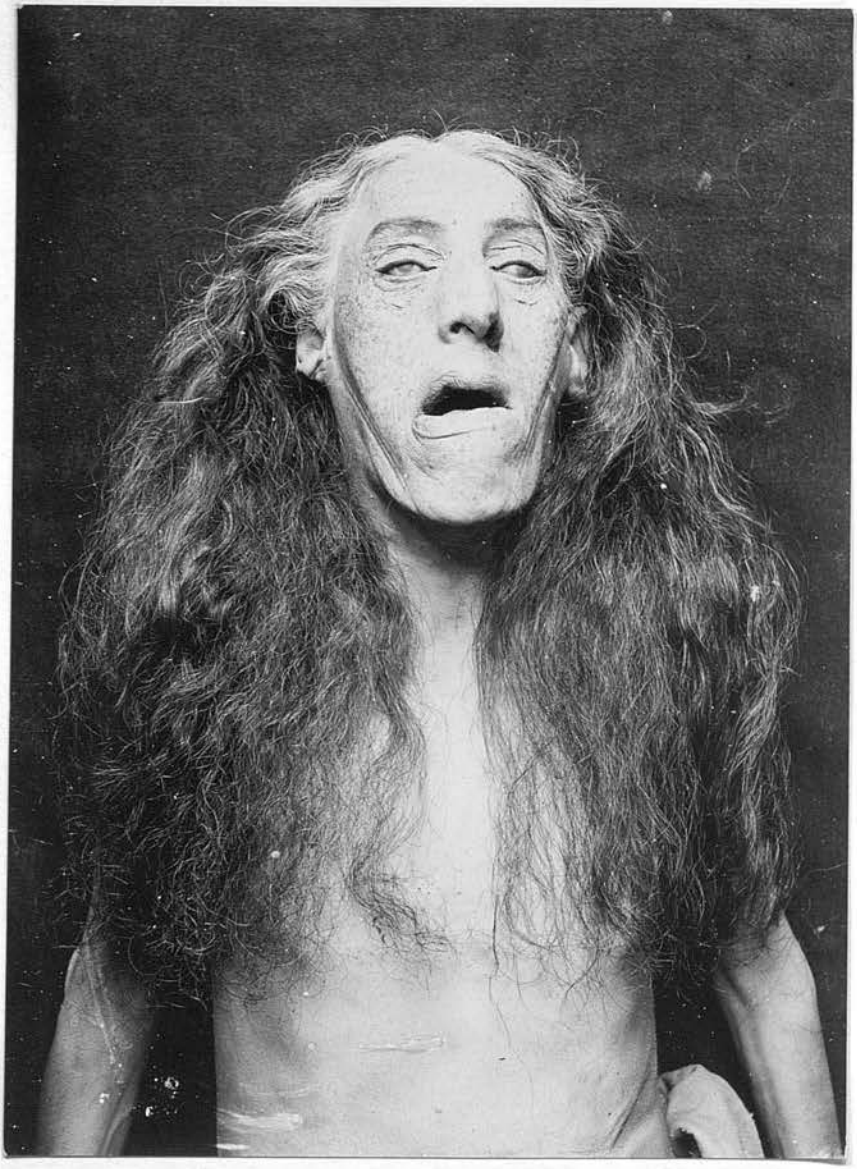
SECTION I. INTRODUCTORY.

As noted above the body E.A.S. 07 was handed over to the Anatomy Department of the University of Edinburgh for dissection. It was preserved by injection of formalin 30% solution into the right common femoral and the left common carotid arteries. As a result of this injection all the tissues were firmly fixed; this added enormously to the difficulties of the subsequent histological examinations. Without it, however, many important observations would have been impossible.

SECTION/

PLATE LXXXVII.

PLATE LXXXVIII.



PLATES LXXXVII. & LXXXVIII.

E.A.S. 07 upon the autopsy table; to show the great wealth of hair, the prominent nose; the gaping mouth; the massive chin; the thin arms and the flat chest.

SECTION II. REPORT UPON THE MACROSCOPIC CHANGES FOUND IN THE BODY E.A.S.07.

The general aspect of the body was remarkable. The wealth and thickness of the hair, the enormous face. The big nose, the gaping mouth, the protuberant tongue, the great hands and feet, the flatness of the chest, the rounded shoulders, the slightly, but permanently flexed thighs, and the chalky whiteness of the skin at once stamped the body as that of no ordinary individual.

As it lay upon the autopsy table it measured 5 feet 3 inches. It was not weighed; but a few days before death the weight was 9st. 2lbs.

The detailed measurements that were made are recorded in the comparative tables already given.

I. Examination of the Head.

The characteristics of the head and face are well shown in the accompanying photographs. (Plates LXXXVII and LXXXVIII). It was found impossible to close the mouth. The reason for this became apparent later; it was, that the coronoid process locked against the lateral cranial wall when any attempt was made to raise the chin. It is unnecessary here to describe in detail the prominence of the nose, the great/

PLATE LXXXIX.

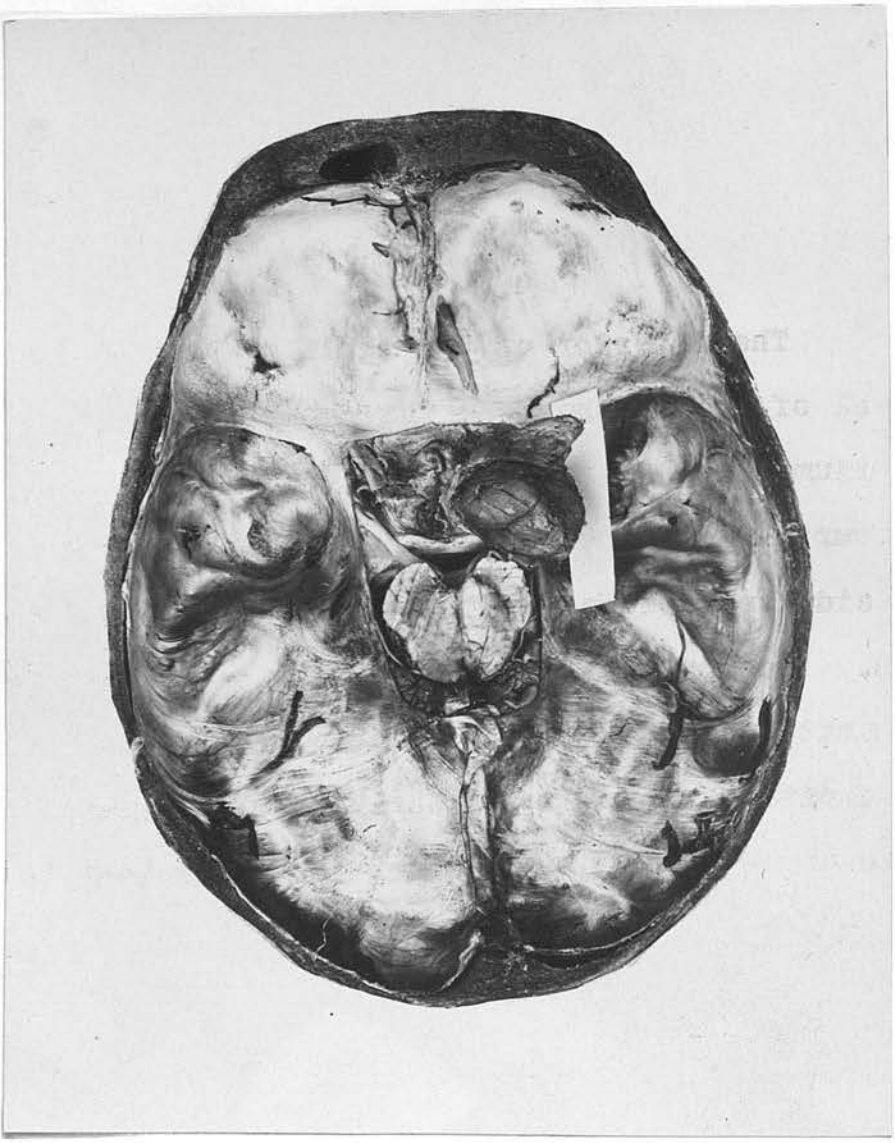


PLATE LXXXIX.

The interior of the skull of E.A.S. 07 after removal of the cerebrum. The upper surface of the tentorium cerebelli; the cut surface of the mid-brain; the fourth nerve on both sides; the third nerve on the left side and the optic nerve on the left side are exposed. Occupying the sella turcica and projecting a bicornuate mass to the right side is the greatly enlarged pituitary. More clearly to show the right margin of the tumour a piece of paper has been laid beneath it.

great size of the mandible and the size of the ears.

The first step in the dissection was to remove en masse the soft parts from the skull and face with the skin and superficial muscles of the neck. A plaster cast of the underlying structures was prepared and over this the soft parts were carefully stitched. The reconstructed head is preserved in the Anatomical Museum of the University.

(a) Report on the condition of the intra-cranial structures.

The skull cap was removed and the brain extracted. To effect this it was necessary to cut through the mesencephalon.

The condition of the parts in the neighbourhood of the sella turcica was:—

The pituitary was enormously enlarged and projected a bicornuate mass, upwards and to the right. As a result of the overgrowth of the pituitary the optic chiasma was torn through; the right optic nerve and optic tract were pressed upon and reduced to the condition of a ribbon of apparently fibrous tissue; the oculo-motor nerve of the right side was pressed upon: the fourth and sixth nerves had apparently escaped injury: the right temporal lobe and the base of the/

PLATE XC.

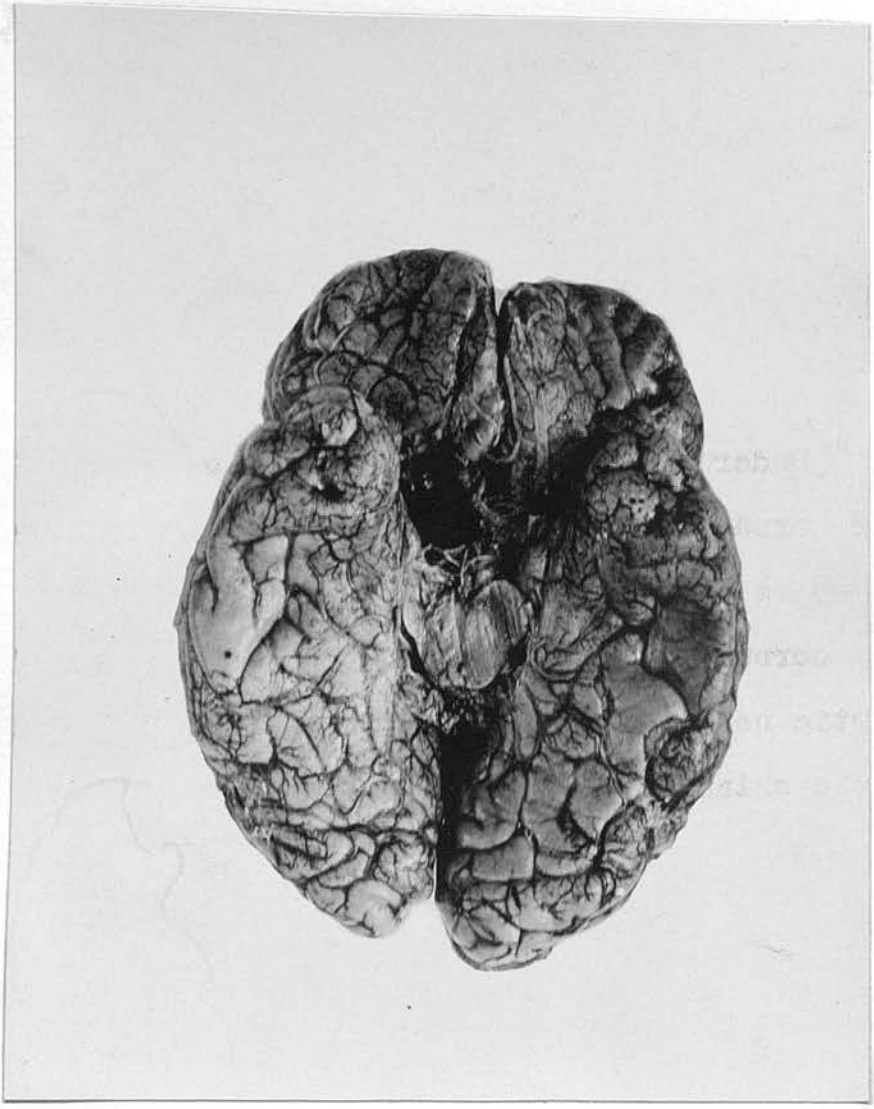


PLATE XC.

Under surface of the cerebrum of E.A.S. 07. The dark area on the under surface of the right hemisphere shows the position of the pit in which the projecting cornua of the pituitary were embedded. The left optic nerve can be seen, but there is no sign of the optic chiasma.

the brain were deeply indented by the pituitary tumour. See Plates LXXXIX and XC.

With considerable difficulty the pituitary was removed from the greatly enlarged sella turcica when it was found to present for examination two portions.

A. A portion lodged within the sella turcica which had the shape of a short cone, the apex of which pointed downwards. This portion had the following measurements:—

Height -- -- -- -- -- --30·8mm.

Antero-posterior diam. -- --27·6mm.

Transverse diameter -- --29·3mm.

B. A portion which projected into the general cranial cavity and indented the hemisphere. This portion projected to the right and consisted of a short stem and two cornua, an anterior and posterior.

The anterior cornu was conoid and had the following measurements:—

Length (base to apex of cone) 17·8mm.

Diameter at base -- -- -- 15·8mm.

The posterior cornu was pyramidal and had the following measurements:—

Length -- -- -- -- -- --28·2mm.

Diameter at base -- -- --16·9mm.

The/

PLATE XCI.

PLATE XCI.

View of the pituitary from the front. The conical dependent portion was lodged in the hollow of the sella turcica: the lateral mass projected free.

The posterior cornu was therefore, considerably the larger.

The cornua were separated by a deep cleft, at the bottom of which lay the anterior cerebral artery. Externally, the cornua were marked off from the body of the gland by concurrent grooves in which the internal carotid, the middle cerebral and the posterior communicating arteries were lodged.

The weight of the pituitary was 15·55gm. The normal dimensions of the adult pituitary are approximately:—

Vertical height — — — 5mm.

Antero-posterior diam. — 7mm.

Transverse diameter — — 12mm.(Piersoll)

The normal weight for the adult pituitary is:—

·35 to 45 grammes (Testut)

·6 grammes (Boyce and Beadles)

The mass of pituitary E.A.S. 07 was, therefore, relatively to the normal, increased approximately thirty times.

Brain:—

The weight of the brain without the pituitary was 3lbs. 5½ozs.

The average proportion of the weight of the brain/

PLATE XCII.

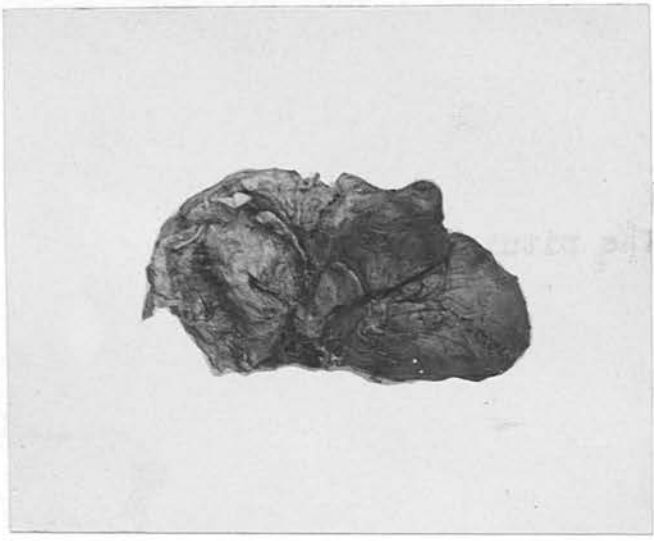


PLATE XCII.

The pituitary from above.

brain to the weight of the body is as one is to fifty (Obersteiner) Therefore, the weight that brain E.A.S. 07 should normally have been is 2·56lbs. (Body weight shortly before death was 9st. 2lbs.) The brain mass was, therefore, increased relatively to the body. It has to be remembered, however, that a brain after hardening with formalin invariably weighs more than before hardening. The difference in this case between the real and estimated weights is so striking that it cannot be entirely due to this cause. Apart from the deep indentation produced by the enlarged pituitary the brain appeared normal in all its parts.

The membranes appeared normal in all their parts.

(b) Report on the condition of the extra-cranial structures.

The eyeballs were enlarged. It was impossible accurately to measure or to weigh them as they were removed with the mask and built into the reconstructed head.

The cartilages of the nose were enlarged. For a like reason it is impossible fully to describe them.

The/

The teeth with the exception of the lower central incisors were carious or absent, their condition is well seen in Plate CXXVII. In addition there were present in the lower gum two pea-like black masses which had no connection with any bone. These were regarded as the stumps of the first right and second left lower molars. Their position was peculiar and suggested that the alveolar margin had atrophied away from them.

The tongue was very large. Its relation to the mandible is well seen in Plate XCIII. This photograph was taken after the superficial soft parts had been removed and before the more deeply placed portions had been disturbed.

Unfortunately the tongue had been hardened in a somewhat crumpled position. Its measurements were:--

Maximum Length -- -- -- --78mm.

Maximum Breadth -- -- -- --72mm.

The surface was much cracked and fissured; the papillae were enlarged.

The tonsils and uvula were much hypertrophied.

The salivary glands were much hypertrophied.

The temporal, the masseter and the pterygoid muscles were large.

II./

PLATE XCIII.

PLATE XCIII.

The head of E.A.S. 07 after removal of the mask. The huge infundibulum ethmoidale; the extraordinary shape of the mandible and the great size of the tongue are well seen.

PLATE XCIV.

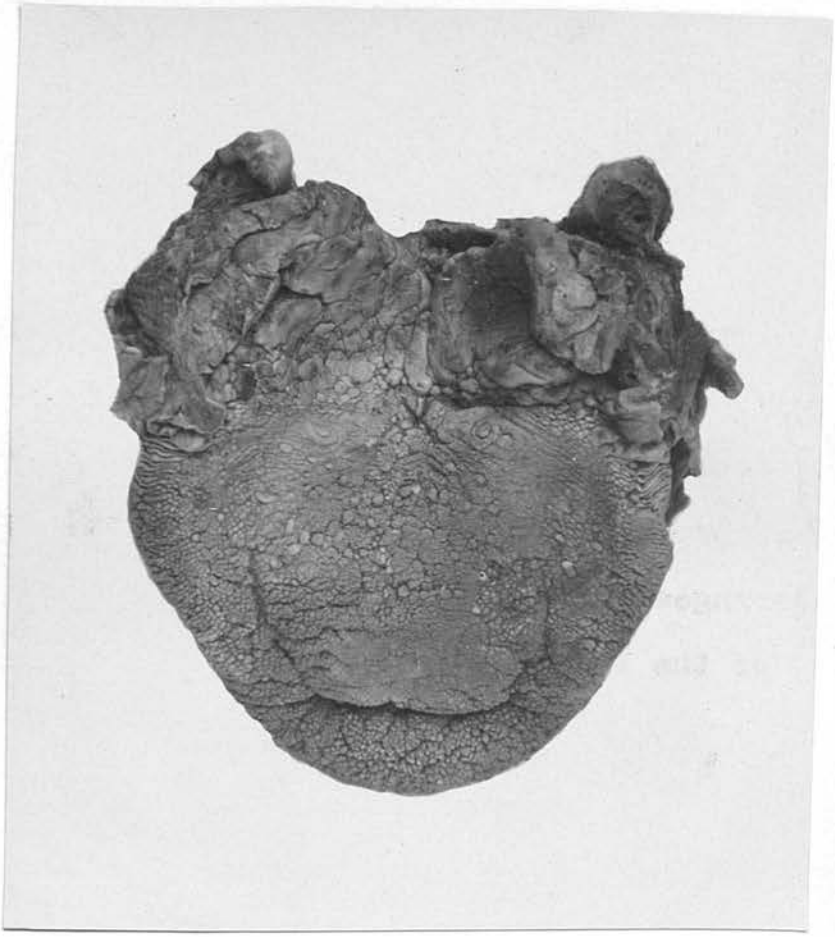


PLATE XCIV.

The tongue of E.A.S. 07 after removal from the body. Its most striking peculiarities are its massiveness; the fissuring upon its surface and the abnormal prominence of its papillae. Posteriorly the pharyngeal portion shows a great increase in the amount of the lymphoid tissue.

II. Examination of the Neck and Thorax.

The anterior half of the thoracic wall was removed in one piece.

(a) General.

The thyroid gland was very large, forming an enormous goitre which, on the left side, reached from the lower border of the mandible to a point behind the manubrium sterni one inch below the level of the upper border of the sternum. It presented on its anterior aspect two deep hollows which corresponded in position to the greatly enlarged inner ends of the clavicles. The veins on its surface were filled with dark blood clot.

The jugular veins were enormously distended and filled with dark blood clot.

The thymus was represented by a vascular leaf-like lamina which lay entirely to the left of the middle line. To the naked eye there appeared to be only a few small areas of thymic substance, the remainder of the lamina being made up of fibrous tissue and fat.

The right lung looked healthy, but shortened from above downwards, its lower margin reached only to the seventh rib in the mid-axillary line.

The/

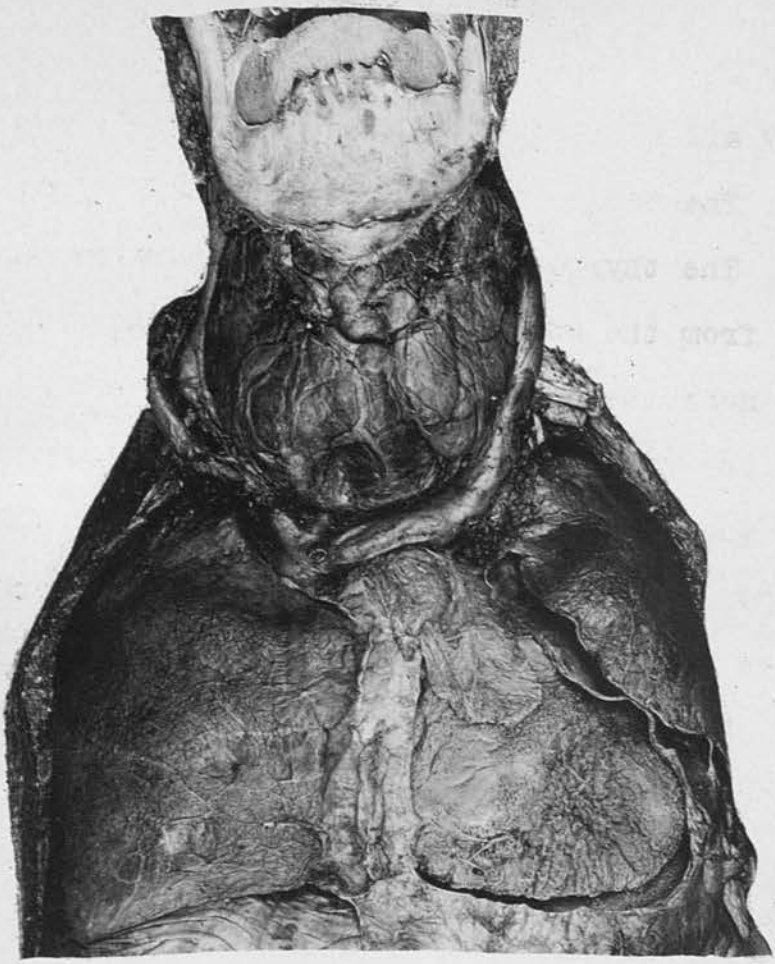


PLATE XCV.

The thorax, neck, lower jaw and tongue of E.A.S.07 after removal of the superficial parts.

The tongue is seen bulging over the mandible.

The thyroid body forms an enormous mass extending from the mandible into the thorax: upon its surface near the lower part are hollows which correspond to the position of the greatly enlarged inner ends of the clavicles. The veins upon its surface are engorged. Round either side of it pass the greatly distended internal jugular veins.

The pericardium is opened and the heart is seen pushed away to the left side: its surface is shaggy with the lymph of pericarditis. Upon it at its upper part lies the thin lamina of thymic tissue.

The shortness of the right lung and the dislocation of the left, so that it almost disappears from view, are well seen.

The heart and pericardium were pushed over to the left, the pericardium was distended and encroached upon the area for the left lung which from the front was only visible in its upper half. (See Plate XCV.)

The convexity of the diaphragm was markedly increased, more especially on the right side, where , a little internal to the mid-clavicular line, it rose to the level of the lower border of the fourth rib.

(b) Particular.

1. The Thyroid.

The lateral lobes of the thyroid were enormously increased; the isthmus was larger than normal, but relatively less hypertrophied.

It measured:—

Maximum Length -- -- -- --120mm.

Maximum Breadth -- -- -- --116mm.

Its weight was 312 grammes. The weight of the normal thyroid is about 30 grammes.

2. The Parathyroids:—

There were five parathyroids, two on the right side, three on the left.

Their weights were:—

1. Right Superior -- -- -- --1·8gm.
2. Right Inferior -- -- -- -- .3gm.

3./

3. Left Superior -- -- -- -- 1.7gm.

4. Left Middle -- -- -- -- ·5gm.

5. Left Inferior -- -- -- -- 2.5gm.

Note:----No. 4 is the abnormal one, it lay between the left lateral lobe and the oesophagus. The identity of all five bodies was established by microscopic examination. The right inferior was 23mm long in place of the normal 6 or 7mm.

3. The Thymus.

The thymic area was very vascular: thymic tissue was apparently confined to a few isolated areas.

4. The Pericardium.

The pericardium was large, its anterior surface was loaded with fat. When opened a large amount of sero-purulent fluid, in which lymph flakes were floating, gushed out. Artificially to produce a corresponding amount of distension a quantity of approximately 300c.c. of fluid was necessary. Owing to the injection of the body with formalin no culture could be made.

The parietal and visceral layers of the serous pericardium were shaggy with lymph and presented most typically the appearance of pulled butter (See Plate XCV.) The heart and pericardium were nowhere adherent/

PLATE XCVI.

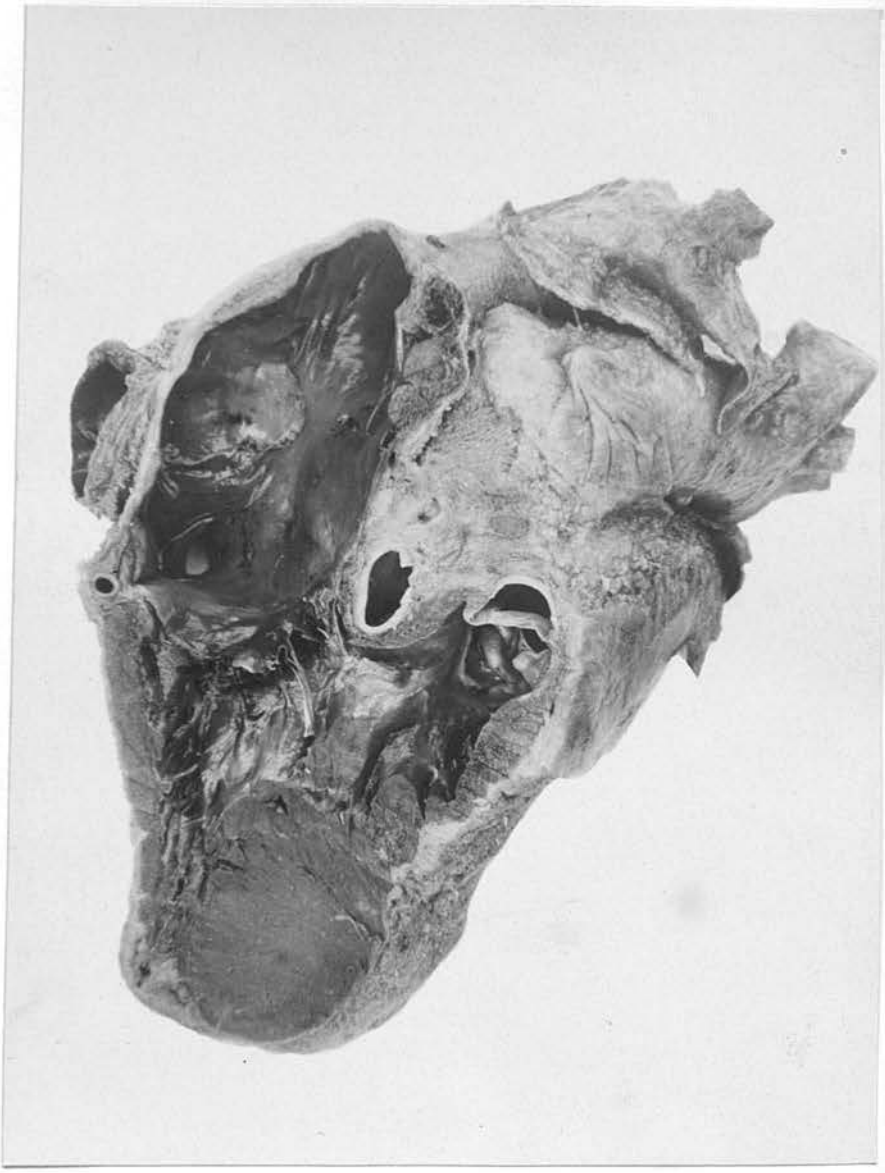


PLATE XCVI.

View of the heart of E.A.S.07.

A thin slice has been removed from its anterior aspect; the right auricle and ventricle are exposed.

To show the relatively great size of the right auricle.

adherent.

5. The Heart:—

The heart was removed from the body and cut into three slices (See Plates XCVI and XCVII.) The endocardium and myocardium were healthy.

The measurements of the heart were:—

Breadth of right auricle -- -- -- --	71mm.
Length of ventricular portion, right auriculo-ventricular opening to apex.	82mm.
Length of ventricular portion Apex to pulmonary orifice.	90mm.
Auriculo-ventricular index -- -- --	86·6.

In normal hearts the index is between 60 and 80. The higher the index the less relatively is the expansion of the auricle during ventricular systole and the less relatively is the collapse of the jugular bulb.(Keith.) From this I conclude that for some reason the venous blood pressure was raised.

The weight of the heart was 531·6gm. In the healthy female the weight of the heart is to the weight of the body as 1:162. The proportionate weight for the heart in E.A.S. 07 would have been 365gm. The increase of mass of the heart was, therefore, nearly fifty/

PLATE XCVII.

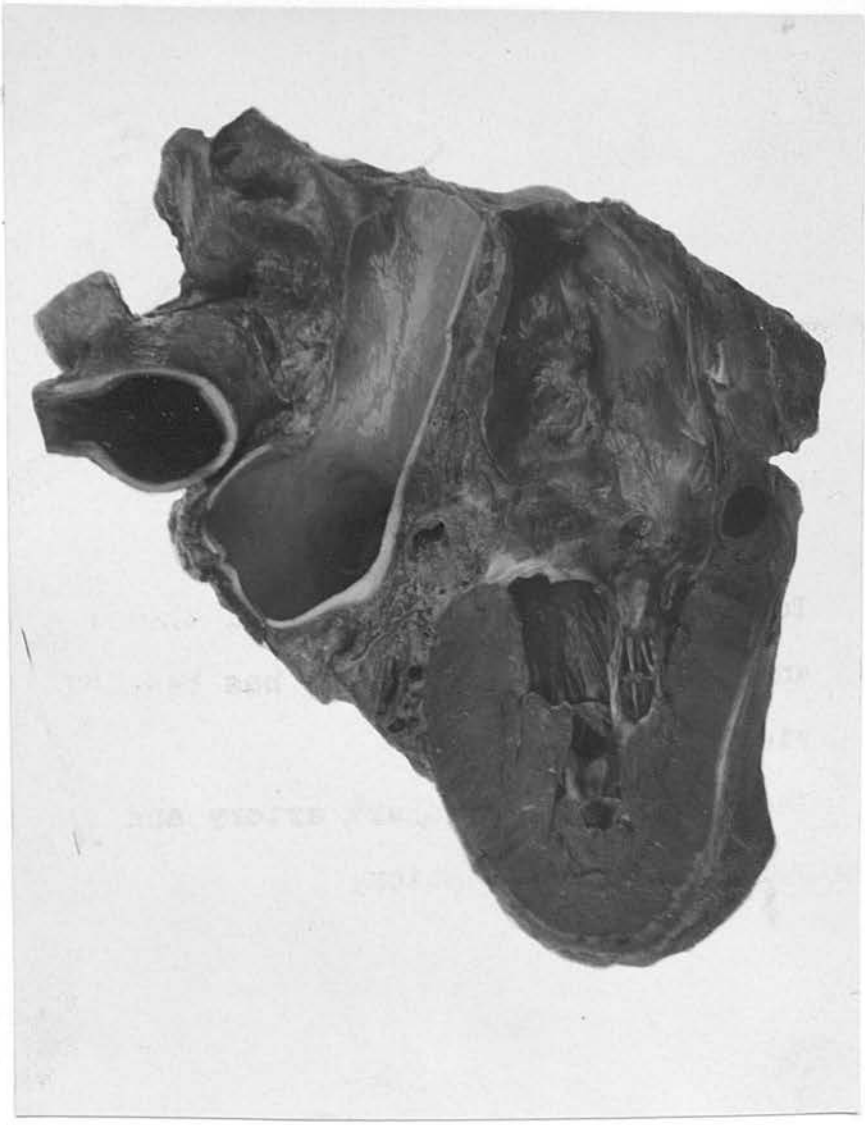


PLATE XCVII.

View of the heart of E.A.S.07.

A thin slice has been removed from its posterior aspect; the left auricle and ventricle are exposed.

To show the great thickness of the ventricular wall and the extent to which it has been affected by the pericarditis.

The aorta, the pulmonary artery and the coronary sinus are seen in section.

fifty per cent.

The valves appeared healthy; owing to the action of the formalin their competence could not be ascertained.

The foramen ovale was patent, the opening being rather larger in diameter than an ordinary lead pencil. The annulus ovalis formed a strongly marked hood; the relations of the parts suggested that an appreciable proportion of the blood from the inferior vena cava passed directly to the left auricle.

Position of the Heart:--

The right border of the heart lay almost exactly in the median line of the body.

The apex of the heart lay 153mm to the left of the middle line.

6. The great vessels were healthy.

7. The lungs, apart from the displacements already described, were normal and healthy. The bronchial glands were enlarged.

III/

PLATE XCVIII.

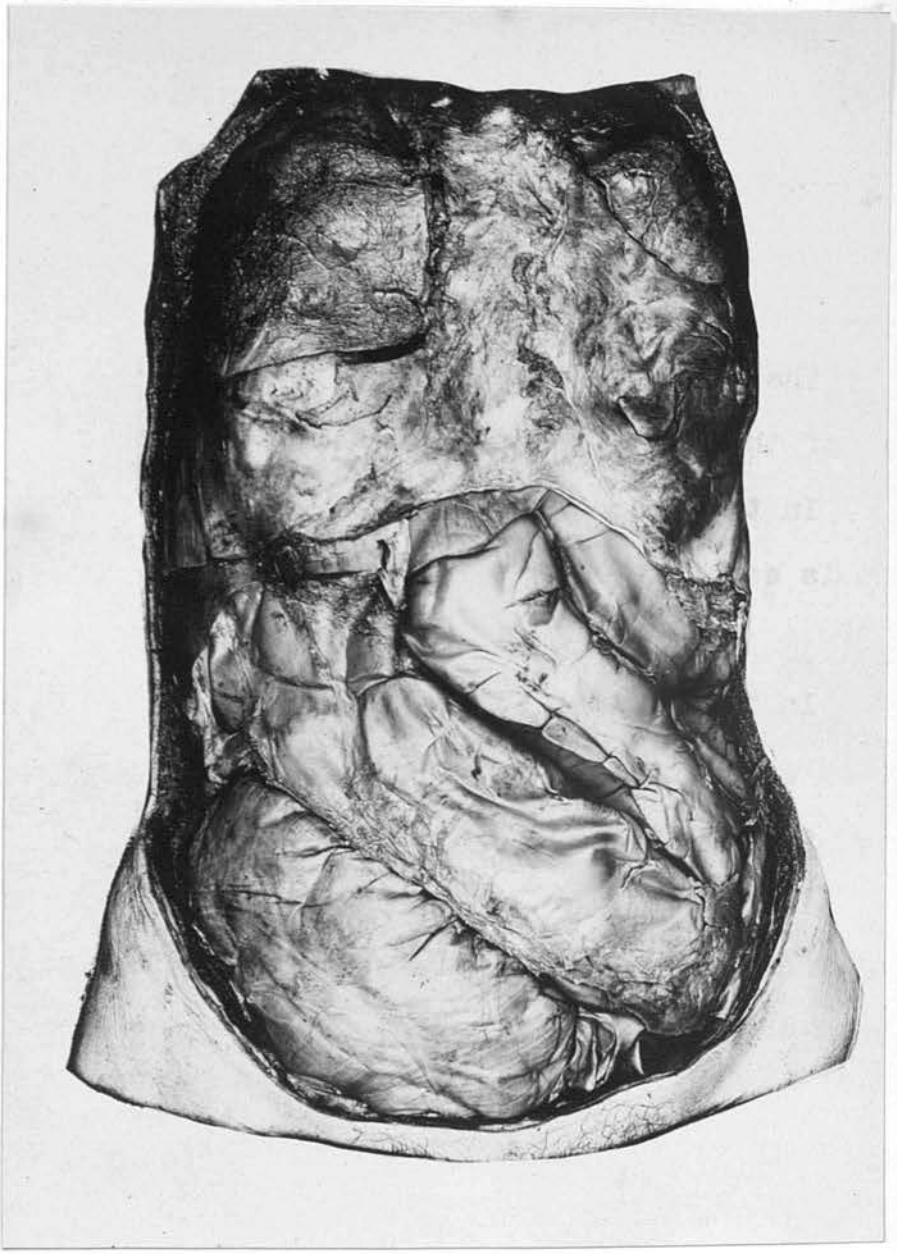


PLATE XCVIII.

The thorax and abdomen of E.A.S. 07 after removal of the more superficial structures.

In the thorax the bulging, fat-loaded pericardium is seen; also its dislocation towards the left.

In the abdomen nothing is seen but the gigantic large intestine. Upon its surface areas of adhesion can be seen.

Viewed as a whole the photograph shows the encroachment of the abdominal space upon the thoracic space and the marked shortening of the right lung.

III. Examination of the Abdomen.

The abdomen was opened by removing the anterior abdominal wall in one piece.

This on the right side was a matter of some difficulty owing to the strong fibrous bands which attached the great intestine to the parietal peritoneum. The adhesions were especially well marked in the right hypochondrium.

When the abdominal wall was removed, the most extraordinary appearance was presented. Absolutely nothing whatever was to be seen, but large intestine. (See Plate XCVIII.) The caecum, and ascending colon were truly gigantic, the transverse colon was large; the descending colon, iliac colon and pelvic colon were normal.

Measurements of Great Intestine.

	Lengths.	Diams.
Length of the Caecum	40mm.	
Greatest diam. of the Caecum		220mm.
Length of the Ascending Colon	860mm.	
Greatest diam. of " "		380mm.
Length of Transverse	350mm.	
Greatest diam. of " "		170mm.
Length/		

PLATE XCIX.

up side down

PLATE XCIX.

View from the right side of E.A.S. 07. To show the position of the liver and diaphragm, the distortion of the lower ribs and the great mass of the large intestine.

Measurements of Great Intestine (continued)

	Lengths	Diams.
Length of remaining portion of large intestine.	595mm.	
Greatest diameter -- -- -- -- --	-- -- --	75mm.
Total Length of great Intestine	2245	
Normal Length of great Intestine	1400	

The different portions of the great intestine were recognised by their arteries of supply.

Position and relations of the Great Intestine.

The caecum occupied the cavity of the pelvis.

The ascending colon occupied the right iliac fossa and formed a great sigmoid loop which passed diagonally across the abdomen. One convexity was in relation to the liver, the other occupied the left iliac fossa.

The transverse colon had risen in front of the stomach which was pressed backwards. It had evidently exerted considerable prsssure on the liver.

Plate XCVIII shows the large intestine in position. Plate C. shows the position of the abdominal viscera, after removal of the large intestine.

The/

PLATE C.

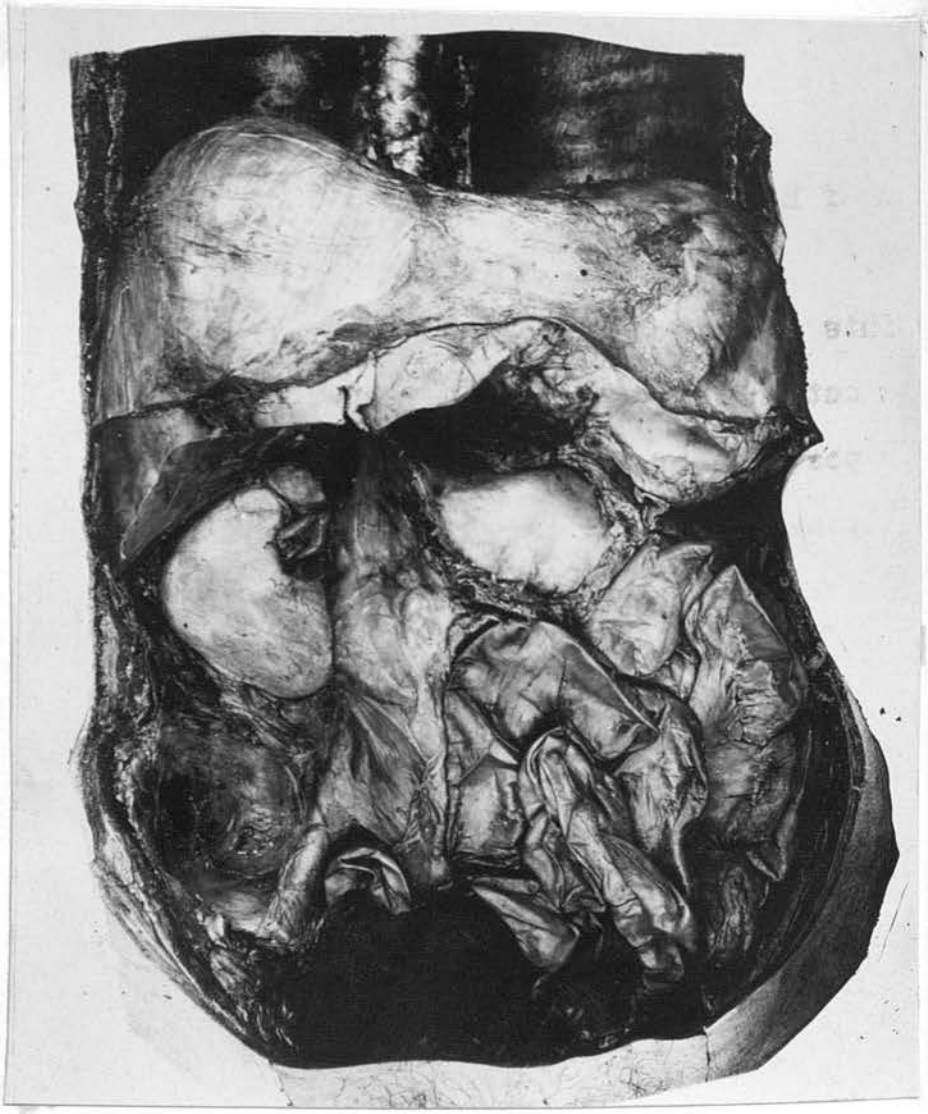


PLATE C.

Abdomen of E.A.S. 07 after removal of the great intestine.

The points of especial interest are:—

The outline of the upper surface of the diaphragm,

The position of the liver and stomach,

The position of the right kidney with its lower pole resting upon the crest of the ilium,

The position of the small intestine entirely to the left of the middle line.

The hilum of the right kidney appears to be situated near the superior pole. This apparent abnormality of shape is to be explained by the deformation that the kidney had undergone as the result of the downward pressure of the posterior part of the liver

PLATE CI.

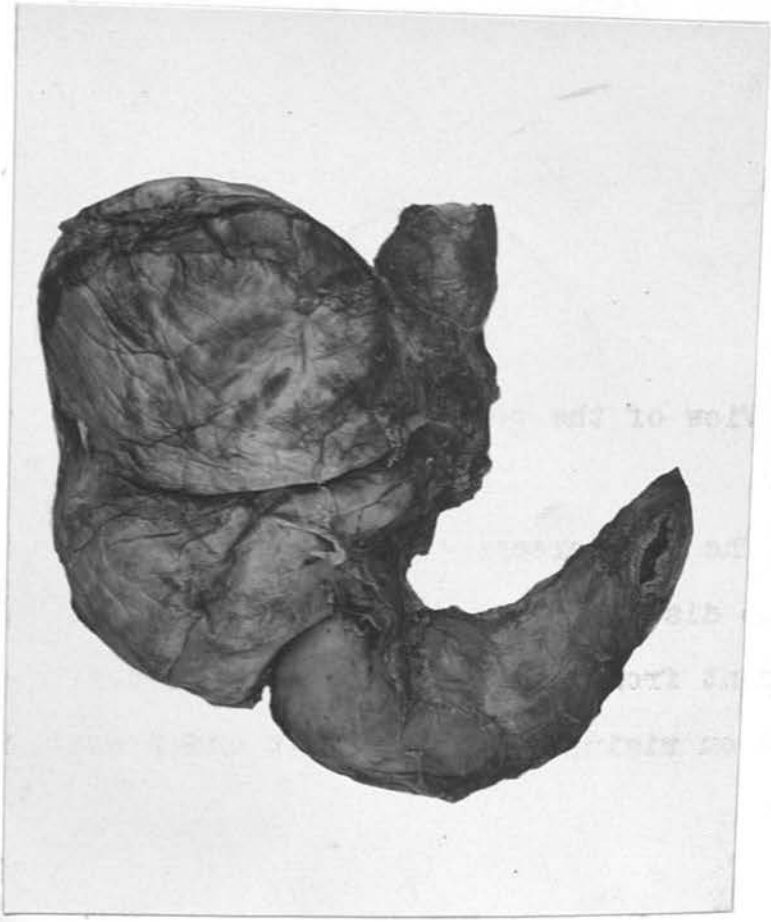


PLATE CI.

View of the posterior aspect of the stomach E.A.S. 07.

The deep crease passing across the body is due to the distortion of the stomach and its partial displacement from its normal horizontal position owing to the colon rising in front of it and pressing it backwards.

The condition of the stomach was most interesting. Its division into a body and pyloric portion were most evident, but far more interesting was the peculiar bending to which the stomach had been subjected by the pressure of the transverse colon rising in front of it. The greater curvature of the stomach, as marked by the line of attachment of the great omentum, pursued from its commencement at the fundus until opposite the middle of the body its normal horizontal course. Here as seen from the left side it suddenly turned downwards in a direction almost at right angles to that in which it originally ran. In short the fundus of the stomach occupied its normal position, but the body and pyloric part had been twisted through a quarter revolution, so that the superior surface became a true anterior surface. This pressure deformity of the stomach is, I think, of some importance to the understanding of the case. I refer to it later.

The duodenum and the ducts opening into it were to all appearance normal.

The jejunum and ilium were pressed over to the left side, but appeared otherwise normal.

Total Length of Small Intestine	3950
Average Length " "	6800

The/

PLATE CII

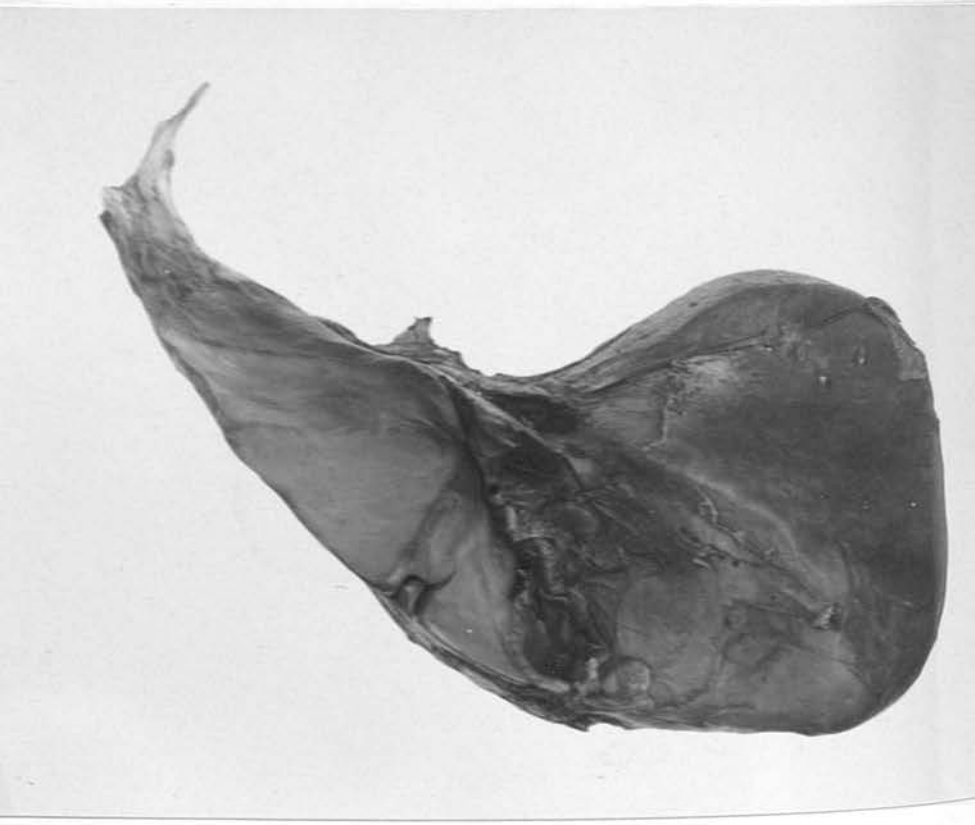
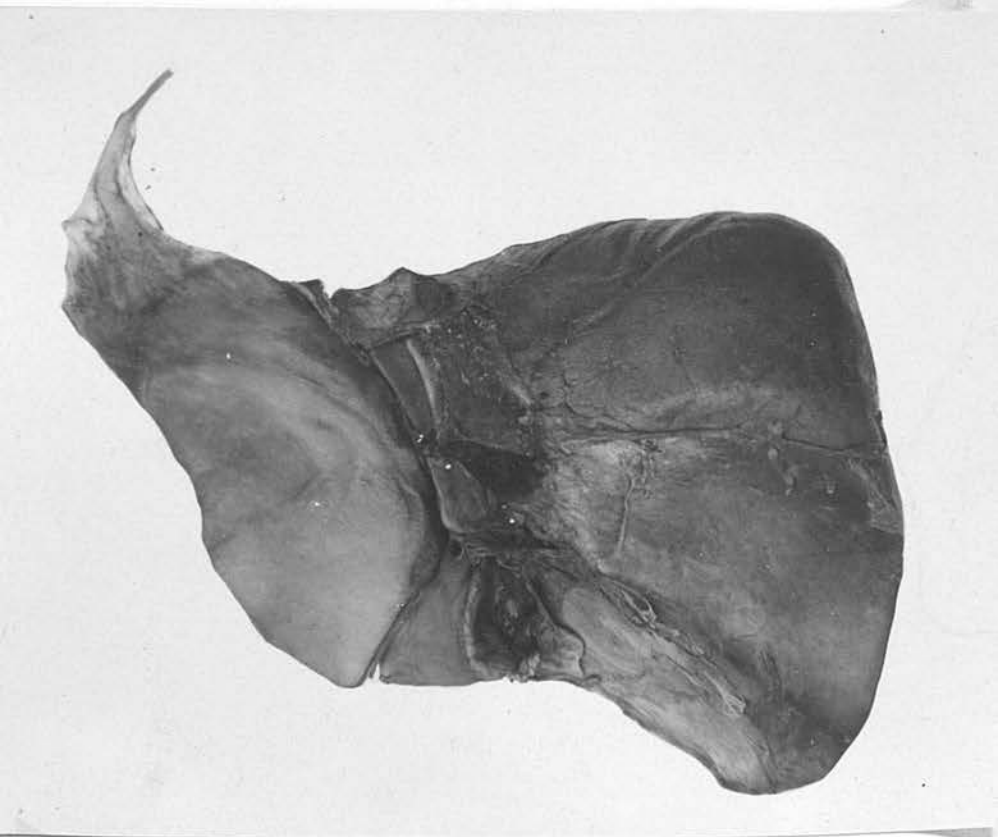


PLATE CIII.



PLATES CII and CIII.

Views of the liver to show the attenuation and lack of definition of the left margin.

The Liver:--

The liver weighed 3.1bs 1½ oz--(1403.3grammes)

The weight of the liver normally is to the weight of the body as 1:40; theoretically, therefore, it should have weighed 3 lbs 3 ozs. Therefore, it was not increased.

Certain appearances suggested that it was undergoing pressure atrophy. The left lobe was exceedingly thin and short and had no definite margin, the liver substance gradually disappearing along an irregular line beyond which small isolated masses of liver cells lay embedded in the pressed out and otherwise empty capsule.

The liver was displaced upward, so that its upper border reached the level of the lower border of the fourth rib, a little internal to the mid-clavicular line. In addition to its general upward translation, the liver was slightly rotated on a transverse axis, so that the anterior half of the inferior surface had passed upwards. In its consequent descent the posterior part of the inferior surface had caught the right kidney and was strongly pressing it down, with the result that the inferior pole of the kidney was carried down to within half an inch of the level of the crest/

crest of the ilium.

The under surface of the liver in its anterior part was deeply indented by abnormal colic impressions.

The gall bladder and bile ducts were healthy.

The Spleen:--

The spleen was rather large, but otherwise normal in appearance and shape. In position it was more horizontal than usual.

Weight of Spleen	212.6grammes.
Average weight	195 "

The Pancreas:--

The pancreas was of normal size, but of unusual shape; the tail being increased in a manner comparable to the normal pancreatic head; the head itself was bulky.

Its total length was	180mm.
Its weight was	76gm.

It was thus slightly longer than the average length 150mm; but its weight was well within the normal range of variation 50-120gm.

Kidneys:--

The/

PLATE CIV.

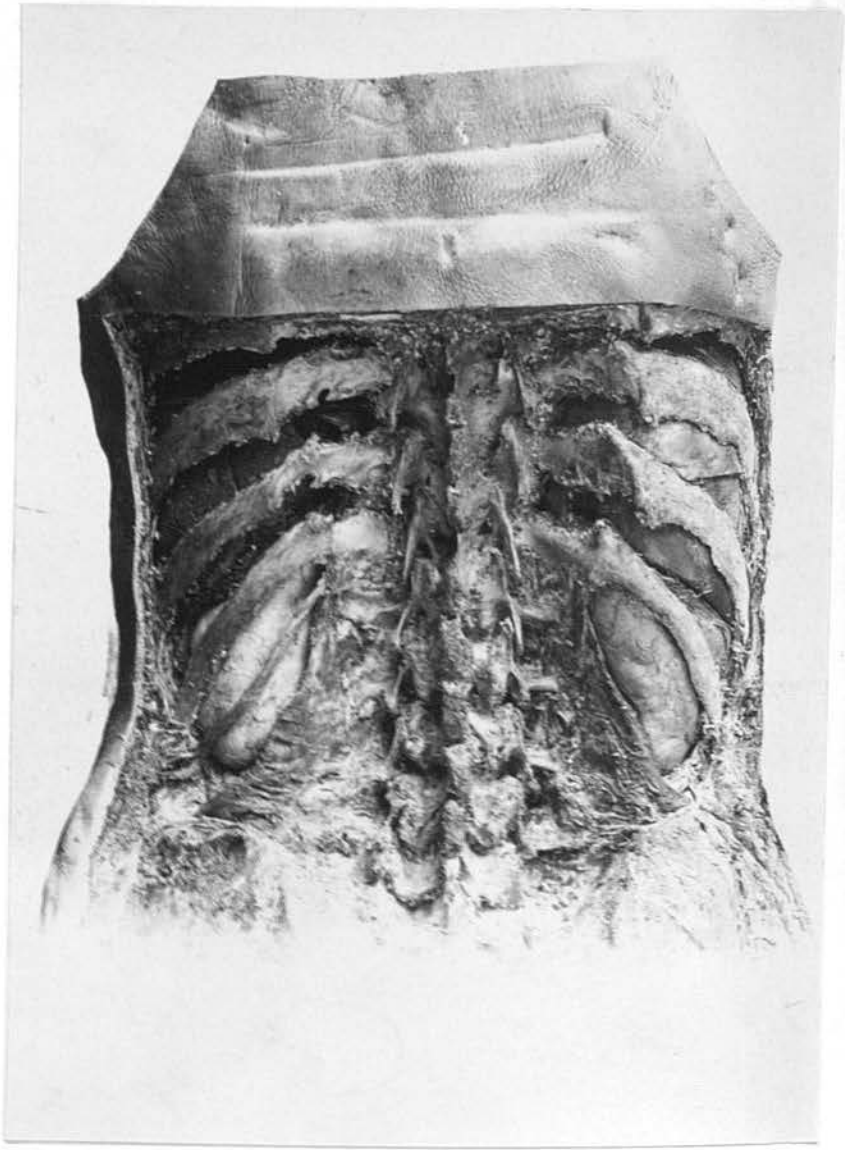


PLATE CIV.

Dissection from behind to show the relations of the liver, spleen and kidneys.

Note, too, the peculiarities of the ribs and the extraordinary processes upon the lower dorsal and lumbar vertebrae. To the tips of each of these stout tendons of the sacro-lumbar portion of the multifidus spinae were attached. Passing across the posterior surface of the left kidney, displaced downwards from its normal position at the lower border of the rib, the gigantic subcostal nerve is to be seen.

The photograph also brings out very well the difference in colour between the healthy right kidney and the fatty left kidney.

The kidneys were very large.

The right weighed -- -- -- -- 262gm.

The left " -- -- -- -- 269gm.

The average weight of a kidney is 130gm.

The shape of the right kidney was most unusual; it was wedge-shaped and presented for examination, an anterior, a posterior and a superior or hepatic surface. Macroscopically it was normal.

The left kidney was of normal shape, but pale and fatty.

Suprarenal Bodies:--

The suprarenal bodies looked considerably larger than normal.

The right weighed -- -- -- -- 9gm.

The left " -- -- -- -- 9.5gm.

Normal weight of suprarenals 6gm.

In texture they appeared normal.

ABDOMINAL PORTION OF THE SYMPATHETIC SYSTEM:--

The bulk of the constituent elements was much greater/

PLATE CV.

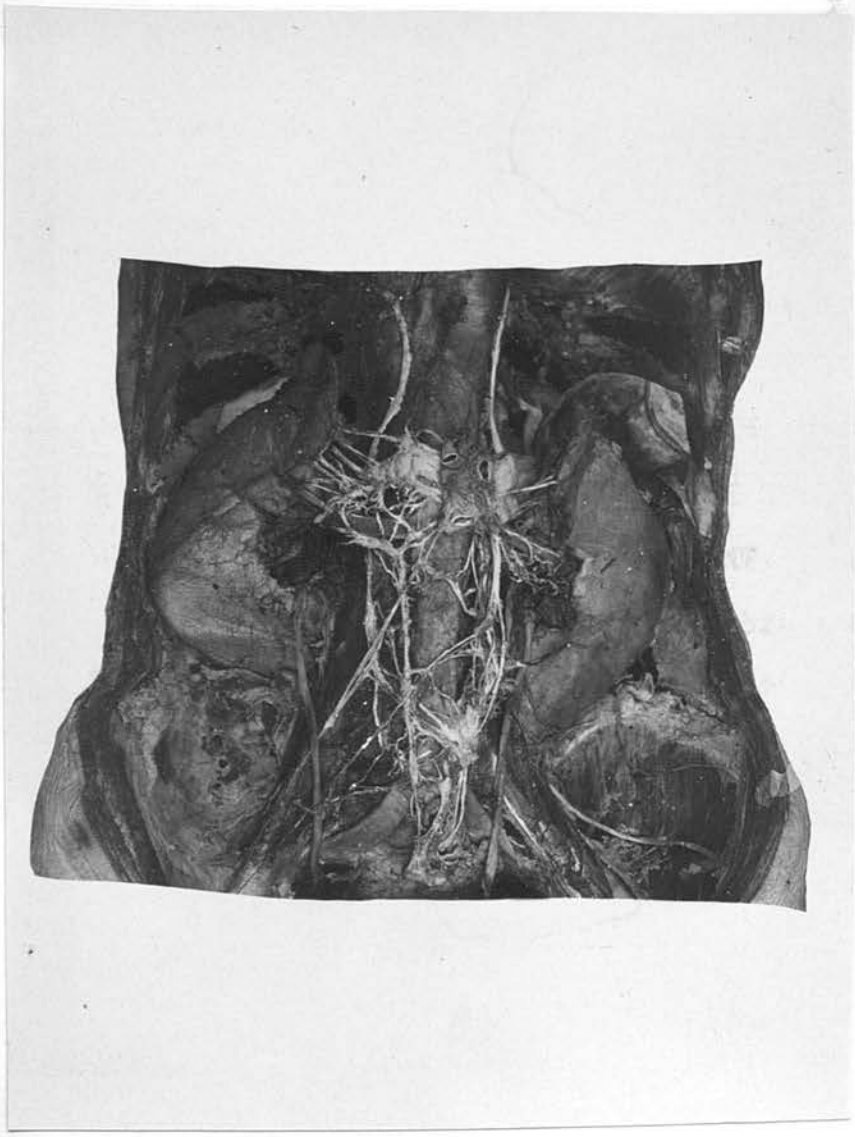


PLATE CV.

Photograph of a dissection of the sympathetic system of E.A.S. 07.

The position of the semilunar ganglia at either side of the coeliac axis and the great mass of nervous tissue surrounding the mesenteric arteries are well brought out.

Incidentally, the peculiar shape of the right kidney is well seen.

PLATE CVI.

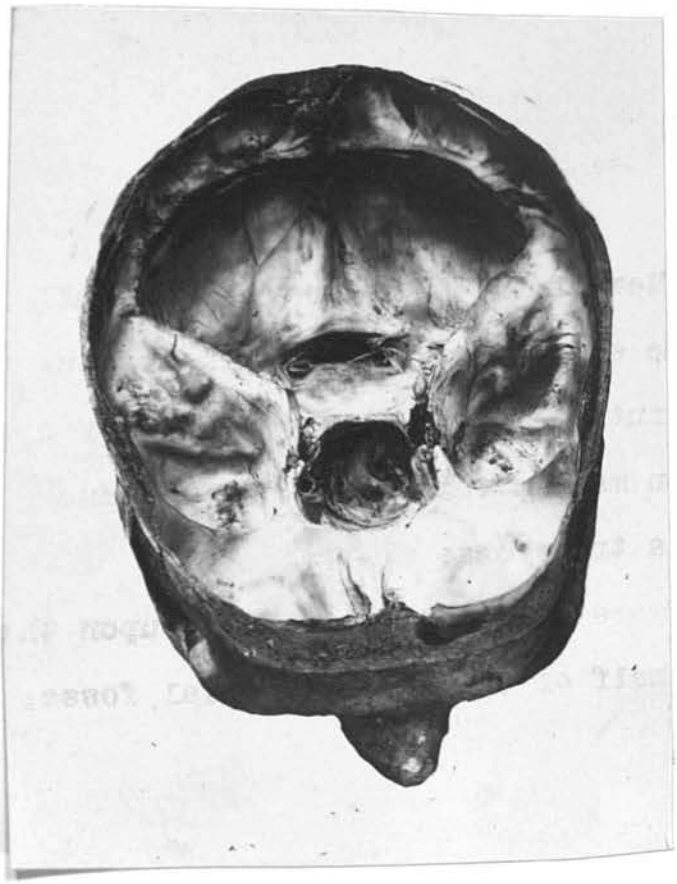


PLATE CVI.

View of the interior of the skull E.A.S. 07 to show the enormous size of the sella turcica and the great diminution in the antero-posterior diameter of the foramen magnum which is thereby reduced to the condition of a transverse slit.

There are some osteophytes upon the floor of the right half of the middle cranial fossa.

PLATE CVII.

PLATE CVII.

Dissection to show compression of the spinal cord at level of the upper border of the fourth cervical vertebrae.

Note the great size of the articular processes and their projection laterally beyond the tips of the transverse processes, the remarkable asymmetry of the spinous process, the roughness of the upper surface of the body and the marked antero-posterior compression of the cord.

great sciatic nerves were not much thickened.

The nerves of the arm were all greatly increased in size.

The palmar portion of the left median nerve was represented by a rounded slightly fusiform mass which measured 54mm. in length and 15mm. in breadth. From this, the normal muscular and cutaneous branches arose.

MUSCULAR SYSTEM:--

The muscles were on the whole well developed. There was a musculus sternalis on the right side. It arose from the skin overlying the third and fourth costal cartilages and was inserted into the skin over the sterno-clavicular articulation, into the sternal head of the sterno-cleidomastoid and into the anterior surface of the manubrium sterni in its upper part.

The gluteus maximus muscle was partly fibrous. The sacro-lumbar portion of the multifidus spinae was also partly fibrous. The muscles of the thenar and hypothenar eminences were not atrophied.

The posterior cervical muscles were strongly developed.

ARTICULAR SYSTEM:--

All/

PLATE CVIII.

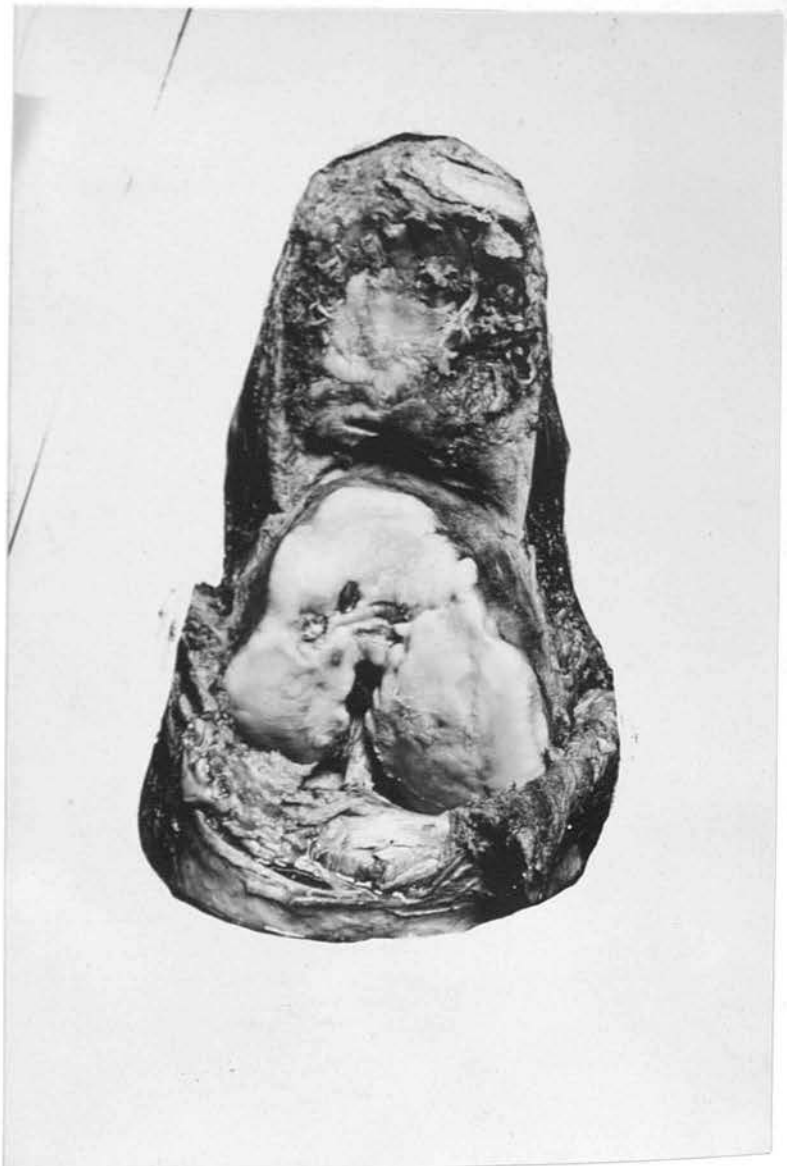


PLATE CIX

PLATES CVIII. and CIX.

Dissections to show the rheumatoid condition of the knee joints and more especially the ulceration of the cartilage on the lower end of the right femur.

All the sutures in the cranium were obliterated.

The tempero-mandibular joint was markedly arthritic.

The upper three cervical vertebrae were ossified together and to the occipital bone.

The joint between the third and fourth cervical vertebrae was movable.

All the other spinal joints were ankylosed, ossification being either partial or complete.

The upper ribs were ossified to the vertebrae.

The sterno-clavicular, the shoulder, the elbow and the wrist joints were arthritic.

The hip joints on both sides were arthritic and incapable of full extension.

The knee joint on the right side was markedly arthritic. The capsule was distended with sero-purulent fluid. The cartilage covering the external femoral condyle was ulcerated.

The knee joint on the left side was also mardedly arthritic, but the effusion was not purulent.

The ankle joints on both sides were arthritic.

All the joints in the hands and feet were arthritic, some were completely obliterated, the bones showing/

PLATE CX.

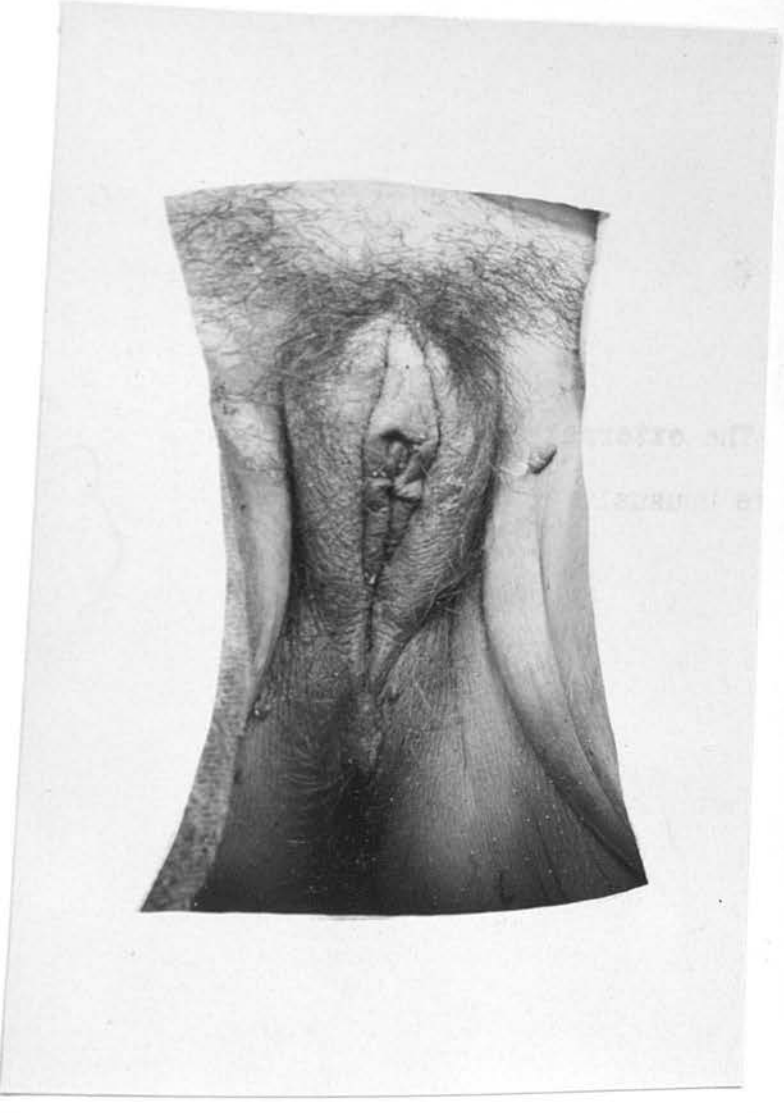


PLATE CX.

The external genitals E.A.S. 07. The labia minora are unusually prominent.

showing osseous union.

The Skin:--

All over the body the skin was thick and redundant. The subcutaneous tissues were thickened especially in the hands and feet. The pad of fat on the right heel was 50mm thick.

The hair of the head was coarse and thick and plentiful.

There were five warts on the body.

The face was blotched with freckles.

THE GENITAL SYSTEM:--

The mammary glands were completely atrophied.

The external genitals:--

The labia minora and the clitoris were unusually prominent.

The internal genitals:--

The vagina admitted one finger: it was small and straight.

The uterus was small and markedly anteflexed, and anteverted.

Measurements:--

Maximum length	30mm.
" breadth	30mm.

Average/

Average length	70mm.
" breadth	40mm.

Ovaries:--

The right ovary was almond shaped.

It weighed	1·5gm.
Its maximum length was	65mm.
" " breadth "	15mm.

The surface was quite smooth and showed no signs of scars. It felt very dense and fibrous.

The left ovary was represented by a hard rounded fibrous cord.

LYMPHATIC SYSTEM:--

Throughout the whole body the lymphatic glands were large and numerous.

Apart from the detailed observations upon the bones of the skeleton this completes the record of the macroscopic observations made.

SUMMARY OF THE MACROSCOPIC OBSERVATIONS.

I.THE DUCTLESS GLANDS:--

The/

The pituitary body was thirty times its normal size.

The thyroid body was ten times its normal size.

The parathyroids were largely increased in size; I estimate the amount of parathyroid tissue as being ten times greater than normal

The thymus was represented by numerous small aggregations of thymic cells. These areas were very vascular. The amount of supra-renal tissue showed a 50% increase.

The ovaries were apparently wholly functionless.

The spleen was slightly increased.

II. ALIMENTARY SYSTEM:--

The tongue, tonsils and uvula were enormously increased. The teeth were carious.

The stomach was normal in size, but deformed by pressure.

The duodenum was normal.

The small intestine was surprisingly short, approximately two thirds of the normal length.

The great intestine was enormously increased in/

in diameter and in length.

The salivary glands were increased.

The liver and pancreas were of approximately normal mass.

III. RESPIRATORY SYSTEM was approximately normal

The cartilages of the larynx were large.

IV. CIRCULATORY SYSTEM:--

There was marked pericarditis.

The heart was increased in mass.

The auricular portion was rather more increased than the ventricular. The foramen ovale was patent.

The great arteries were normal.

The great veins of the thorax were distended. The veins of the neck and extremities were distended.

The veins of the portal system were distended. The vena cava inferior was empty and collapsed.

The lymphatic glands throughout the body were markedly increased.

V. NERVOUS SYSTEM:--

The/

The brain was increased in mass.

The lower part of the medulla oblongata and the cervical portion of the spinal cord were compressed antero-posteriorly.

The spinal nerves were greatly increased in diameter and in length, frequently being longer than necessary. The great sciatics were exceptional being increased neither in length nor diameter.

The palmar portion of the left median nerve was characterised by an extraordinary gangliform enlargement.

The sympathetic system was markedly enlarged.

VI. MUSCULAR SYSTEM:--

There was hypertrophy of the posterior muscles of the neck: fibrous atrophy, consequent on hypertrophy (?) of the glutei maximi and of the sacro lumbar portion of multifidus spinae.

The thenar and hypothenar muscles were not atrophied.

VII. GENITO URINARY SYSTEM:--

The kidneys were very large; the left was fatty.

The/

The uterus and vagina were small.

The ovaries were atropnied.

The external genitals were slightly increased.

The mammary glands were atrophied.

VIII. MISCELLANEOUS:—

The skin was thick and the hair, plentiful.

The joints were all affected by rheumatoid arthritis. The right knee was affected with purulent synovitis and ulceration of the joint cartilage.

ANALYSIS OF THE MACROSCOPIC OBSERVATIONS.

I. THE LARGE INTESTINE:—

The increase in the size of the large intestine was probably a recent and progressive feature.

This I deduce from:—

1. The dislocation of the heart to the left; its right border being at no point to the right of the middle line. In the case record it is recorded as being 1½ inches to the right of the sternum. The mechanism of dislocation obviously was that the liver and diaphragm were pushed upwards on the right side whereas the heart, prevented by the inferior vena cava from moving/

moving upwards, was compelled to move to the left.

2. The appearances suggestive of pressure atrophy of the liver indicate that the upward pressure of the abdominal contents was increasing. The portion of the liver atrophied and of which the capsule alone remained was that between the loop of the transverse colon and the immovable pericardium.

3. The pressure deformity of the stomach must, I think, have been a recent acquirement. Had the conditions producing it existed early in life it is hardly conceivable that a plastic organ like the stomach would not have adapted itself in its entirety to the shape of its altered bed.

4. The abdominal circumference increased at a time when the circumferential measurements of the body generally were tending to decrease.

I, therefore, conclude that the greatly increased bulk of the large intestine was a recent acquirement.

The developmental history of the intestine shows that the upper part of the large intestine is latest in developing. At birth the caecum is applied to the under surface of the liver and after birth descends to the right iliac fossa as a result of the growth/

growth of the ascending colon and in some measure of the transverse colon. I, therefore, include it in the list of ontogenetically youthful areas of the body.

The results of the enormous growth of the large intestine, in addition to the displacement of the liver, its translation and its rotation and in addition to the secondary displacement of the heart and to the deformation of the stomach, were apparently acutely to anteflex and to antevert the uterus and to press upon the ovaries and to press upon the inferior vena cava.

The pressure upon the cava I regard as important. Firstly, the atrophy of that portion of the liver interposed between the colon and heart shows that the intestine was pressing upon the surrounding structures. Secondly the complete emptiness of the cava after death suggests that the pressure upon it had been considerable, at least sufficient to empty it of blood. If this condition existed during life, there must have been partial obliteration of the abdominal venous cistern and consequent disturbances of the blood distribution. Evidence that this was so is forthcoming from the heart where as we have already seen there was, even with the great ventricular increase, a/

a disproportionate auricular increase which is known to be associated with a failure of the great veins of the neck to empty. With this I associate the prominence of the annulus ovalis projecting like a cowl over the opening of the inferior cava and directing part of the abdominal venous flow through the patent foramen ovale.

I, therefore, conclude that the progressive enlargement of the large intestine lead to a partial functional obliteration of the abdominal venous cistern and that as a result a condition of venous congestion of all the other parts of the body was established and that through the accidental presence of a patent foramen ovale there was an appreciable venous admixture of the arterial blood.

Microscopic examination of the tissues has conclusively demonstrated that general venous congestion did in fact exist. The importance of these observations in such a case is too obvious to be overlooked.

I am not at all certain that part at least of the ovarian atrophy was not due to direct mechanical pressure. The caecum directly impinged upon the left ovary/

ovary and it was found to be reduced to a fibrous cord. The right ovary protected from direct pressure by the pelvic brim was less atrophic.

On the other hand it is not impossible that the hypertrophy of the ventricular portion of the heart was due partly directly, partly indirectly to the same cause, the direct cause being the high abdominal pressure, the indirect cause the high venous pressure.

II. The Brain:--

The increased brain weight I regard as evidence of brain growth. I regard the advancing akrocephaly which from a comparison of the 1898-1907 measurements we have seen to have existed as evidence that the brain growth was progressive. This is an important consideration.

III. THE MUSCULAR SYSTEM:--

I regard the fibrosis of the glutei maximi and sacro lumbar portion of the multifidus spinae as the result of atrophy consequent upon hypertrophy. The hypertrophy, in turn, being consequent upon the impossibility of complete extension of the thigh and upon the/

the spinal curvatures; this I refer to later.

In the next section I describe the results of the microscopic examination of the tissues.

SECTION III. REPORT UPON THE MICROSCOPIC CHANGES FOUND IN THE BODY E.A.S.07.

Preliminary Note:--

The tissues were fixed with 30% formalin injected into the blood vessels. During the period of dissection the body was kept wrapt in formalin cloths from which evaporation was prevented by covering the whole with waterproof sheeting. However excellently adapted to preserving the body for dissection, the method was far from the best for preserving delicate tissues for microscopic examination.

The tissues examined were:--

A. THE DUCTLESS GLANDS.

1. The pituitary.
2. The thyroid.
3. The parathyroids.
4. The thymus.
5. The suprarenals.
6. The ovaries.
7./

7. The spleen.

8. The tissues lying behind the bifurcation of the common carotid, for the intercarotic body.

9. The tissues lying at the root of the inferior mesenteric artery, for Zuckerkandls chromaffin bodies.

10. The tissues surrounding the middle sacral artery for the ano-coccygeal body.

11. Bone marrow from the femora.

B. THE ALIMENTARY SYSTEM:--

1. The salivary glands.

2. The liver.

3. The pancreas.

4. Numerous pieces from the small intestine.

C. THE GENITO URINARY SYSTEM:--

1. The ovaries.

2. The kidneys.

D. THE NERVOUS SYSTEM:--

1. Nerves (optic, anterior crural, and median)

2. Spinal cord (cervical, dorsal and lumbar regions)

3. Sympathetic ganglia.

E/

E. MUSCULAR SYSTEM:—

1. Muscles of the Thenar Eminences.

2. Muscles of the Arm.

3. Muscles of The Thigh.

F. OSSEOUS SYSTEM:—

1. Portion of the occipital bone.

2. Portions of the femora.

G. INTEGUMENTARY SYSTEM:—

1. Skin from back, chest and arm.

2. Mammary Gland.

H. LYMPHATIC SYSTEM:—

1. Abdominal lymphatic glands.

2. Numerous lymphatic glands from neck.

I. CIRCULATORY SYSTEM:—

1. Carotid arteries.

2. Jugular veins.

Certain features common to all the sections examined may be noted:—

1. Throughout the whole body the walls of the arteries were definitely thickened;

2. everywhere there was evidence of great vascularity;

3./

PLATE CXI.

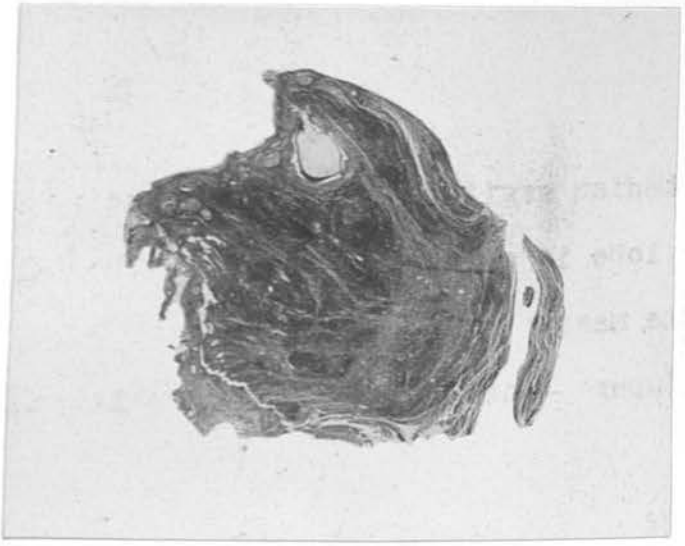


PLATE CXI.

Median sagittal section of the pituitary. The posterior lobe is seen spread out on the supero-posterior part of the mass.

Supero--anteriorly is seen a large colloid space.

PLATE CXII.

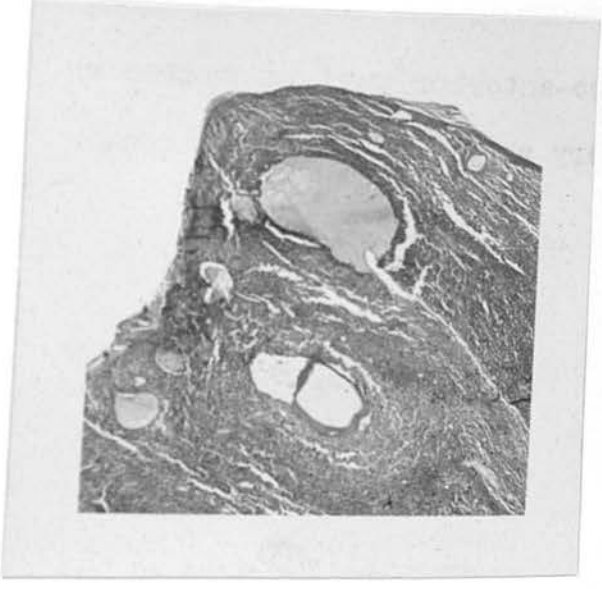


PLATE CXII.

Supero-anterior part of median sagittal section of the pituitary showing colloid spaces.

3. everywhere there was evidence of venous congestion.

ABRIDGED REPORT UPON THE MICROSCOPIC STRUCTURE OF THE TISSUES EXAMINED.

A. THE DUCTLESS GLANDS:--

A. The Pituitary.

(Note:--Pituitaries of individuals dead of diseases in which venous congestion was a prominent symptom were used as guides in the interpretation of the structural alterations discovered.)

On examination, it was found that the great increase in the bulk of the gland was due to a proliferation of the cells of the anterior lobe; the posterior was of apparently normal size, but somewhat flattened by pressure.

The structure of the anterior lobe was similar to that found in venously congested, but otherwise normal pituitaries.

The arrangement of the cells was normal.

The cells were normal in size and in appearance.

There was one large colloid space in the antero-superior region of the anterior lobe, and numerous small/

PLATE CXIII.

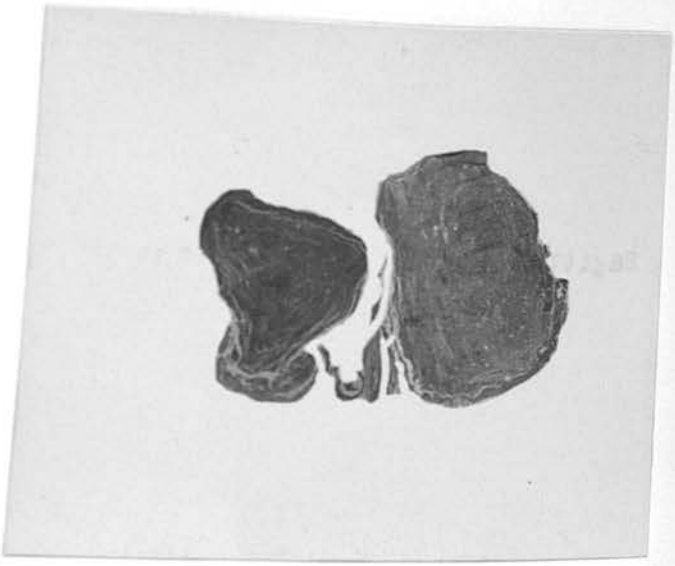


PLATE CXIII.

Sagittal section through the pituitary cornua.

PLATE CXIV.

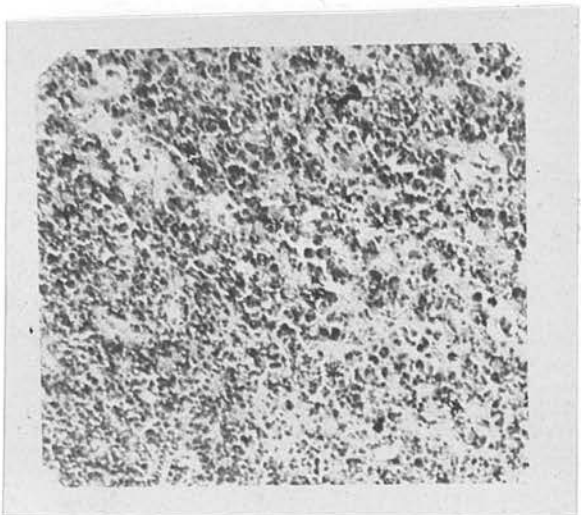
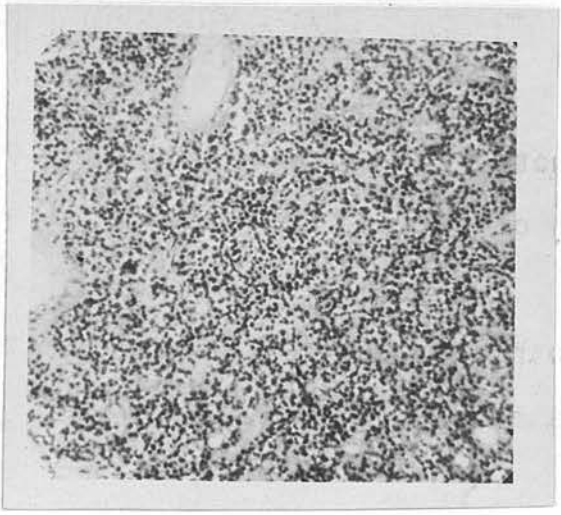


PLATE CXV.



PLATES CXIV. and CXV.

Photographs of sagittal sections showing the arrangement of cells in the anterior lobe of the pituitary.

Both of these might be photographs of normal human pituitaries.

PLATE CXVI

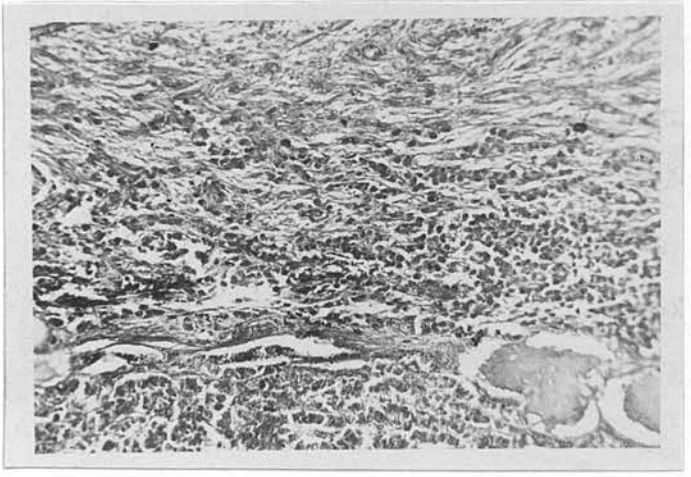


PLATE CXVI.

Area of junction of posterior and anterior lobes of pituitary; to show the cells of anterior lobe type apparently invading posterior lobe.

Zona intermedia showing condition of venous congestion.

small spaces in the pars intermedia.

From the microscopic appearances I think that the increased size of the gland was due to an excessive, but simple hyperplasia and not to an adenoma.

B. THE THYROID:--

A large number of sections cut from different parts of the gland were examined. Without exception these showed the effects of venous congestion. In spite of some slight differences in the amount of fibrous tissue found in different sections and sometimes in different parts of the same section the general appearances were most certainly those of a progressive parenchymatous goitre. Some of the colloid follicles were very large and branching and were lined by a single layer of cells; others apparently were in various stages of the process of formation, all forms varying from almost solid masses of cells with intracellular vacuoles containing colloid to the completely formed large follicles being frequently met with.

C. THYMUS:--

The/

PLATE CXVII.

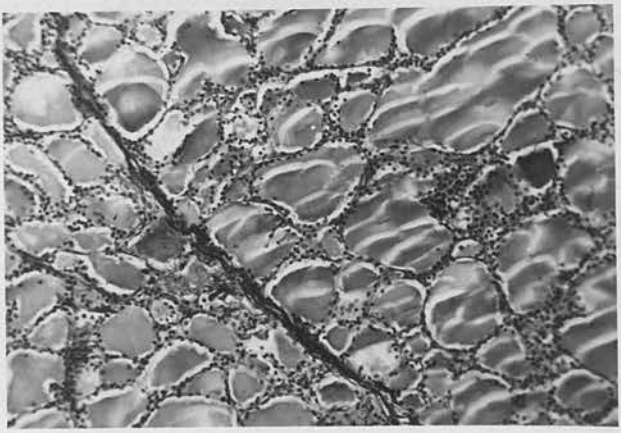
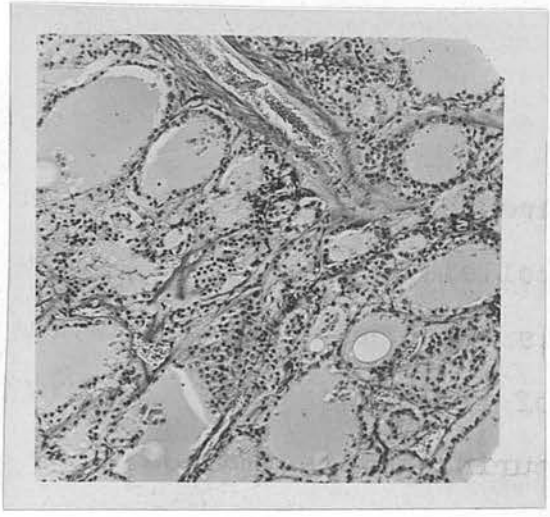


PLATE CXVIII.



PLATES CXVII. and CXVIII.

Micro-photographs of the thyroid. In Plate CXVII. the colloid material is seen cracked and fissured. This is an artefact and is due presumably to the method of fixation. In Plate CXVIII. the cracking and fissuring is less marked.

PLATE CXIX.

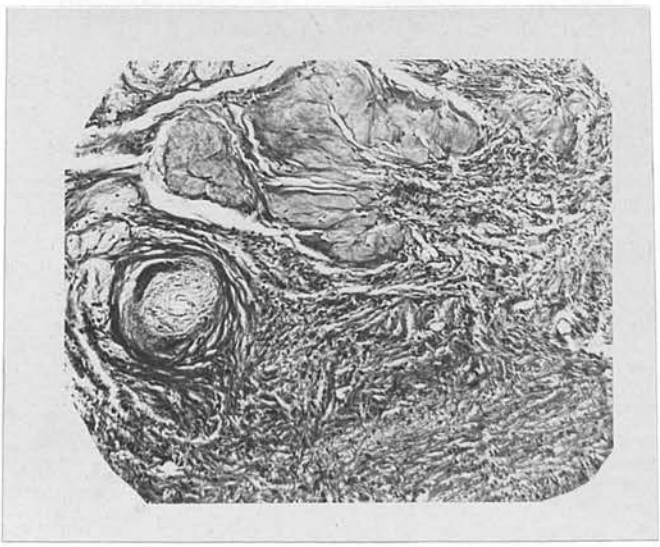


PLATE CXX.

PLATES CXIX. and CXX.

Micro-photographs of medium and high power views of sections of the right ovary.

In Plate CXIX. the great amount of fibrous tissue and the arrangement of the degenerated cellular elements are well seen.

In Plate CXX. the thickened stroma and the degenerated follicles are seen.

In other sections nothing but fibrous tissue was to be seen.

PLATE CXXI.

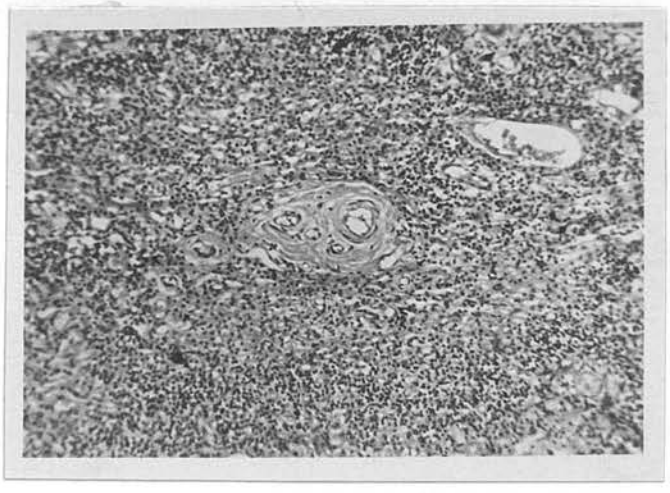


PLATE CXXI.

Micro-photograph of a section of the thymus.

The total amount of thymic tissue was small; in what there was the veins and capillaries were engorged, otherwise there were no abnormalities either in cell structure or arrangement.

D. SUPRARENALS:—

The suprarenals appeared to be in every respect normal. The capsule, the zona glomerulosa, the zona fasciculata and the zona reticularis were almost diagrammatically evident.

E. THE OVARIES:—

The left ovary was reduced to a fibrous cord.

The right ovary was also extremely fibrous. Some of the sections showed only fibrous tissue. At the centres of others were degenerated Graafian follicles. The general appearance would have been normal in an extremely aged woman; for a woman of fifty they can only be described as those indicative of an extraordinarily precocious senility. At no place in the numerous sections examined was any sign of a corpus luteum discovered, nor was any indication of surface scarring observed. The germinal epithelium had entirely disappeared from the surface.

F./

PLATE CXXII.

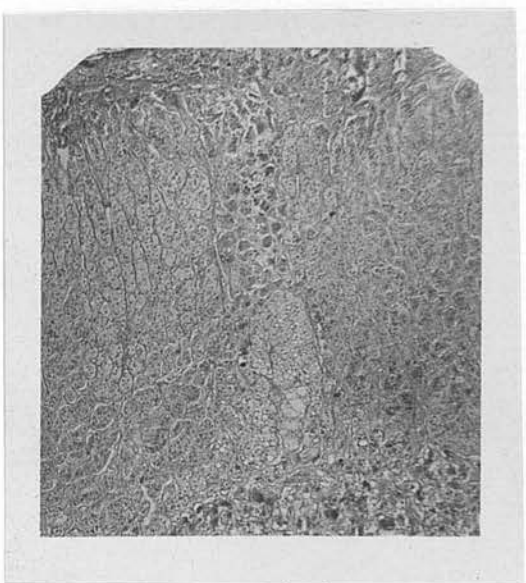
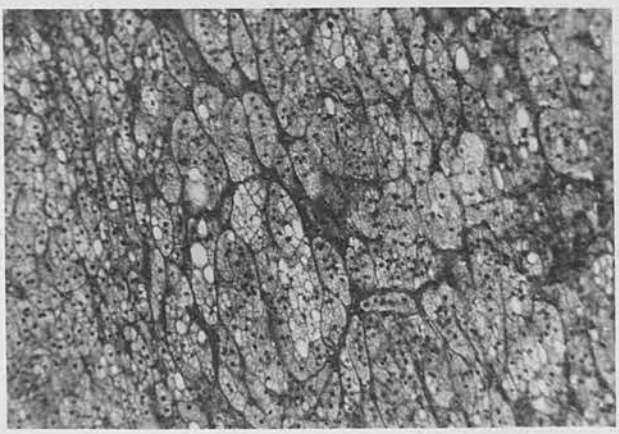


PLATE CXXIII.



PLATES CXXII. and CXXIII.

Low and high power views of the suprarenal body.

F. THE SPLEEN:--

Apart from a slight increase in the fibrous trabeculae the spleen appeared normal. There were no marked signs of chronic venous congestion.

G. THE INTERCAROTIC GLAND:--

The intercarotic gland was examined; no abnormality of structure was observed.

H. ZACKERKANDLS CHROMAFFIN BODIES:--

The lymphatic glands lying near the origin of the inferior mesenteric artery were examined microscopically. No chromaffin cells were discovered.

I. THE COCCYGEAL GLAND:--

Serial sections were made of the tissues lying around the branches of the middle sacral artery and the coccygeal gland in this way sectioned. No abnormality of structure or of cell type was observed.

K. THE MARROW:--

Marrow was removed from the shafts of both femora. It was of red colour. On microscopic examination this was found to be chiefly due to the great amount/

PLATE CXXIV.

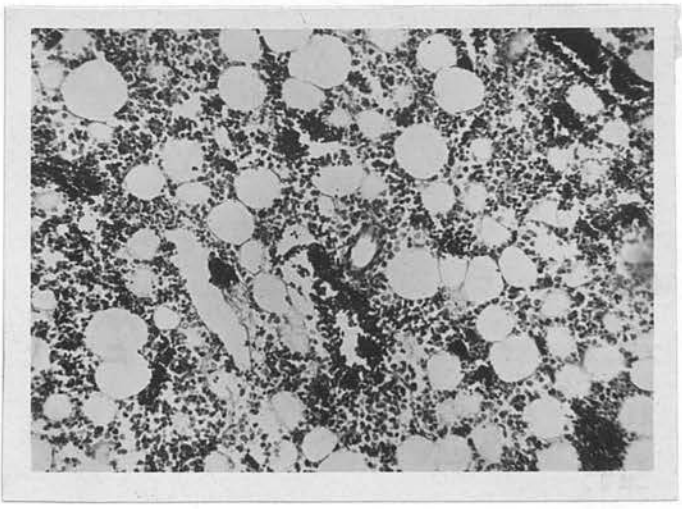


PLATE CXXIV.

Micro-photograph of the marrow from the shaft of the right femur. To show the unusual persistence of the cellular elements and the relatively slight amount of fat.

amount of blood present, and partly to the abnormal persistence of actively functioning marrow elements which were present in considerable quantities round the fat cells.

The detailed appearances of the marrow elements were in no way unusual.

L. THE PARATHYROIDS:—

The amount of parathyroid tissue was largely increased: its vascularity was enormous, at parts a vesicular structure had been developed. At one place in the parathyroid from the back of the left lobe there was a mass of granular debris which stained freely with eosin.

II. THE ALIMENTARY SYSTEM:—

A. The Salivary Glands:—

The salivary glands showed the ordinary structure and appearance of these glands in cases of venous congestion.

B. THE LIVER:—

The liver was very fatty, the result apparently of both fatty degeneration and fatty infiltration. The condition/

condition was, however, so advanced that it is difficult to speak with certainty. Most of the cells were distended with fat, but at the centre of the lobules there were numerous rather atrophied cells which contain fat droplets and granules. The centres of many of the lobules were, however, completely disorganised as the result of chronic venous congestion.

At the left margin of the left lobe of the liver, the gland cells had almost completely disappeared and been replaced by dense fibrous tissue. In some of the remaining lobules the venous congestion was most intense.

C. THE PANCREAS:--

The examination of the pancreas was not satisfactory: so far as could be made out the structure and appearance were normal.

D. THE SMALL INTESTINE:--

The small intestine was normal in structure and appearance throughout its length.

III. THE GENITO-URINARY SYSTEM:--

KIDNEYS.

A./

A. RIGHT KIDNEY:--

The right kidney showed the changes ordinarily associated with chronic venous congestion, but not to a very great degree. The glomeruli appeared large; the venules and capillaries were engorged and dilated.

The epithelium of the secreting tubules was as a whole little altered: at some places there were catarrhal changes; a few granular casts were noted in the collecting tubules.

B. LEFT KIDNEY:--

The left kidney was fatty: the essential elements of the organ showed the changes ordinarily associated with subacute nephritis. The interstitial connective tissue was increased in amount and fibrocellular; many of the tubules contained granular debris and degenerated cells. The Malpighian bodies were enlarged: in some there was interstitial thickening of the tuft and leucocytic infiltration. Some of Bowman's capsules were thickened and showed concentric laminae of connective tissue with flattened cells between; others were almost normal in appearance.

The signs of venous congestion, dilatation of the veins and venules were also present; several small infarcts were noted.

C./

C. THE OVARY has been already described along with the ductless glands.

IV. THE NERVOUS SYSTEM:—

A. The Spinal Cord.

The microscopic examination of the spinal cord was most unsatisfactory.

The method of preparation and fixation (intravascular injection of 30% formalin) was little suited to preserve fully the staining properties of the tissues.

The following notes are all that can be offered. The cord in the dorsal and lumbar regions was markedly unsymmetrical, the right side being the more bulky.

There was throughout a fairly definite increase in the amount of the supporting structures.

No degenerations of the essential elements were discovered although carefully looked for.

B. THE SYMPATHETIC GANGLIA:—

The increase in the bulk of the semilunar ganglia was due to an increase in the amount of the fibrous tissue. There were no visible changes in the essential elements.

C./

PLATE CXXV.

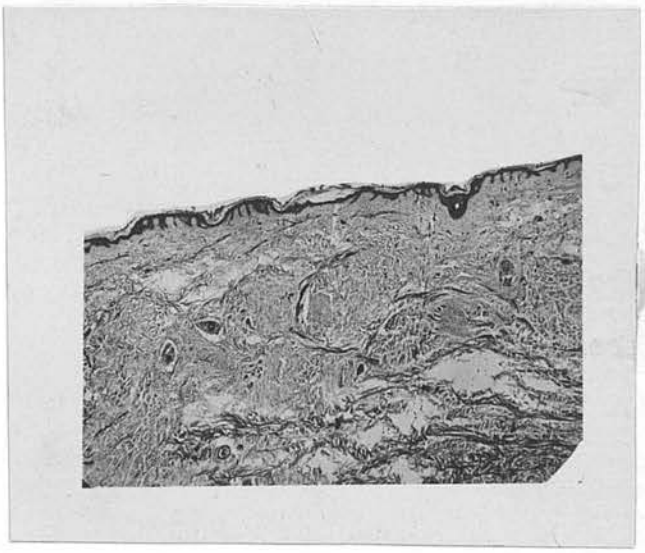


PLATE CXXV.

Micro-photograph of the skin, to show the relatively great thickness.

C. THE PERIPHERAL NERVES:--

The increased diameter of the peripheral nerves was due to a great increase in the amount of the fibrous tissue. There were no visible changes in the essential elements.

V. THE MUSCULAR SYSTEM:--

The muscles examined were normal in appearance.

VI. THE OSSEOUS SYSTEM:--

The bone of cranial vault (occipital squame) was remarkable for its extreme vascularity and for the thinness of the bony trabeculae. There was neither true outer table nor true inner table, the whole thickness being diploic.

The bone of the femur was remarkable for the enormous dilatation of its vascular spaces and for the thinness of the surface layer of really compact bone.

VII. MISCELLANEOUS:--

The subcutaneous tissues were markedly increased in thickness, but were normal in appearance.

The/

The mammary gland was completely atrophied.

The lymph glands were the seats of a simple hyperplasia.

The walls of the arteries were thickened.

SUMMARY OF MICROSCOPIC REPORT.

The pituitary was the seat of a simple hyperplasia(?) The thyroid was enlarged and apparently hyperfunctioning; the parathyroids were extremely active and resembled in appearance those found in cases of thyroid insufficiency: the ovaries were functionless. The left kidney was degenerating and the seat of a subacute nephritis: the liver was fatty and degenerated. The bones were abnormally vascular.

The other tissues of the body showed in greater or less degree the ordinary signs of chronic venous congestion.

CONCLUSIONS DRAWN FROM THE CLINICAL AND POST-MORTEM RECORDS OF CASE E.A S. 07.

From a consideration of the clinical and post-mortem records of case E.A.S. 07 I conclude:—

1. That the case was undoubtedly one of Acromegaly./

Acromegaly.

2. That the tissues were the seat of a markedly precocious senility.

3. That the thyroid was actively functioning, but that there was a great demand for its products which it was unable to meet.

4. That death was due to a septic pericarditis, secondary to an acute septic synovitis of the right knee.

CHAPTER XXI.

ABRIDGED DESCRIPTION OF AN ACROMEGALIC SKELETON AND THE RELATION OF ACROMEGALY TO GIANTISM.

SECTION I. METHOD OF PREPARATION OF THE SKELETON.

The skeleton was cleaned by hand, the soft parts being picked away piecemeal with ordinary dissecting forceps. This method of preparation was adopted in preference to maceration as it was feared that the bones would be damaged by prolonged immersion in water and by lying for months in sand.

The cleaned bones have been preserved in weak formalin.

SECTION II DESCRIPTION OF THE SKELETON.

The special characteristics of the different bones will be described later. There are, however, certain general features common to all the bones.

1./

PLATE CXXVI.

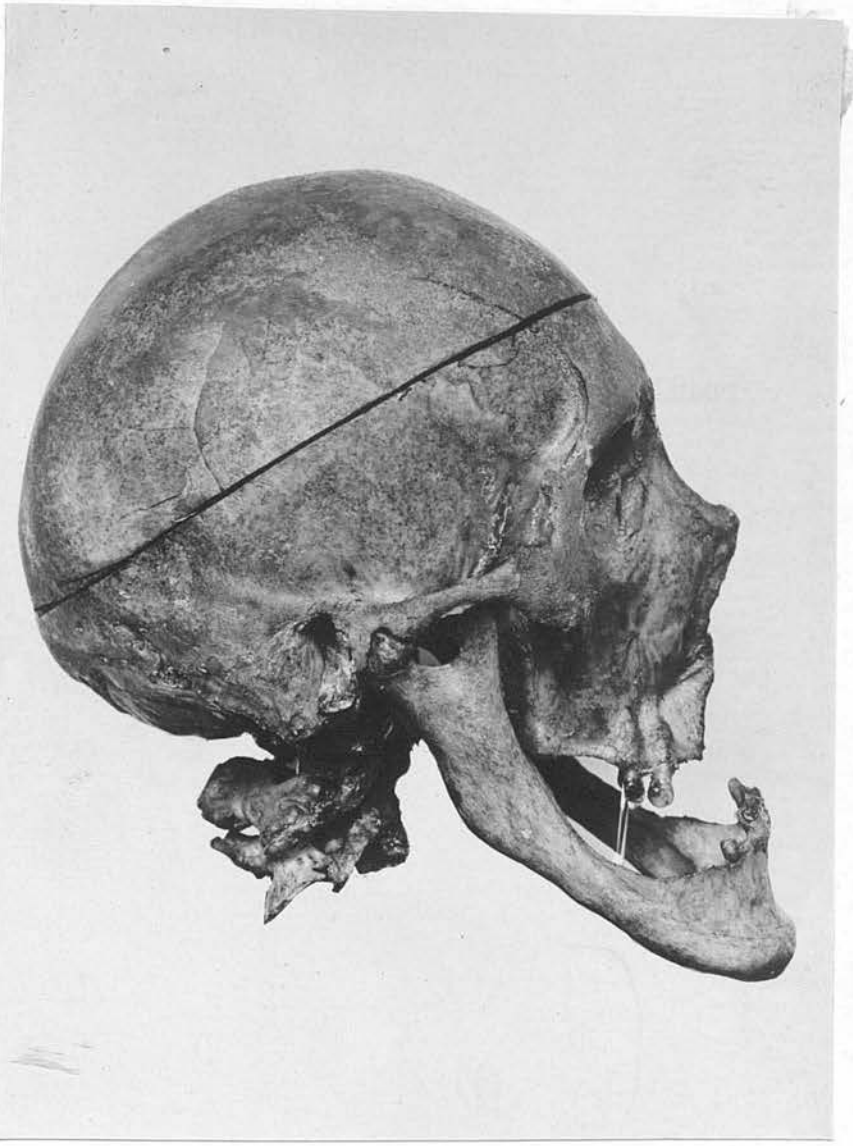


PLATE CXXVI.

Profile view of the skull E.A.S. 07.

For description see text.

1. In every bone of the skeleton there are signs of unusually great vascularity. This reaches its maximum in the bones of the cranial vault: its minimum in the mandible.

2. With the exception of the bones of the cranial vault every bone of the skeleton shows changes of the so-called disease rheumatoid arthritis. This reaches its maximum at points of tension and compression, its minimum on bone surfaces in contact with the fleshy portions of muscles.

3. Without exception, every bone of the skeleton is abnormal in shape and in appearance.

A. THE SKULL.

The skull E.A.S. 07. possesses some remarkable peculiarities. The colouring of the bones when first exposed was very extraordinary, the cranial vault was almost chocolate coloured from the presence of blood coagulated in the vascular channels and spaces of the bone: the mandible was pearly white, the result of its relatively slight vascularity.

At parts, the bone is thin and almost as transparent as wet tissue paper. The anterior superior dental/

PLATE CXXVII.

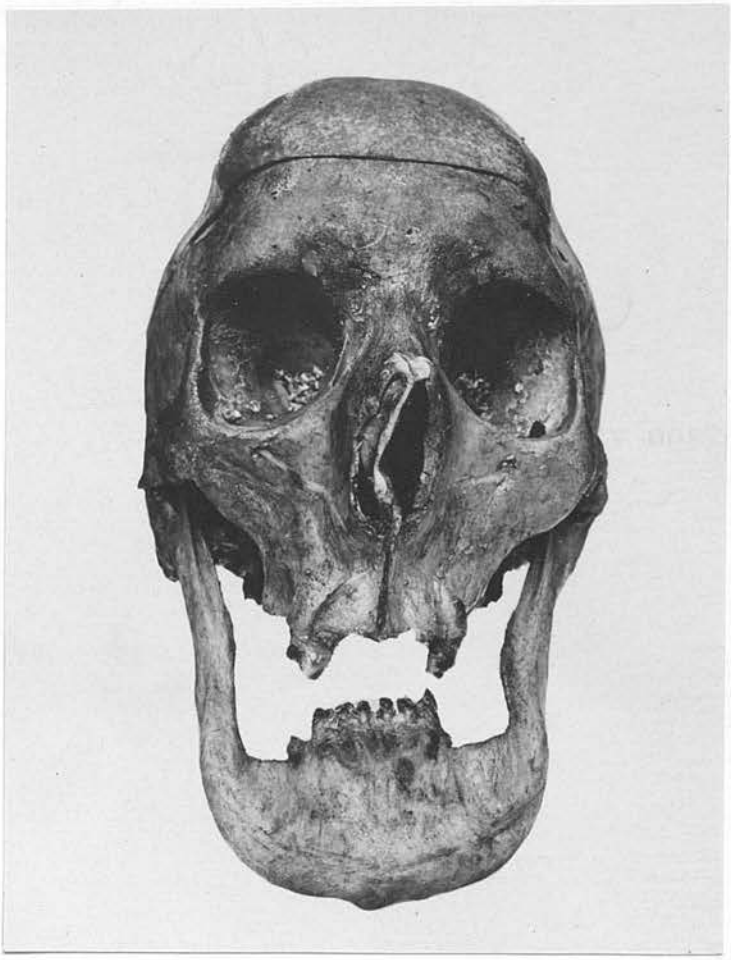
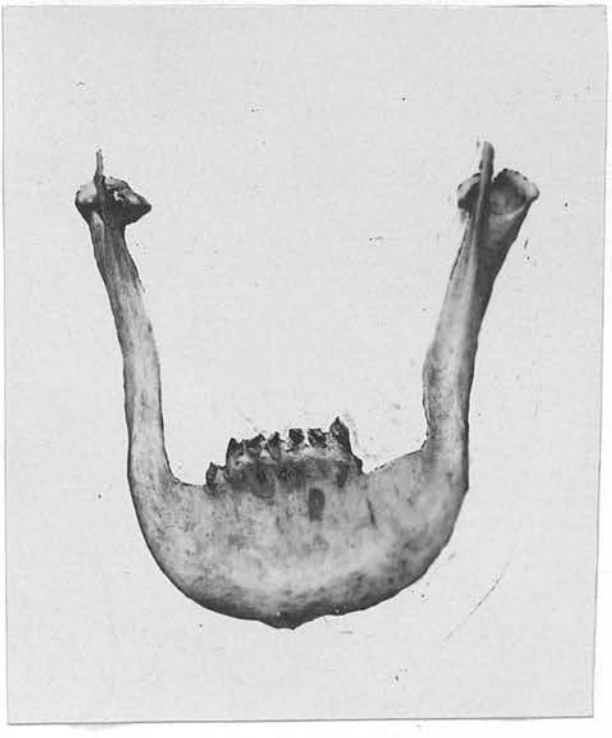


PLATE CXXVII.

Full face view of the skull E.A.S. 07.

For description see text.

PLATE CXXVIII.



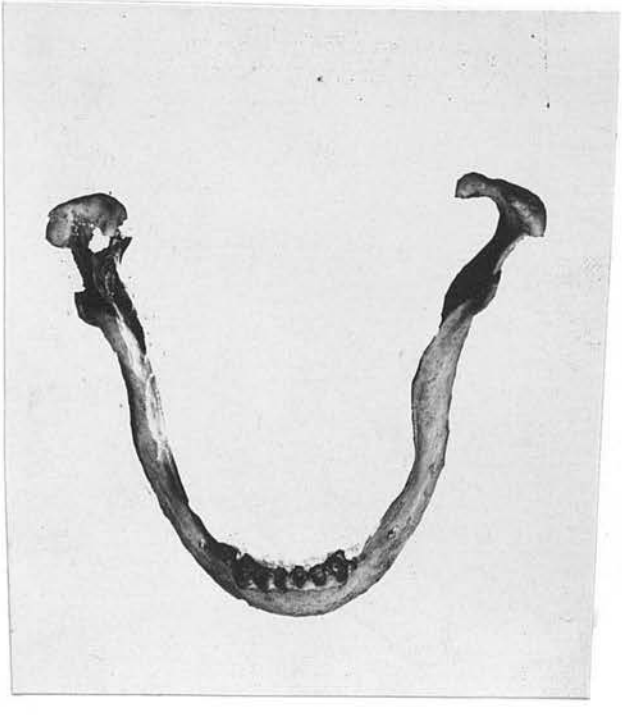


PLATE CXXVIII.

Two views of the mandible E.A.S. 07.

Note the asymmetry and the marked rheumatoid changes in the articular surfaces.

dental nerves are plainly visible within the substance of the superior maxillae. It is evident, too, upon the most cursory examination that the maxillary antra are enormously dilated. As a result of the skull being preserved wet they are partly filled with fluid, the surface level of which is readily visible through the bone.

The alveolar margin of the mandible has been the seat of a most pronounced atrophy. Its edge is razor-like. It is possible to see through it and to recognise colours through it. In contrast with the alveolar margin, the mental prominence and body are rounded, thick and strong. When the mandible is articulated with the cranium it is not only impossible to bring the lower incisors against the stumps of the upper, but it is impossible to raise them to the same plane. This is due to the locking of the coronoid processes against the cranial wall, that to the enormously increased length of the body of the bone which swings the incisors far in front of the superior maxillae.

The cranial sutures are entirely obliterated with the exception of that between the tympanic and squamo-zygomatic portions of the temporal bone. The outer/

PLATE CXXIX.

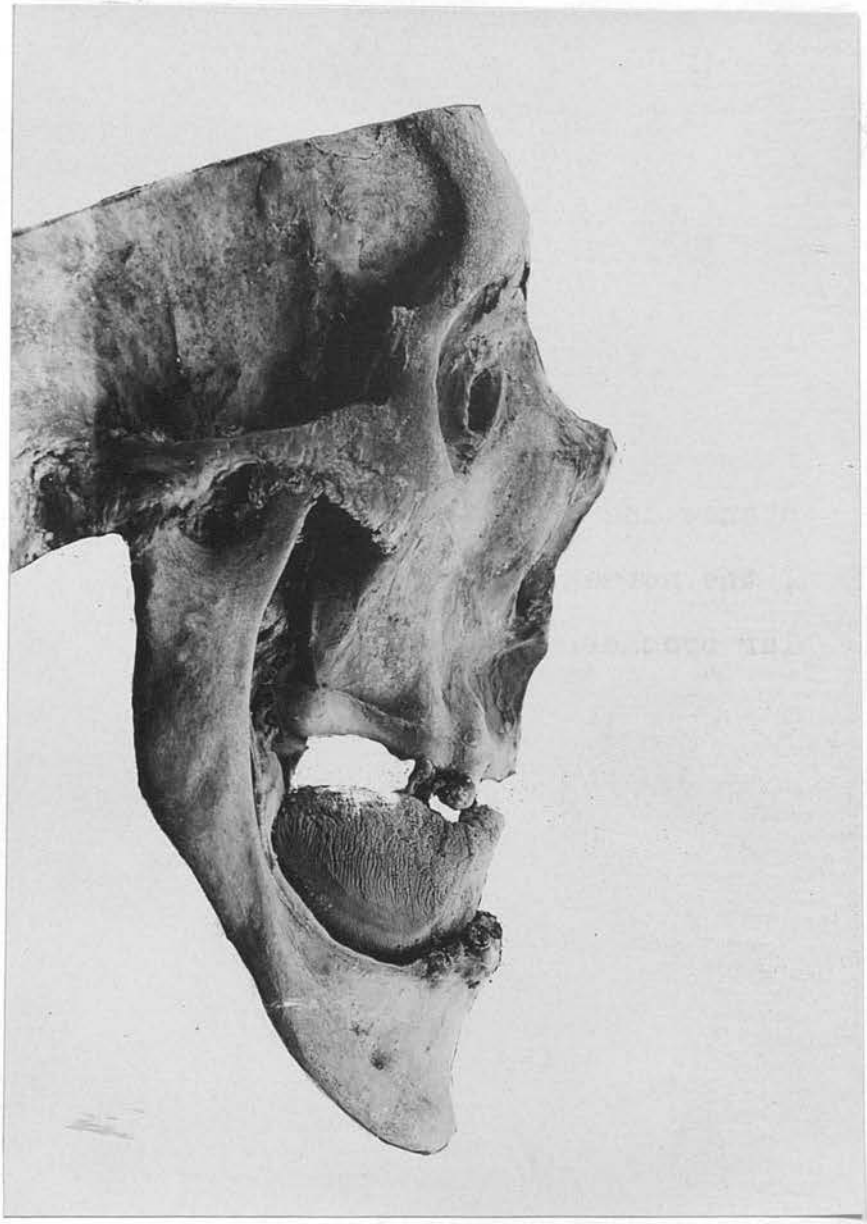


PLATE CXXIX.

To show the enormous size of the infundibulum ethmoidale, the normal position of the mandible and the naso-alveolar bracket.

outer margin of the tympanic plate projects on either side as a rough and rugged crest, crescentric in outline which reduces the external auditory meatus to a vertical slit. The walls of the cranial vault are of unequal thickness; the mesial part of the frontal squame is nearly as thick as the diameter of a three-penny bit; the bone in the region of the pterion is nearly as thin as a sixpence.

The zygomatic arches are exceedingly thin and weak; the cavities of the orbits are circular in outline: the bony bridge of the nose is peculiarly outstanding and prominent; the infundibulum ethmoidale on either side is exceedingly large; the frontal sinuses are large, their anterior wall is formed by the thinnest scale of bone.

In the superior maxilla, the alveolar margin projects and is supported at its centre by a bracket-like vertical plate of bone which passes from the anterior nasal spine to its centre.

The base of the skull is remarkable for four things; first, the upper three cervical vertebrae are firmly ankylosed together and to the occipital bone; second, the right styloid process has a bulbous end; third, the pterygoid plates do not descend so low as the/

the tuberosities of the superior maxillae: fourth, there is a mesially situated abnormal foramen which perforates the basilar portion and leads into the greatly enlarged pituitary fossa.

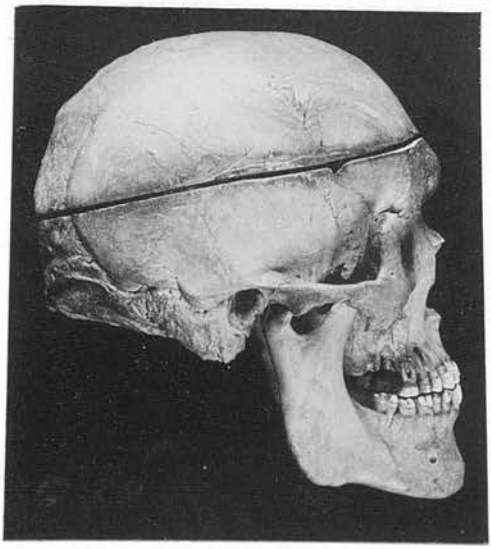
The interior of the cranium is remarkable for three things; first, for the enormous size of the pituitary fossa which is bowl shaped, in its expansion it has encroached upon the surrounding bone, thinning out the dorsum sellae to such a degree that it has been necessary to leave the dura mater in place to support it: second, for the great antero-posterior compression of the foramen magnum which is reduced to a transverse slit; third, for some prominent osteophytes which project from the floor of the right middle cranial fossa in its anterior part.

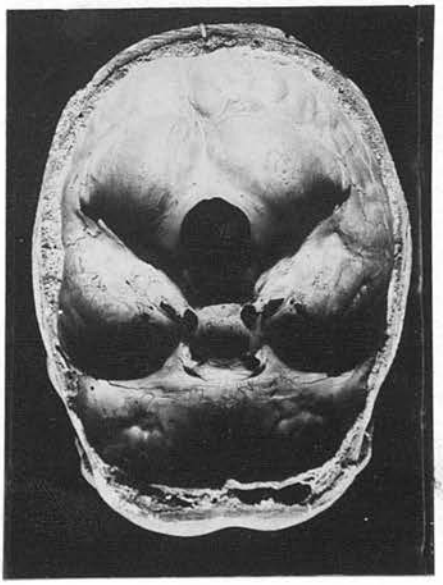
The tempero maxillary joint is markedly arthritic.

Measurements:--

Into the table of measurements E.A.S. 07. Table VI. I have introduced Professor Cunningham's figures for the skull of Cornelius Magrath, and for seven normal Irish skulls, Hinsdale's figures for the skull of the American Giant, and Mr.Alexis Thomson's figures for the skull E.A.S.79, which I have remeasured and/

PLATE CXXX.





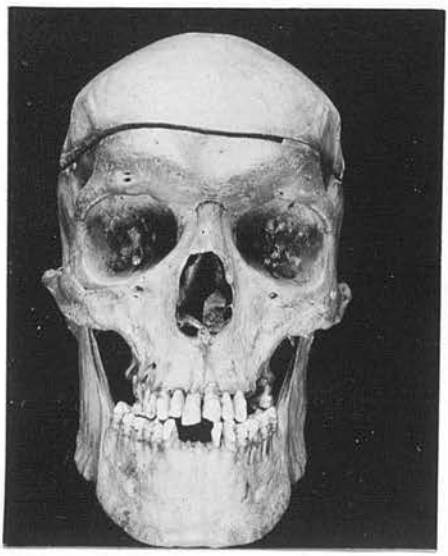


PLATE CXXX.

Three views of the skull E.A.S. 79.

and at one or two places slightly altered.

E.A.S.07.

TABLE VI.

SKULL MEASUREMENTS.

	E.A.S. 07.	E.A.S. 79.	Magrath	American Giant	Seven Irish skulls
Glabello Occipital length.	189	201	198	234	189
Basi bregmatic height	137	143	139	---	137
Vertical Index	72·5	71·5	70·2	---	72·4
Min. frontal diam.	90	104	109	---	94·4
Stephanic diam.	--	130	136	---	121·5
Asterionic diam.	126	119	144	---	111·5
Max. breadth	146	148	155	145	143
Cephalic Index	77·25	74	78·3	---	75·7
Horizontal Circumference.	534	563	568	640	526
Frontal longitudinal arc.	---	130	139	---	128·2
Parietal do.	---	115	135	---	129·6
Occipital do.	---	164	120	---	119·3
Total do.	380	409	394	---	377
Vertical transverse arc.	330	336	340	---	307·3
Vertical/					

TABLE VI. (continued)

	E.A.S. 07.	E.A.S. 79.	Magrath	American Giant	Seven Irish Skulls
Vertical height	133	131	---	---	---
Vertical height Index	70·3	64·8	---	---	---
Length of Foramen magnum	10	33	40	51	36·7
Breadth of Foramen magnum	25	32	---	39	---
Basi-nasal length	126	106	105	---	103
Basi-alveolar length	118	105	107	---	98·6
Gnathic Index	93·65	99·1	101·9	---	95·6
Interzygomatic breadth	133	150	156	147	131
Intermalar breadth	119	126	127	133	111·1
Ophryo-alveolar length	127	124	---	---	---
Broca's Facial Index	95·5	82·6	---	---	---
Naso-alveolar length	98	82	96	90	73·4
Cunningham's Facial Index	73·7	54·6	61·5	62·6	55·7
Nasal height	65	59	72	---	53·7
Nasal width	20	24	29	---	24
Nasal Index	30·8	40·7	40·2	---	44.4
Orbital/					

TABLE VI. (continued)

	E.A.S. 07.		E.A.S. 79.		Magrath	American Giant	Seven Irish Skulls
Orbital width	40		44		44	52	41
Orbital height	40		36		43	42	35·1
Orbital Index	100		80		97·7	80·8	85·3
Palato maxillary length	61		67		50	---	53·3
Palato maxillary breadth	63		70		65	---	60·3
Palato maxillary Index	103·3		104·4		130	---	113·2
Ophryo-mental length	212		190		---	---	---
Naso-mental length (1)	183		148		156	148	120
Mandible:--							3 Irish Mandibles
Symphyseal height	46		46		46	40	34
	R.	L.	R.	L.			
Coronoid "	75	70	96	81	98	---	67
Condyloid "	69	65	92	95	95	---	70
Gonio mental length	108	116	113	106	113	---	95
Gonio alveolar length	92	96	107	105	104	---	91
Breadth/							

(1) Owing to the impossibility of bringing the lower incisors against the upper these measurements were taken with the mandible in the position it occupied in life. This method is, in a sense, fallacious, but it gives a better index of the real face length than any other.

TABLE VI. (Continued).

	E.A.S. 07.		E.A.S. 79.		Magrath	American Giant	Seven Irish Skulls
	R.	L.	R.	L.			
Breadth of ascending ramus	24	21	38	41	34	40	33
Intergonial width	100		113		113	113	100

ANALYSIS OF THE MEASUREMENTS. (1)

To the eye, the most striking thing about the shape of the skull is its marked akrocephaly. The vertical index 72·5 does not support the general impression. The vertical height index, found by comparing the vertical height and antero-posterior length is, however, 70·3 whereas that of E.A.S.79 is only 64·8. The reason for this is the peculiar outline of the cranial vault which in profile forms a large segment of a small circle. This taken in conjunction with the progressive increase of the glabello-occipital arc demonstrated by comparison of the 1899-1907 measurements seems to me to be a most important observation.

Of all solid figures of any given surface area the sphere contains the greatest mass and it seems necessary to conclude that in this case the brain increase in/

(1). I have used Professor's D.J.Cunningham's Analysis of the measurements of Magrath as my general model.

in mass after the onset of the acromegaly and forced the skull to adapt itself to the new bulk of its content. Comparing the glabello-occipital length with the similar measurement of the skull of the American Giant and of the seven normal skulls (189:234:189) there is an obvious suggestion that there also the brain increased in mass after the onset of the giantism, but that the occipito-sphenoidal synchondrosis being unobliterated cubic capacity was gained by an increase of base length.

In the face, the most outstanding features of the bones have been already referred to: an analysis of their proportions, however, well repays investigation.

First the superior maxillae are markedly increased in height, as is shown by the following table:--

E.A.S. 07. TABLE VII.

Naso alveolar length compared with stature.

Stature = 100

	Naso Alveolar length	Stature	Index
E.A.S.07	98	1574	6·22
E.A.S.79	82	1830	4·42
Magrath	96	2177	4·40
American Giant	90	2295	3·94
Seven Irish skulls	73·4	1710	4·26

This/

This brings out in a most striking way the very great size of the superior maxillae in E.A.S.07. The comparison with stature tends, however, markedly to minimise the great development of the bones in the two giants. If instead of stature we take the cranial circumference as the basis of comparison we obtain the following results:--

E.A.S. 07 TABLE VIII.

Naso alveolar length compared with cranial circumference.

Cranial circumference = 100.

	Naso-alveolar length	Cranial Circumference	Index
E.A.S.07	98	534	18·5
E.A.S.79	82	563	14·5
Magrath	96	568	16·8
American Giant	90	640	14
Seven Irish Skulls	73·4	526	13·8

A comparison of these indices shows the great growth of the superior maxillae. In E.A.S.79 the result is somewhat masked by the inclusion in the cranial/

cranial circumference of the enormously heavy superciliary ridges and in the case of the American Giant by the altogether abnormal length of the skull base. In spite of these disturbing factors, however, it is quite evident that in these skulls the superior maxillae are definitely larger than normal.

It is interesting to discover in which part of the superior maxillae the growth changes were most active. This can be sufficiently accurately determined by comparing the nasal height and the naso-alveolar length.

E.A.S. 07 TABLE IX.

Nasal Height compared with Naso-Alveolar length.

Naso-Alveolar Length = 100.

	Nasal Height	Naso-Alveolar Length	Index.
E.A.S.07	65	98	66·3
E.A.S.79	59	82	72
Magrath	72	96	75
Seven Irish Skulls	53·7	73·4	73·1

The lower the index in this table, the greater relatively has been the growth of the lower or alveo-

lar/

alveolar portion of the superior maxillae.

The proportion borne by the length of the face to the total stature is also not without interest. It is easily brought out by comparing the naso-mental length with the total stature. Theoretically the ophryo-mental length would be a preferable unit to employ, but in practice the ophryon is difficult to determine. I therefore follow the method adopted by Professor Cunningham for calculating this index. It is to be noted, however, that in E.A.S.07 the naso-mental measurement includes the length of the buccal gape consequent upon the locking of the coronoid processes.

E.A.S.07 TABLE X.

Vertical Height of Face (Naso-Mental Length). compared with Stature.

Stature = 100

	Length of Face	Stature	Index
E.A.S.07	183	1574	11·62
E.A.S.79	148	1830	8·08
Magrath	156	2177	7·16
American Giant	148	2295	6·44
Seven Irish Skulls	120	1710	7·01

Just/

Just as before, when dealing with the height of the superior maxillae, comparison with stature tends to mask the growth changes in the giants: it is as well therefore, to compare the face length with the cranial circumference though, as we have seen, this puts both E.A.S.79 and the American Giant at a disadvantage.

E.A.S.07 TABLE XI.

Vertical Height of Face (Naso-Mental Length) compared with Cranial Circumference.

Cranial Circumference = 100

	Length of Face.	Cranial Circumference	Index
E.A.S.07	183	534	34·2
E.A.S.79	148	563	26·3
Magrath	156	568	27·4
American Giant	148	640	23·1
Seven Irish Skulls	120	526	22·8

The extraordinary face length of E.A.S.07 is well brought out by these indices. It is not uninteresting to notice that in absolute length of face E.A.S.07 exceeds the average for the seven male Irish skulls by almost exactly 50%.

Before/

Before passing from the face it is well to compare the maxillary and mandibular heights even though it gives but little information as to the relative growth of the bones, since it compares the whole growth of the maxillae with the symphyseal increase in the mandible.

E.A.S.07 TABLE XII.

The Mandibular Symphyseal Height compared with the Naso-Alveolar Height.

Naso-Alveolar Height = 100.

	Symphyseal Height	Naso-Alveolar Height	Index.
E.A.S.07	46	98	46·95
E.A.S.79	46	82	56·4
Magrath	46	96	47·9
American Giant	40	80	44·4
Seven Irish Skulls	34	73·4	46·5

From this table it is evident that in E.A.S.07 the mandibular height increased relatively, slightly more than the maxillary: in E.A.S.79 and Magrath, considerably, more.

With regard to the mandible itself it is important/

important to note that the growth has affected chiefly the body of the bone. This is well brought out in the following tables in which the condylar height and gonio-mental length are compared with the cranial circumference and with one another.

E.A.S.07 TABLE XIII.

Condylar Height compared with Cranial Circumference.

Cranial Circumference = 100.

	Condylar Height	Cranial Circumference	Index
E.A.S.07	65	534	12·17
E.A.S.79	95	563	16·69
Magrath	95	568	16·72
Three Irish Mandibles	70	526	13·3

E.A.S.07 TABLE XIV.

Gonio-Mental Length compared with Cranial Circumference.

Cranial Circumference = 100.

	Gonio-Mental Length	Cranial Circumference	Index.
E.A.S.07	116	534	21·72
E.A.S.79	106	563	18·65
Magrath	113	568	19·89
Three Irish Mandibles	95	526	18·06

E.A.S.07/

E.A.S.07 TABLE XV.

Gonio-Mental Length compared with Condylar Height.

Condylar Height = 100.

	Gonio-Mental Length	Condylar Height	Index.
E.A.S.07	116	65	178
E.A.S.79	106	95	111·5
Magrath	113	95	118·9
Three Irish Mandibles	95	70	135·7

It is necessary, before drawing from these figures any conclusions as to growth, to admit the probability of atrophy and absorption rounding off and reducing the angle of the mandible to the detriment of the measurements of height.

So far as it is possible to judge of the effects of growth in an atrophic bone it is evident from a comparison of the gonio-alveolar and gonio-mental lengths that the lower part of the body of the mandible has grown more than the upper.

E.A.S.07 TABLE XVI.

Comparison of the Gonio-Alveolar and Gonio-Mental Lengths.

	Gonio-Alveolar Length	Gonio-Mental Length
E.A.S.07	96	116
E.A.S.79	105	106
Magrath	104	113
Three Irish Mandibles	91	95

The Facial Indices have already been given in E.A.S.07, Table VI.

They are:--

E.A.S.07	73·7
E.A.S.79	54·6
Magrath	61·5
American Giant	62·6
Seven Irish Skulls	55·7

SUMMARY OF ANALYSES OF SKULL MEASUREMENTS.

The face is enormously increased in length; all the bones of the face participate in this increase. In/

In the superior maxillae the growth has been relatively greatest in the alveolar portion: in the mandible, the body and chin have grown most.

B. THE BONES OF THE TRUNK.

1. The Vertebral Column.

All the joints of the vertebral column are ankylosed, except that between the third and fourth cervical vertebrae. In all the other cervical joints and in all the thoracic joints the intervertebral discs have been entirely absorbed. The lumbar discs persist, the ankylosis being situated posteriorly. The ankylosis of the vertebral bodies is not marked by projections, except in the lumbar region where there is a slight tendency to the formation of marginal protuberances.

There is a marked cervico-dorsal kyphosis with compensatory cervical and lumbar curves.

The sacrum is rotated so that its long axis is horizontal, and is bent under the weight of the spinal column. The whole appearance suggests that there has been a primary rarefying osteopathy, a kind of osteomalacia and that the subsequent ankyloses are the result of crude attempts at repair.

The/

PLATE CXXXI.

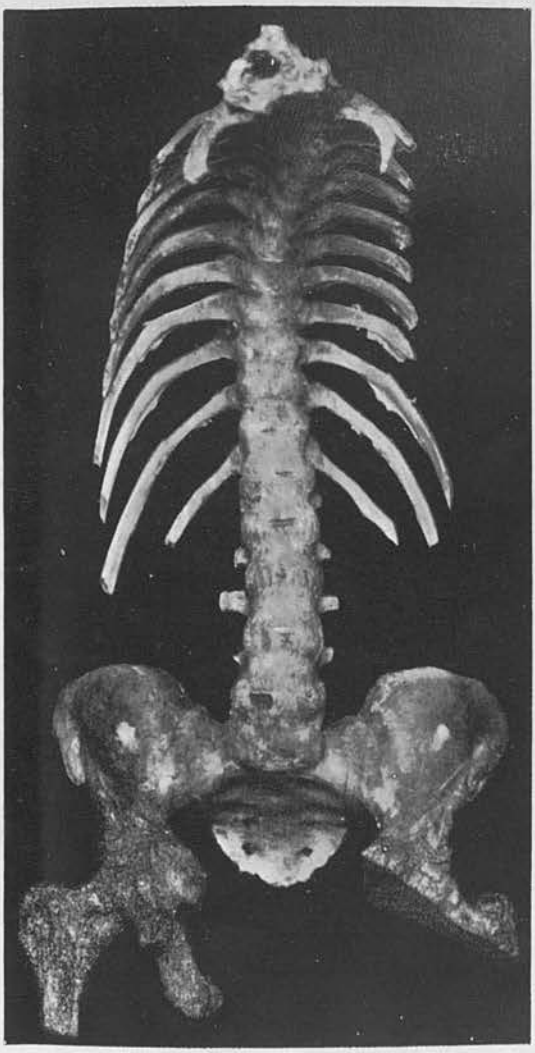


PLATE CXXXI.

Spondylose Rhizomélique.

---- After Léri.

PLATE CXXXII.

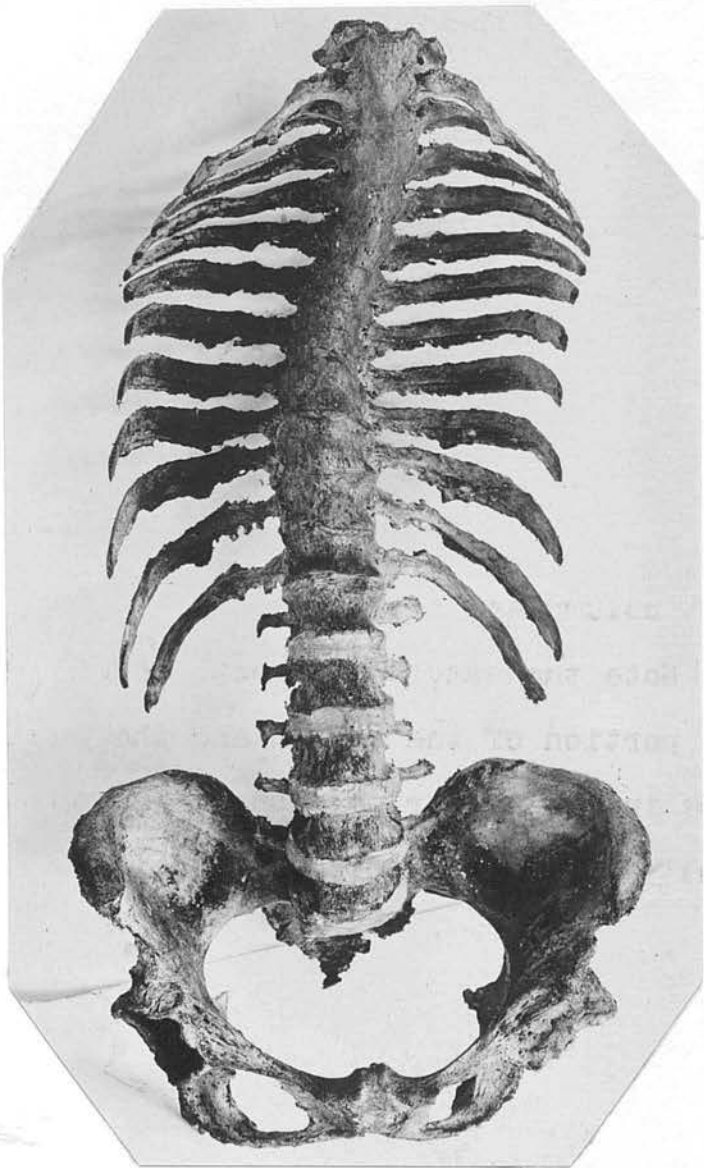


PLATE CXXXII.

Vertebral column and pelvis.

Note the complete, smooth ankylosis of the thoracic portion of the column and the persistence of the discs in the lumbar portion; also the great width of the pelvis and the horizontal position of the sacrum.

PLATE CXXXIII.

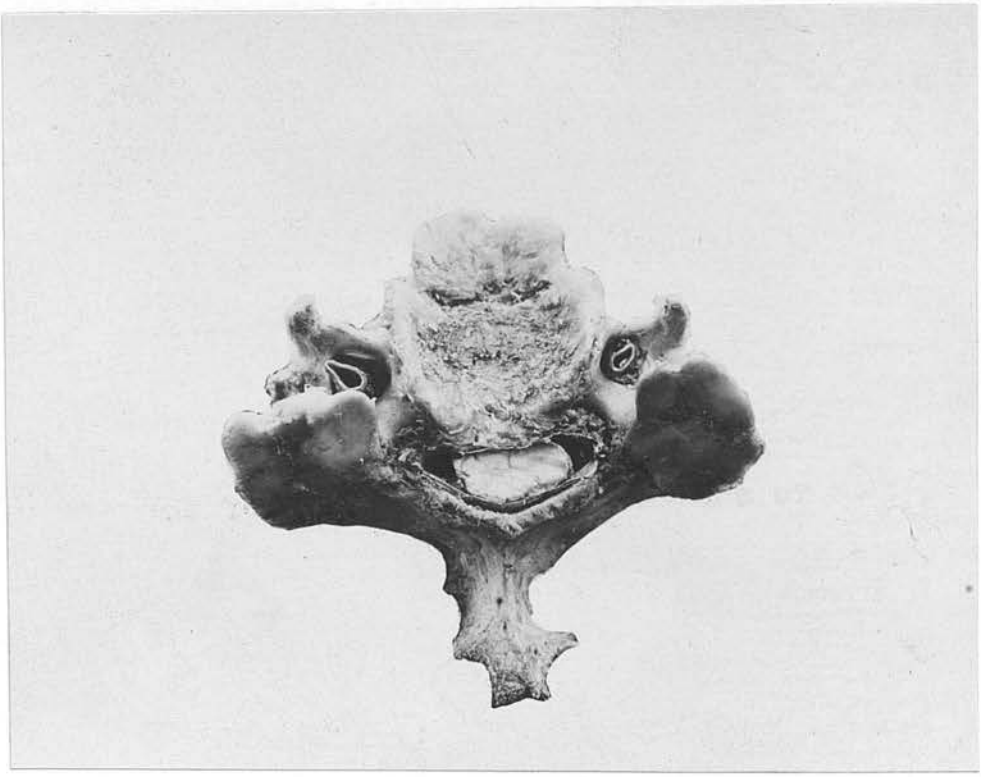


PLATE CXXXIII.

To show the characteristics of the cervical vertebrae.

The condition is obviously one of advanced spondylose rhizomelique and conforms almost in every detail to Léri's[1] description of that condition. There is, however, one very remarkable change in the lumbar region. All the lumbar vertebrae and the three lower dorsal vertebrae have had developed upon them spine-like anapophysial processes similar to those found in the Cercopithecidae. To the tips of these processes strong tendons of the sacro-lumbar portion of the multifidus spinae were attached. Whether the presence of these processes should be regarded as evidence of reversion, or as a use acquirement is a question which at the present time it is unnecessary to discuss. It is, however, not without significance that the sacro-lumbar portion of the multifidus spinae was fibrous and that this was thought to be the result of an atrophy consequent upon hypertrophy. Mechanically it is certain that the sites of attachment of the tendons to the bone were points of strain and, therefore, points at which abnormal ossification was to be looked for.

2. The ribs, more especially at their anterior ends, and the sternum are greatly increased in size.

C./

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(1) Review of Neurology and Psychiatry, February 1908.

PLATE CXXXIV.

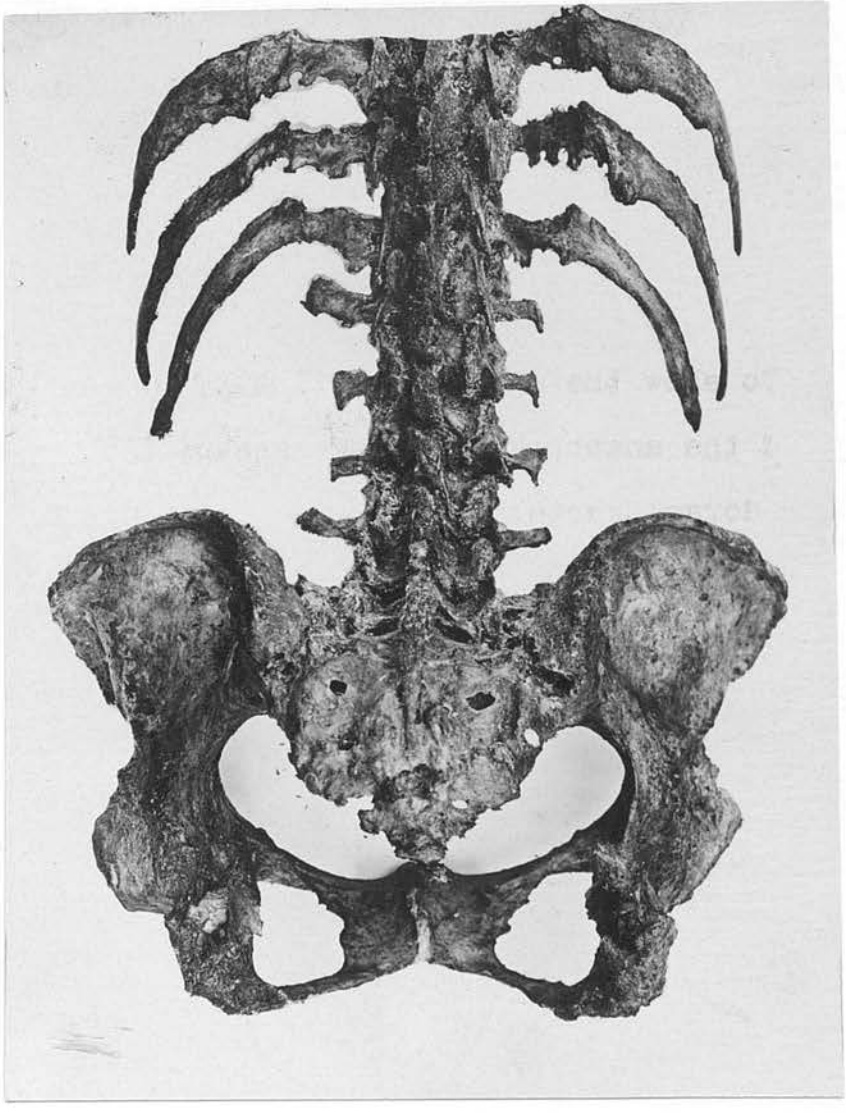


PLATE CXXXIV.

To show the characteristics of the pelvis from behind and the anapophysial processes upon the lumbar and lower dorsal vertebrae.

PLATE CXXXV.

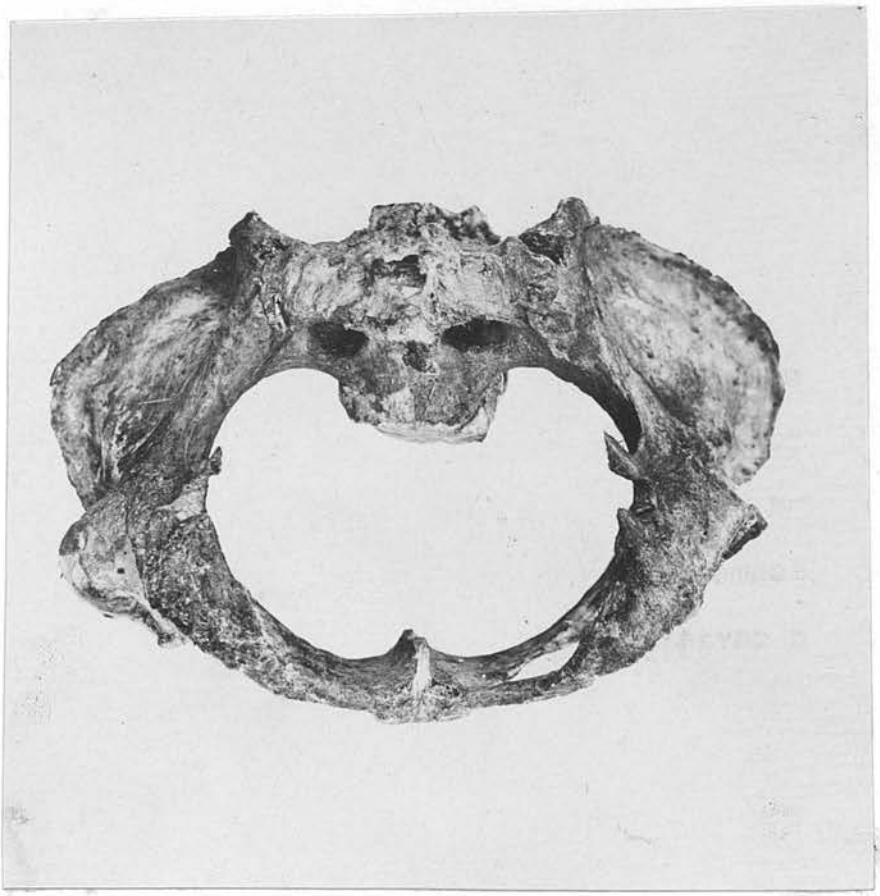


PLATE CXXXV.

The pelvis from below.

To show the condition of the ischial tuberosities and the bony growths round the acetabula, also the encroachment of the region of the symphysis upon the pelvic cavity.

C. THE LIMB BONES.

All the bones of the limbs are affected with the most extraordinarily strongly developed changes of the so-called rheumatoid type, extreme general atrophy with local hypertrophies. In the humerus, for example, the insertion of the deltoid is marked by a very rough and very prominent V shaped line.

In the pelvis there is extreme atrophy of the bone forming the floor of the iliac fossae and extreme hypertrophy and rugged outgrowth of the iliac crest. The sub pubic angle is extraordinarily wide and flat.

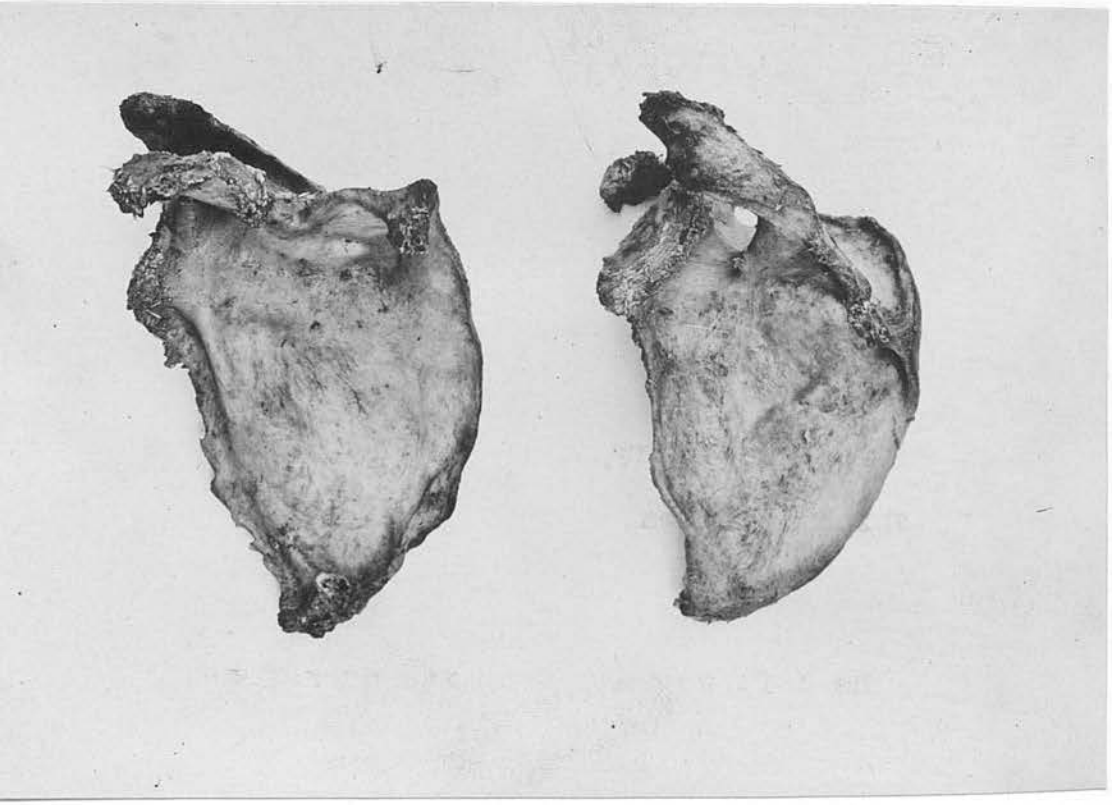
The accompanying photographs give a better idea of their appearances than many pages of verbal description could convey. The bony ankylosis affecting the carpus, metacarpus, tarsus and metatarsus and the peculiar fusiform swelling affecting the upper third of the left radius are worthy of notice.

The Measurements, in millimètres, of the bones are:--

Scapula	Right	Left
Length	157	149
Breadth	104	101
Infra-spinous length	120	115

Humerus:--/

PLATE CXXXVI.



1. 2.

PLATE CXXXVI.

1. The right scapula from its ventral aspect. Note the great development of the angle and the direction in which it faces.

2. The left scapula from its dorsal aspect.

The Measurements, in millimetres, of the bones (continued)

		Right	Left
Humerus:--	Length	329 5	318
Radius:--	Total length	220	226
	Length without styloid	215	220
Ulna:--	Total length	248	242
	Length without styloid	248	242
Femur:--	Head to Internal Condyle	421	423
	Oblique length	420	420
Diameters:--	(just below lesser trochanter)		
	Antero-Posterior	30	34
	Transverse	45	48
	(at middle of shaft)		
	Antero-Posterior	23	20
	Transverse	33	32
	(Junction of lower and middle thirds)		
	Antero-Posterior	25	18
	Transverse	35	32
Tibia:--			
Maximum Length		347	343
Length without malleolus		338	334
Diameters:--	(at middle of shaft)		
Antero-Posterior		30	27
Transverse		20	17

Fibula:--/

PLATE CXXXVII.

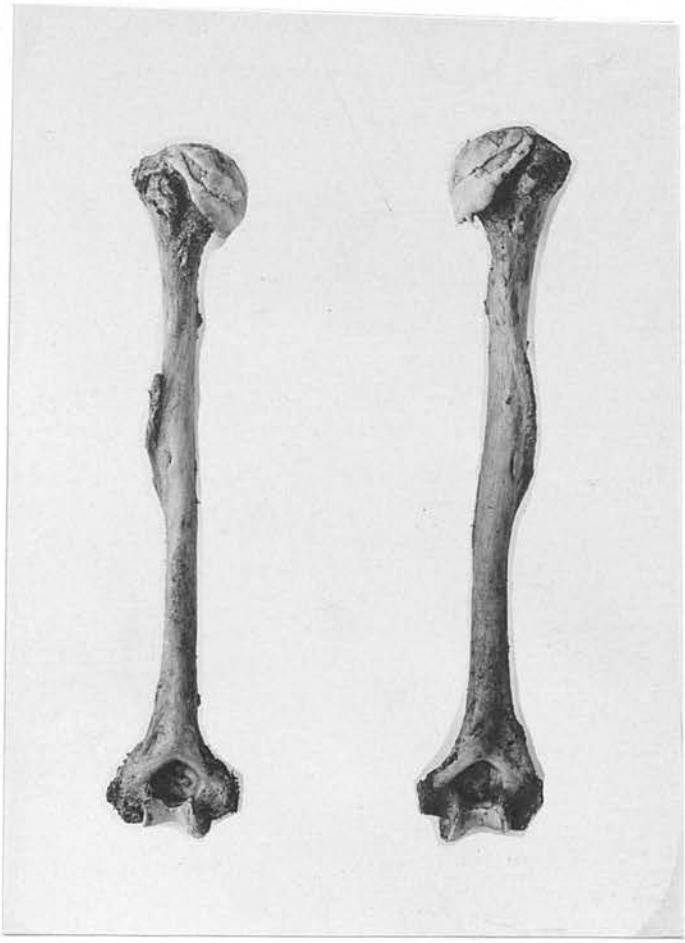
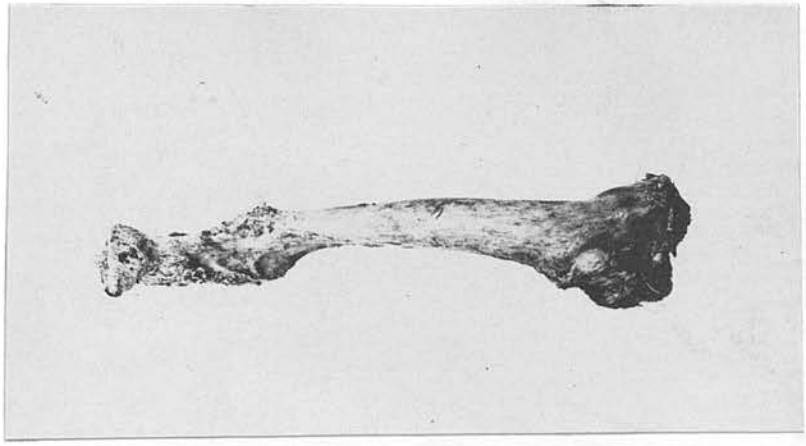


PLATE CXXXVIII.



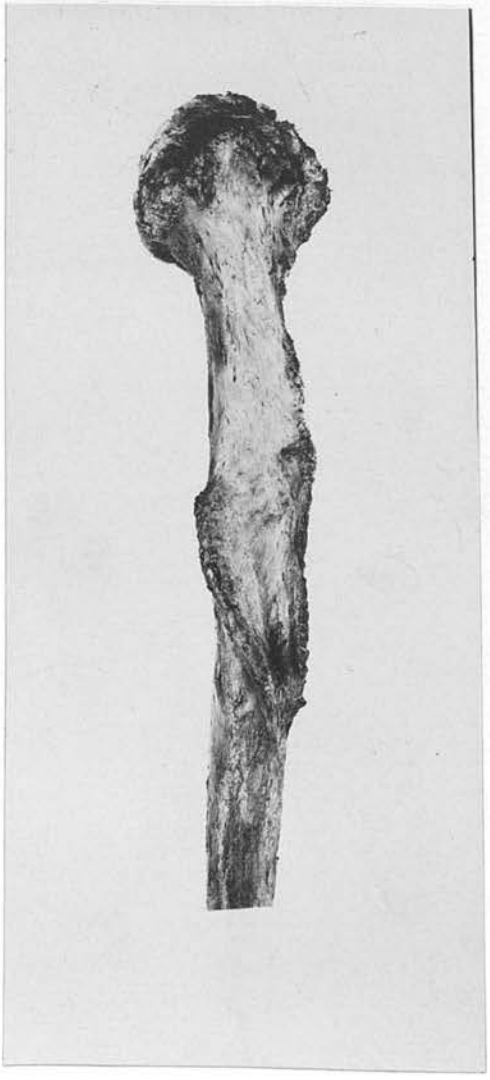


PLATE CXXXIX.

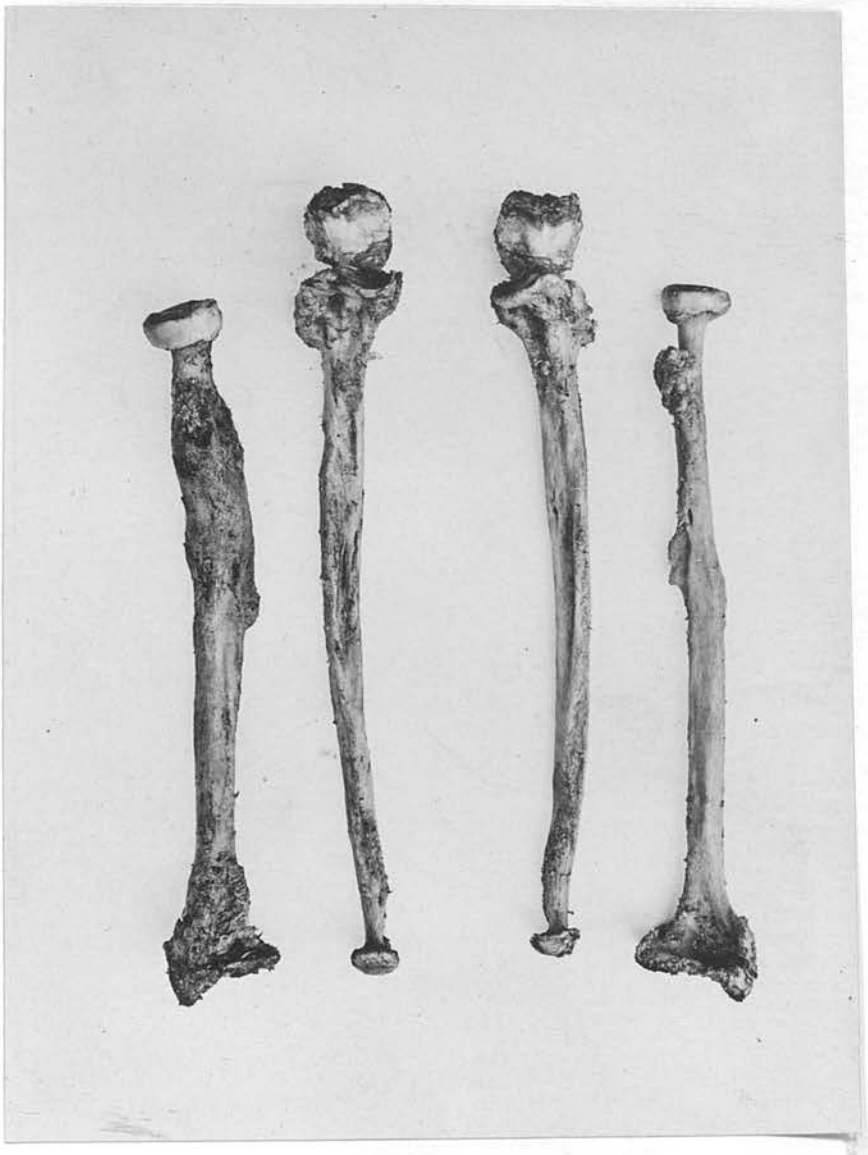


PLATE CXL.

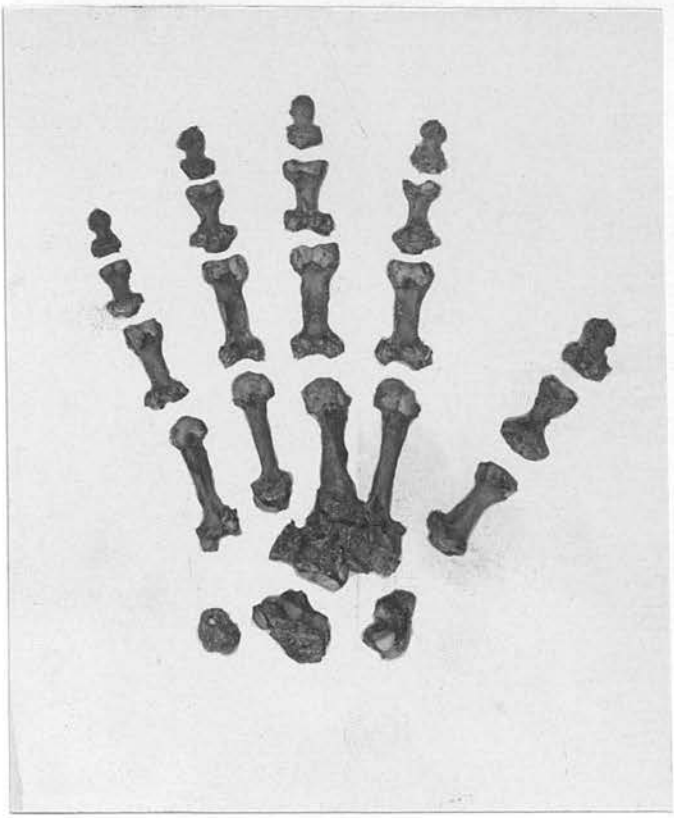
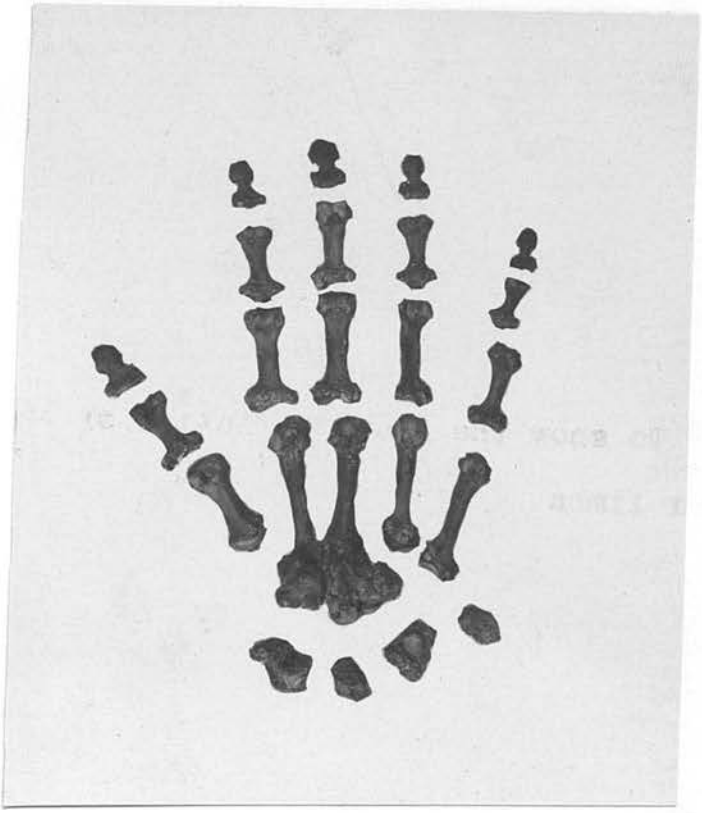


PLATE CXLI.



PLATES CXXXVII.-- CXLI.

To show the characteristics of the bones of the upper limbs.

The Measurements, (continued).

	Right	Left
Fibula:--		
Total Length	337	327

Pelvis:--

Breadth	316
Height	218
Breadth length Index	68·9
Breadth between anterior-superior spines	270
Breadth between posterior-superior spines	125
Breadth between Ischial tuberosities	195
Breadth between Ischial spines	140
Diameters of Condyloid:--	
Vertical	47
Transverse	51
Diameters of Obturator Foramen:--	
Vertical	32
Transverse	52

True Pelvis:--

Transverse width between ilio pectineal lines	166
Antero-posterior diameter	90
Brim Index	54·2
Oblique diameter R. sacro-iliac	148
L. do. do.	150
Inferior sagittal diameter	127
Coccygeo Pubic diameter	114

Intertuberal/

PLATE CXLII.

PLATE CXLIII.

PLATE CXLIV.

PLATE CXLV.

PLATE CXLVI.

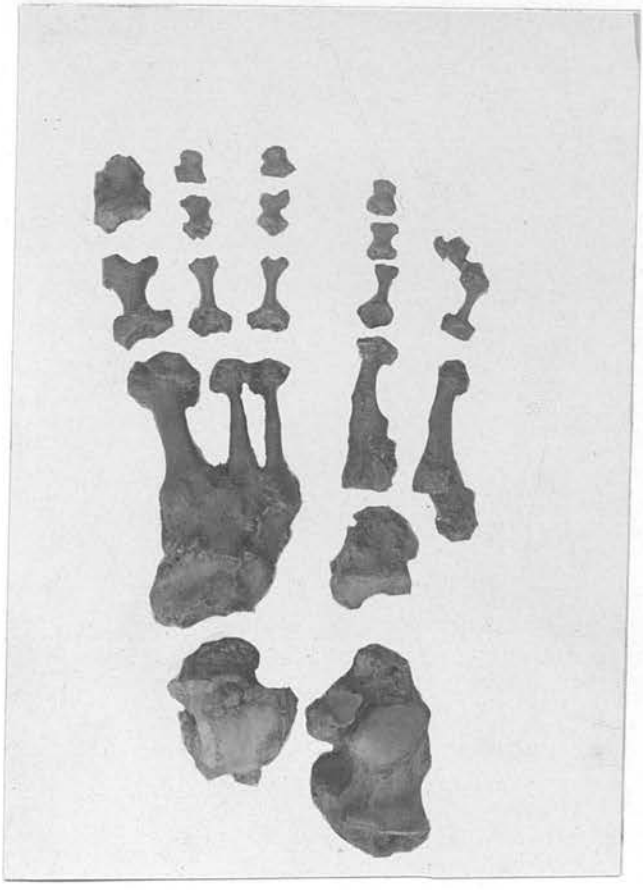
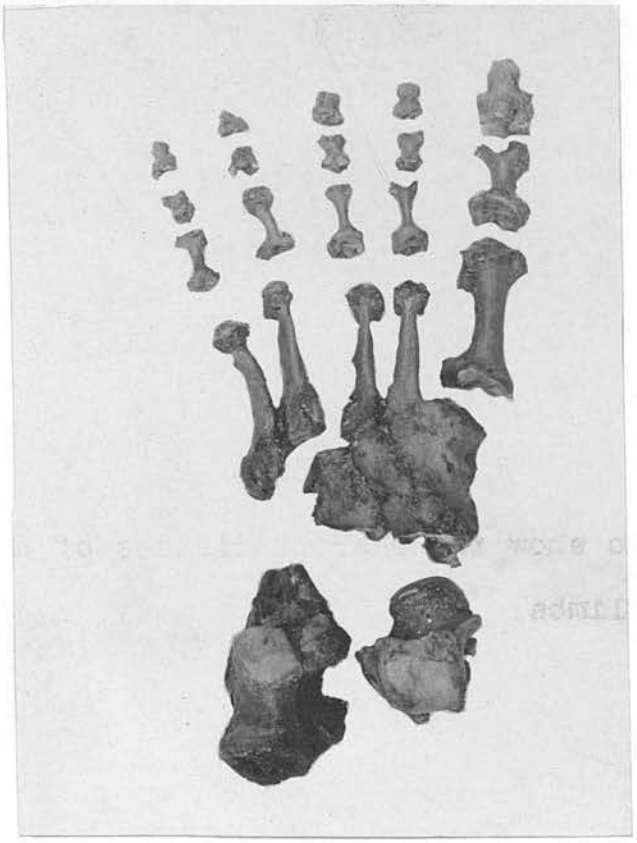


PLATE CXLVII.



PLATES CXLII. — CXLVII.

To show the characteristics of the bones of the lower limbs.

The Measurements, in millimètres, of the bones (continued)

Intertuberal diameter	141
Depth of pubic symphysis	51
Depth of pelvic cavity	91

Of the points brought out by these measurements the most important are:--

1. The extraordinary breadth of the pelvis as shown by the pelvic index 68·9, the average for the white races being 73.

The same feature is well brought out by the brim index 54·2: in this it is, however, exaggerated as a result of the subsidence of the lumbar vertebrae consequent upon the yielding of the sacrum which has given to the pelvic inlet a shape not unlike the heart on a playing card.

2. The femora are markedly platymeric, index (66.6), the right has a third trochanter; the condyles are rotated backwards. The tibiae are markedly platycnemic (index 66·6) and the heads are retroverted. The association of these conditions with an inability fully to extend the thigh is most interesting. Manouvrier has associated them with "la marche en flexion" and the skeleton under consideration fully supports his view,/

view, for it is necessary for an individual who cannot extend his thigh to walk with the knee flexed, otherwise balance could not be maintained. The additional association of the condition with marked eurysplasia is also of interest. Further consideration of the point is, at the present time, unnecessary.

Deductions made from an Examination of the Skeleton

The skeleton is essentially that of an individual who has been the subject of a precocious senility. General bone absorption has been progressing, but at points of strain and pressure bone hypertrophy has occurred. Preceding the development of the precocious senility there have, however, been changes characteristic of acromegaly.

The precocious senility I regard as due to the existence of a generalised protoplasmic food shortage consequent primarily upon the development of an undue body bulk, secondarily, upon the establishment of a condition of venous congestion and venous admixture of the arterial blood, which, in turn, were secondary to a partial or complete functional obliteration of the abdominal venous cistern.

In/

In the face, the growth changes affected especially those parts which are phylogenetically and ontogenetically the most youthful, thus in the parts derived from the nasal fold of the embryo the tip of the process, the alveolar margin of the maxillae was most increased; in the parts derived from the mandibular process the chin and body were most increased. With this I associate the great size of the infundibulum ethmoidals due to the growth of the structures formed in the tip of the maxillary process.

With these growth changes in the face it is necessary to associate the enormous increase of pelvic width to which the title gigantic may, without exaggeration be applied. Now, increase of pelvic width is due to endochondral ossification occurring at the margins of the cartilages of the sacro-iliac joint and of the pubic symphysis.

In a general review of acromegaly it would be necessary to add to these the fact that in cases in which the onset immediately precedes maturity there is ossification in the cartilages of the ontogenetically youthful hands which leads to the evolution of the hand type called by Marie the "type en long."

It, therefore, appears that the stimulus to growth/

PLATE CXLVIII.

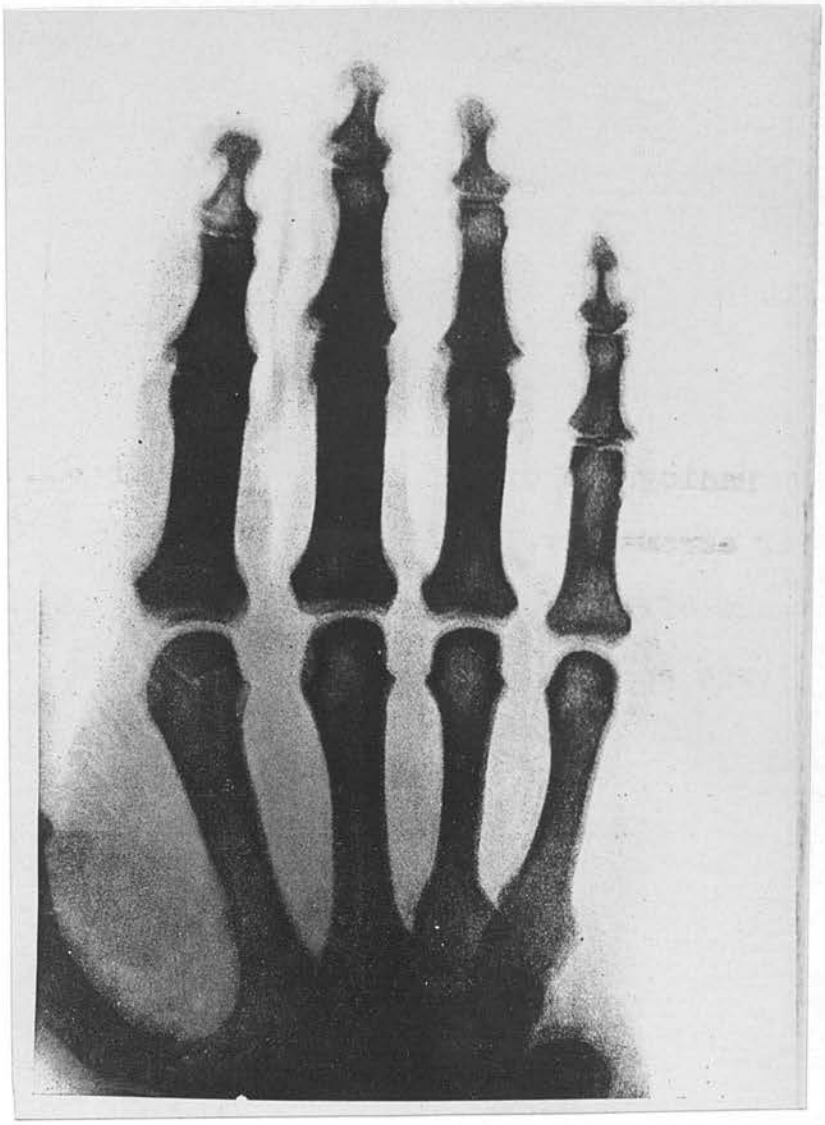


PLATE CXLVIII.

Radiograph of the hand of an individual, a victim of acromegaly, aged twenty-seven, to show the persistence of the epiphyseal plates in the evolution of the "type en long."

—After Murray.

growth in acromegaly affects primarily whatever cartilages may persist and secondarily the periosteum, but especially that of the phylogenetically and ontogenetically most youthful areas of the body.

It has already been shown that in the giantism of nutritive overloading the stimulus to growth affects primarily whatever cartilages may persist and secondarily the periosteum, but especially that of the phylogenetically and ontogenetically most youthful areas of the body.

It, therefore, is evident that Acromegaly and the Giantism of Nutritive Overloading are one and that Acromegaly is, as was suggested, the result of the onset of nutritive overloading at the time of the establishment, or immediately after the establishment, of full maturity.

I am now in a position to state in detail the central hypothesis of this thesis.

SECTION III. STATEMENT OF THE HYPOTHETICAL RELATIONS OF ACROMEGALY AND GIANTISM.

A condition of uncontrolled and excessive protoplasmic food supply established in childhood or adolescence causes hypermacroplasia and, later, as the absorptive/

absorptive power of the somatic cells diminishes and the concentration of the nutritive material in the body fluids falls, hypereuryplasia; whereas, uncontrolled and excessive protoplasmic food supply established after maturity causes hypereuryplasia.

In both cases the hypereuryplasia especially affects those parts of the body which in virtue of their phylogenetic or ontogenetic youth possess unusual absorptive power.

Further, as the amount of growth is normally determined by the interplay of two forces, cell absorptive power and food supply, and as the latter is dependent upon two factors, concentration of nutrition in the body fluids and amount of blood supply which, in turn, is dependent upon the stimulus of active function, the growth changes will affect, in amount varying directly as their absorptive power those tissues which normally receive least functional increase of blood supply. Thus cartilage, bone, fibrous tissue, fat and skin will increase most; nerve, glandular substance and muscle least, unless these are subjected to unusual functional stimulus when they too will grow to excess.

The reason for this is, I think, not obscure. Local/

Local increase of blood supply is normally provoked by local blood shortage. If, therefore, as the result of increased nutritive concentration there be no local blood shortages, there will be no local increments of blood supply. Actively functioning tissues, therefore, may have delivered to them little, if any, more nutritive material than normally they are accustomed to receive.

In this way I seek to explain the growth changes of Acromegaly and Giantism.

In the next chapter I discuss the definitive classification of the giantisms.

CHAPTER XXII.

DEFINITIVE CLASSIFICATION OF THE GIANTISMS.

SECTION I.

There are two distinct classes of giants, the physiological; and the pathological. Physiological giantism has been already discussed with sufficient fulness. Pathological giantism has been seen to be the result of an excessive supply of nutriment to the tissues. This may be the result of reduced nutritive requirements, as in eunuchs and eunuchoids, or, of increased nutritive supply, as in failure of the mechanism of the exogenous metabolism.

I propose first to deal with some further points in connection with the giantism of reduced nutritive requirement.

SECTION/

SECTION II. THE GIANTISM OF REDUCED NUTRITIVE REQUIREMENT.

There is an essential difference between this form of pathological giantism and the other. Here, there is no loss of what I have called the safety margin of nutritive supply, because the controlling mechanism is intact. The period of decline will, therefore, not be associated with the acuter forms of food shortage. In consequence, the clinical symptoms will vary in the sexes.

In normal men the reproductive drain continues until extreme old age, therefore, we may say that in them the safety margin is more than sufficient to meet the requirements of their body cells. In the eunuchs and the eunuchoids, therefore, although the safety margin may be small relatively to their increased mass, there is every reason to suppose that it will be sufficient to prevent absolute food shortage.

In normal women, however, sexual drain ceases at the climacteric and thereafter every woman is in effect a eunuchoid. To the action of the nutritive material set free for the use of the body cells I attribute the somewhat acromegaloid changes frequently seen in the early menopause. These have so struck some of the/

the continental writers, more especially the Italian, that the menopause has been described as a physiological acromegaly. This use of the term, although possibly literally accurate, severely strains its accepted connotation and is, I think, undesirable.

Briefly, I prefer to say that if the sexual drain on nutritive supply be artificially or naturally removed before the epiphyses are closed, the resulting hyperanabolism causes gigantoid changes; if after the epiphyses are closed the resulting hyperanabolism causes acromegaloid changes. But, that owing to the action of the nutritive controlling mechanism the starvation decline is slow and indistinguishable from old age; in women, indeed, it is old age.

This type of phenomenon I propose to refer to as:-- EUNUCHOID GIGANTISM.

SECTION III. THE GIANTISM OF FAILURE OF NUTRITIVE CONTROL.

To recognise a form of giantism as dependent upon failure of internal nutritive control is to establish a convenient portmanteau class which probably contains a large number of cases of essentially different pathogeny. They will, however, have two points in/

in common, first, there will always be protoplasmic nutritive overloading with its age dependencies hypermacroplasia and hypereuryplasia; second, there will be complete loss of the safety margin in nutrition and its absolutely inseparable dependency, relatively rapid anabolic decline, or, if the term seem preferable, its precocious senility.

From the connotation of Marie's word, acromegaly, it seems to me proper to retain it. I do so, however, unwillingly, because it is clumsy and ill-constructed. I should prefer to make use of Professor Cunningham's suggested term "megalacria," but the word acromegaly has passed far from its original meaning and now, in common use, undoubtedly connotes peculiar growth changes of the face, the hands, the feet, spinal curvatures and precocious senility. I think, however, that the term acromegaly alone should be given up as it fails to connote the results of early failure of nutritive control. I therefore propose to refer to the phenomena consequent upon failure of nutritive control as:—

ACROMEGALIC-GIGANTISM.

I use the Greek form gigant in preference to giant because it seems to me that the popular connotation of that word is more nearly akin to "superman" than/

than to "patient suffering from a definitely pathological condition."

SECTION IV. DEFINITIVE CLASSIFICATION OF GIANTS.

I propose, therefore, to recognise three classes of wholly or partially gigantic persons.

1. Physiological Giants, healthy men and women of stature and bulk greater than normal. With these I associate the cases of partial physiological giantism.

2. Eunuchoid Gigants, sexually imperfect individuals, in whom there is no failure of nutritive control, but in whom gigantoid or acromegaloid growth changes occur because of the abnormal supply of food stuffs to the somatic cells consequent upon the non-existence of the reproductive drain.

3. Acromegalic Gigants. A portmanteau class, admission to which is qualified for by the possession of deficient nutritive control with its associated hypermacroplasia and hypereuryplasia and its inevitable precocious senility.

Of Physiological Giantism I have nothing more to say. To Eunuchoid Gigantism it will be necessary briefly/

briefly to refer later. The next part of this thesis is devoted to a detailed consideration of some of the problems of Acromegalic-Gigantism.

End of Part III.

PART IV.

ACROMEGALIC - GIGANTISM.

CHAPTER XXIII.

SOME PROBLEMS OF ACROMEGALIC GIGANTISM.

SECTION I. ETIOLOGY AND PATHOGENY.

Acromegalic Gigantism sporadically affects individuals of all races and in all countries, and is not a condition of modern evolution.

Whatever the underlying causes may be, they are independent of sexual peculiarities. In 210 cases 104 were men, 106 women.(1)

Age governs the growth symptoms but does not influence the underlying causes.

The influence of heredity is apparently of no moment.

Emotional disturbances are sometimes associated by the patients with the commencement of their troubles.

Syphilis/

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(1). Sternberg.

Syphilis, chronic alcoholism and lead poisoning have no necessary connection with the condition.

Infectious diseases, especially scarlet and typhoid fevers, frequently precede the onset of the symptoms; their influence in determining the onset of the condition is unknown.

Injury is frequently reported as immediately preceding the onset of the symptoms; its influence also is unknown.

In attempting to assess the relationship of such conditions to an insidious growth process like acromegalic-gigantism it is well to appreciate the fact that any one of them may lead to an unusually critical examination of the body with the result that unnoticed but long existent pathological conditions are brought to light. It is known, however, that pre-existing morbid processes may be intensified by the mental and physical strains of profound emotion, severe infectious disease or gross bodily injury.

In the absence of knowledge, many wild guesses as to the nature of the condition have been made. None of them is satisfactory. The more important of these are:--

1. The "Theory" of Nervous Origin:

According/

According to this idea the disease is the result of changes in the nervous system. This may mean anything: it explains nothing.

2. The "Theory" of Atavistic Growth:

Freund and Dr. Harry Campbell have stated that acromegaly is no disease but a reversion to the type of the anthropoid ape. Superficially examined, an acromegalic skeleton is somewhat anthropoid; critical analysis of the growth changes has shown that far from being reversive they are progressive.

3. The "Theory" of Sexual Failure:--

Freund has suggested that the disease is directly the result of sexual failure. From what has been said with regard to the eunuchoids it is obvious that this "theory" is insufficient to explain the facts.

4. The "Theory" of Persistent Activity of the Thymus:

Fritsche and Klebs advanced the following "theory". In cases of giantism the thymus is hyperactive; in it angioblasts are formed to excess, are carried away by the blood stream, are deposited in distant capillaries and there develop to form new vessels through which an increased amount of blood is delivered to the body cells. Hypertrophy results.

The/

The "theory" is attractive. The idea of the tissues receiving more than their normal supply of blood is supported by many facts. There are, however, two fatal objections to this idea; the first that in the majority of cases the thymus is not hyperactive; the second, that there is no evidence to show that the thymus does send off showers of vaso-formative cells.

5. The "Theory" of Pituitary Perversion:

This theory was introduced by Marie and Souza Leite. Baldly it is, that enlargement of the pituitary causes acromegaly or that the normal growth of bone is dependent upon the normal functioning of the pituitary. Since first advanced it has frequently been enlarged and modified, but in its existing form it means nothing and explains nothing. Its attractiveness is spurious, resting on some supposed analogy to the relationship of thyroid failure and myxoedema.

SECTION II. HYPOTHESIS OF THE CAUSATION OF ACROMEGALIC-GIGANTISM.

I base my hypothesis of the causation of Acromegalic-Gigantism upon a fact which I believe to be not open to serious challenge. From a consideration of/

of the sharp limitation of body mass and from the long continuance of human maturity, it is inevitable to conclude that the amount of nutritive material made available for the use of the body cells is in early life only a small proportion of the total potential cell food absorbed by the intestine. Were this not so, growth after grafting as in John Hunter's famous experiment would be unexplainable, and further it would be necessary for the intestinal absorptive power to increase with age that the diminished anabolic power of aged cells might be counterbalanced by an increased concentration of nutritive material in the body fluids. From this hypothetical conclusion there is no escape, in this way and in no other can the facts of the physiology of growth and of human maturity be explained.

Turning from hypothesis to experiment the work of Folin (1) and of Noël Paton (2) yields ample evidence that only a small proportion of the total nitrogen absorbed by the intestine is made use of in the essential metabolism of the body. From the experimental results obtained by these observers it is evident that in the katabolism of muscle protoplasm, the nitrogen containing part must be capable of repeatedly combining with the/

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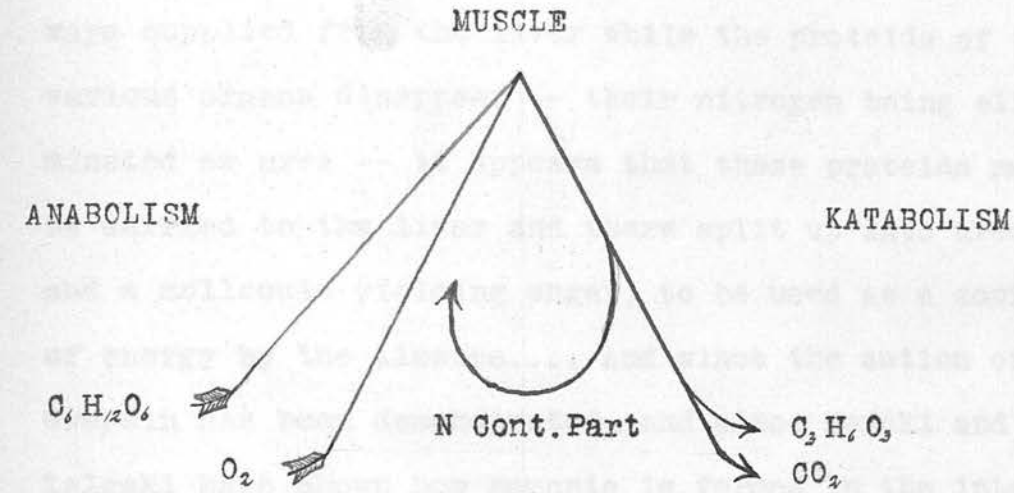
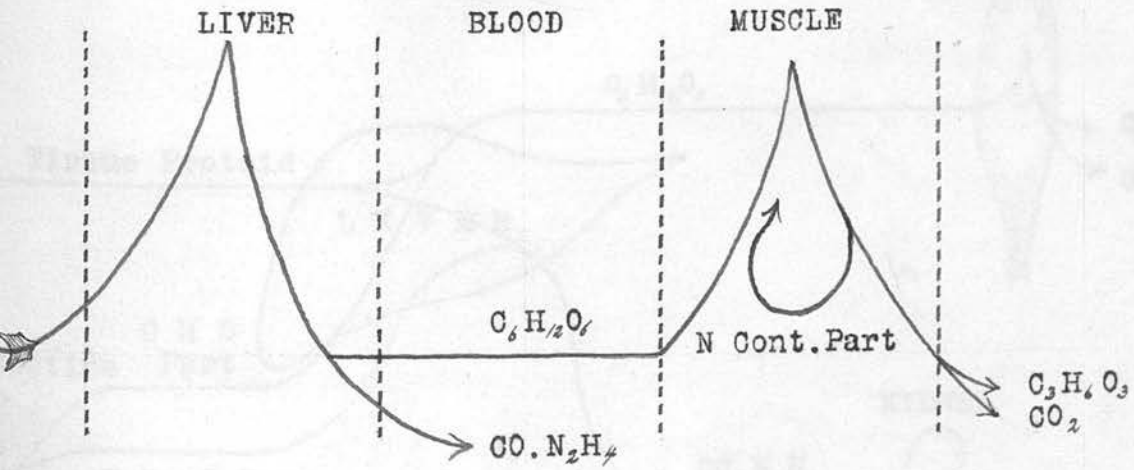
(1). Folin, Amer.Journ. of Physiol. XIII.p.117, 1905.
(2). Noël Paton, Journ. of Physiol. XXIII. p.1, 1905.

The oxygen and the carbohydrates supplied to it. Noël Paton represents this by the following diagram:--



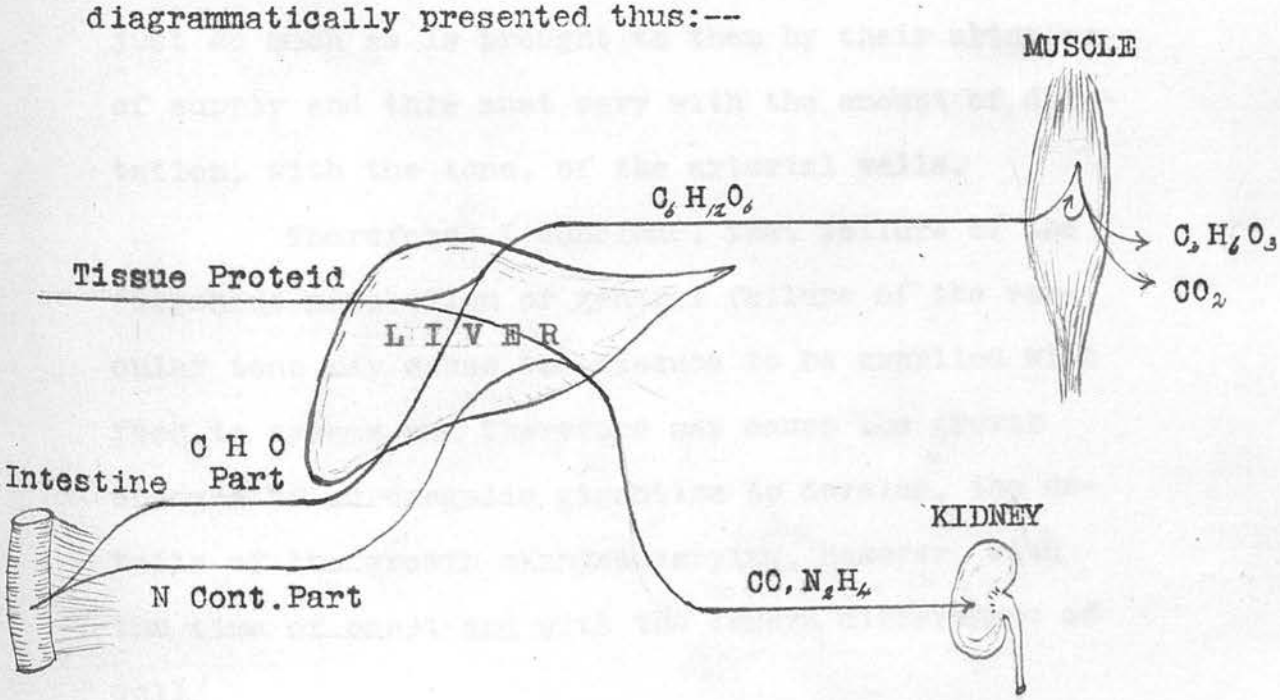
"Hence", he says, "no very large supply of proteid is necessary for ordinary muscle metabolism, and, when any excess of proteid is taken the nitrogen is split off and excreted as urea while the rest of the molecule is changed to sugar or glycogen --



Further,/

Further, from the fact that, during fasting, the sugar of the blood does not diminish in amount, but is always supplied from the liver while the proteids of the various organs disappear -- their nitrogen being eliminated as urea -- it appears that these proteids must be carried to the liver and there split up into urea and a mollecule yielding sugar, to be used as a source of energy by the tissues.... And since the action of erepsin has been demonstrated, and since Nencki and Zaleski have shown how ammonia is formed in the intestinal wall and carried thence to the liver as ammonia compounds, we have a clearer picture of the fate of the food proteids".

This conception of proteid metabolism can be diagrammatically presented thus:--



This/

This view does not exclude the absorption of a quantity of proteid sufficient for the needs of cell replacement and cell repair. That it is in the main correct I do not doubt and that in some such way the nitrogen supply is forced to maintain a safety margin, a reserve against the coming scarcity, is certain. Were it not so, processes of decline would immediately ensue upon the cessation of growth and the long continued maturity of men would be biologically unthinkable.

But in addition to this systemic control of food supply there must be a secondary, local or vascular control.

It is evident that the amount of nutritive material made available for the use of the tissues is just so much as is brought to them by their arteries of supply and this must vary with the amount of dilatation, with the tone, of the arterial walls.

Therefore, I conclude, that failure of the exogenous metabolism or general failure of the vascular tone may cause the tissues to be supplied with food to excess and therefore may cause the growth changes of acromegalic gigantism to develop, the details of the growth changes varying, however, with the time of onset and with the inborn differences of

cell absorptive power.

Add to this the development of precocious senility necessary in all cases of uncontrolled cell proliferation and the essential picture of acromegalic-gigantism receives a full and adequate explanation.

From this it is evident that in all cases there will be three classes of symptoms; the primary, which indicate the causal affection of the liver, of the ductless glands, of the nervous system or of whatever it may be; the secondary, which are abnormal growth and its attendant, precocious senility; the tertiary, which are accidental or mechanical in their origin.

In the next section I consider in detail some of those cases in which the protoplasmic nutritive overloading was dependent upon vascular conditions which in turn were secondary to lesions affecting the nervous system.

SECTION III. CASES OF ACROMEGALIC-GIGANTISM DEPENDENT UPON GENERAL FAILURE OF THE VASCULAR TONE.

A case of Acromegaly in a Negress. (1)

Mary Mack, aged 60, coloured, was admitted to the/

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(1). Henry J.Berkely, M.D., Bulletin John Hopkin's Hospital 2, 1891, pp.134-136.

the City Insane Asylum in May 1888 for delusions of persecution. Her family history was negative: her personal history, uneventful. The patient was married and had borne six living children, there was one miscarriage.

Condition, March 1891.

The patient came under observation in October 1890, at which time she attracted attention, apart from her mental symptoms, by the large size of her hands and feet, the peculiar thick and drooping appearance of the lower lip and the humped back attitude with which she carried herself. Between October and March there was no change in her general condition, except, that trophic lesions of the arms and hands developed.

She was a rather undersized negress, 1445mm in height, rather heavily built for her stature, though the panniculus on the trunk and extremities was but slightly developed.

Her appetite was large, but her thirst was not increased. Her urine was high coloured and deposited a cloud of phosphates but contained neither albumen nor sugar. No abnormalities of the respiratory or circulatory systems were discovered.

Her eyesight was reasonably acute; her colour sense was well-preserved.

Her/

Her pupils reacted to light and accommodated perfectly. No ophthalmoscopic examination was made.

Hearing was much dulled.

Taste was perfect.

Tactile sensation was somewhat diminished in acuteness; heat, cold and pain were readily distinguished.

Cutaneous secretion was increased and foul smelling.

Glandular secretions were normal.

The muscular sense was well preserved: there was no loss of equilibrium on standing with the eyes closed.

The deep reflexes were somewhat exaggerated, the cutaneous, normal.

The skin over the face, trunk and legs was comparatively well nourished; on the arms and hands, more especially on the right, there were numerous old scars, the cicatrices of which were attached to the deeper tissues; between the first joints of the fingers were large blebs, which healed slowly, and upon the tip of the little finger there was a subcutaneous ecchymosis which had been present for a number of weeks. At the right elbow was a large ulcer, the result/

result of a bruise, which had assumed a perforating character and penetrated down to the ligaments of the joint. The hair, all over the body, was thick and coarse; on the legs it had a distinctly flattened appearance.

Mentally, she was suspicious, at times very refractory and always very talkative. Her delusions were of persecution as evidence of which she showed the bruises which she inflicted upon herself by striking her extremities against the bed or the door of her cell when she was restless and excited at night.

CEPHALIC EXTREMITY:--

The skull was dolichocephalic, rather small but regular, the bones were not increased in size. The ears were well formed and not thickened. The orbital arches were prominent for a negro; the eyebrows were peculiarly curved and there were large quantities of pigment deposited about the eyelids. The nose was uniformly thickened, broad but not prominent, the increase in size being due equally to the enlargement of the osseous and of the soft tissues. The malar bones were prominent and the tissue overlying them was thickened. Both lips were thick but the lower projected considerably outward beyond the upper, giving/

giving the face a prognathous aspect. The upper teeth were in part lost; the lower, were well preserved and slightly separated from one another. The tongue was not markedly increased in length but seemed thickened. The voice was high pitched and disagreeable; articulation did not seem to be impeded.

The mandible was slightly increased in vertical measurement. The face, while much more oval than the average negro's did not present that extreme elongation apparent in the majority of described cases. Races characteristics doubtless here played an important part.

The neck was normal in size. There was a marked dilatation of the veins, but this was even more apparent about the forehead and over the upper part of the thorax and arms where the vessels were markedly varicose. The thyroid gland could not with certainty be felt and, if altered at all, was smaller than usual. The larynx was prominent. When the patient sat the chin rested on the breast.

TRUNK:--

The right shoulder was held much higher than the left: the scapulae were not notably altered: the clavicles seemed broadened at their sternal extremities:/

extremities: the supra-clavicular fossae were very deep: the manubrium sterni was prominent and apparently enlarged, the gladiolus less so; the ensiform cartilage was very prominent and hypertrophied.

There was a well marked retro-sternal dulness over the whole of the manubrial region: the heart dulness was not unusually great, the percussion note over the lungs was clear.

Posteriorly, a pronounced scoliosis of the vertebral column was very striking: there was no pronounced kyphosis. The ribs were thickened: the lower part of the thorax projected outwards.

SUPERIOR EXTREMITIES:—

The arms and forearms did not show any disproportion to the general development; the hands were large, out of proportion to the size of the arms. There was a difference in the muscular development which was probably due to an old standing dislocation of the right shoulder. Scars, blebs and ulcers which affected the arms have been already described: these were more marked on the left than on the right side.

There seemed to be some increase in the soft parts, but not in the bones, of the wrists.

The/

The hands, relatively to the size of the forearms, were enormous; they were broad rather than long; the fingers were thick, the nails broad and short, but not ridged; the skin over the whole hand was wrinkled and creased. The thenar and hypothenar eminences were large but flabby: the abductor of the right thumb was the larger. The phalangeal joints were considerably thickened.

INFERIOR EXTREMITIES:--

No abnormality of the thighs was noticed. The patellae were apparently increased in all their dimensions; otherwise, the knee joints were normal.

The bones of the leg were normal: the calf muscles, more especially the left, were firm and prominent; the Achilles tendons were broad and thick.

The feet were large in proportion to the legs and thighs; the bones of the tarsus and the first phalangeal joints were especially hypertrophied. The soft parts of the heel and outer margin of the foot were thick; the natural plantar lines were deeply marked. The nails were broad, short and striated.

----------oOo----------

Obviously in this case there was a syringomyelic element/

element and it is not without interest to place beside it a brief synopsis of a recent case in which, though the evolution of the disease was very slow, the completed clinical picture was typical of acromegaly.(1) In it death was due to tubercular pericarditis. Post-mortem it was discovered that there was no enlargement of the pituitary, although anatomical changes characteristic of acromegaly were found. The bones of the cranium were, however, very thin and the foramina at the base of the skull were dilated. There was a very high degree of bathrycephaly.

Microscopically the changes in the pituitary were limited to a slight sclerosis which might have been due to the age of the individual (fifty.)

Examination of the spinal cord revealed an unexpected syringomyelia which had given rise to no clinical symptoms. The site of the anatomical changes which occupied the region of the central canal and the base of the anterior horns, was sufficient explanation of this. The posterior horns were of almost normal structure. The lesions were most extensive in the third and fourth dorsal segments, where the anterior horns were almost completely destroyed.

The/

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(1) Petren: Virchow's Archiv. Bd 190, 1907.

PLATE CXLIX.

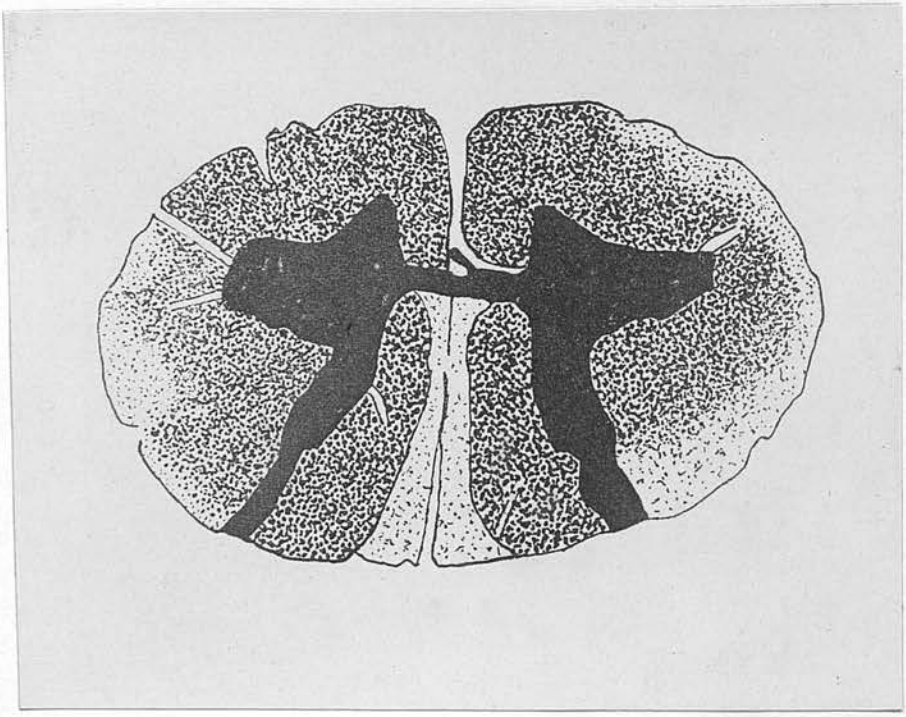


PLATE CL.

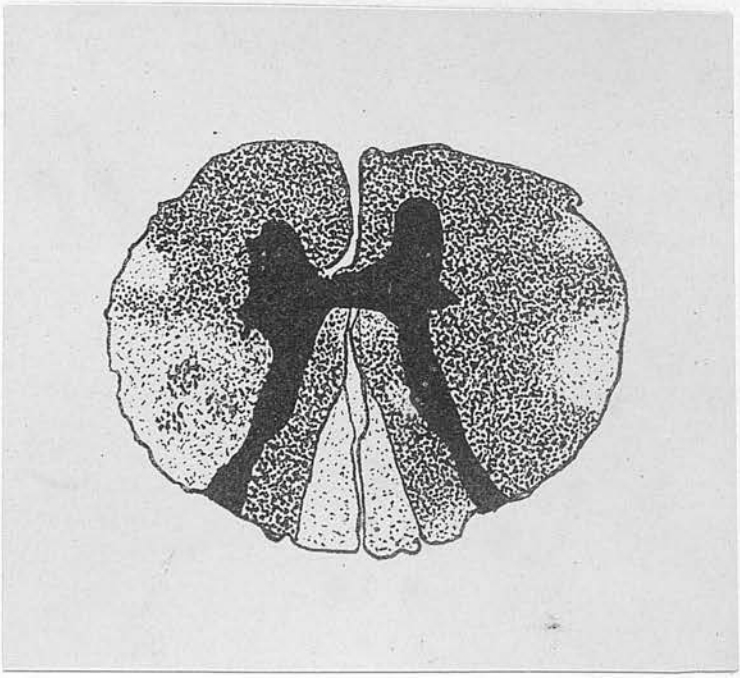
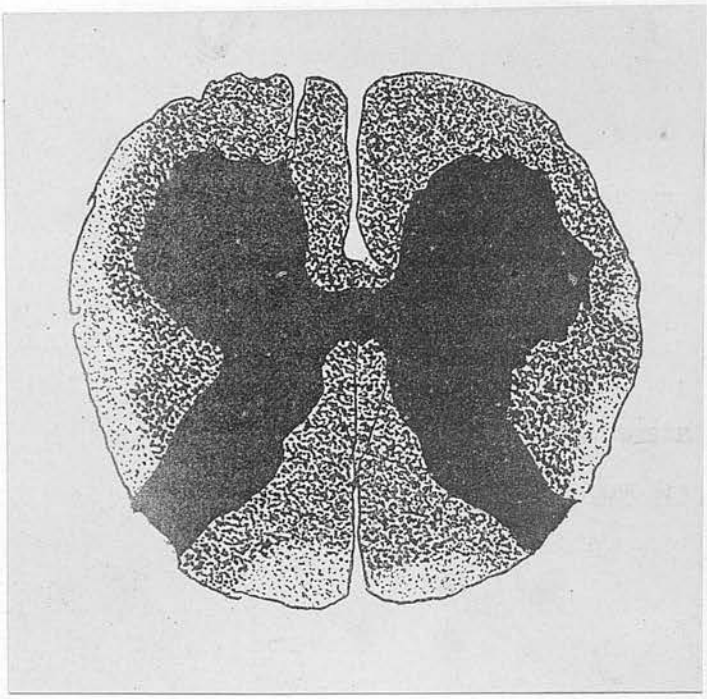


PLATE CLI.



PLATES CXLIX.--CLI.

To show the lesions in the spinal cord commonly met with in acromegaly.

---- After A. Souques.

The syringomyelia had not the usual microscopical appearances, true gliomatous tissue not being found. The affected parts of the cord contained epithelial cells, similar to those in the central canal, and fibrous tissue connected the markedly sclerosed blood-vessels. The central canal of the cord throughout the greater part of its length was enlarged, usually in the form of a narrow transverse slit. In connection with it were found bands of epithelial cells which formed irregular masses without any visible connective tissue.

These changes in the cord are certainly different from those found in the ordinary type of case.

Dallemagne, Mitchell, Huchard and Launois have also published cases of Acromegaly in which the pituitary was macroscopically and microscopically normal.

In this connection, too, the case of the child with congenital unilateral hypertrophy described by Finlayson (1) is worthy of brief reference. In it the hypertrophied side was distinctly warmer than the unhypertrophied. This obviously must have been dependent upon a unilateral hyperaemia which in turn must have/

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(1) Finlayson, Glasgow Medical Journal, Vol. XXII, p.327,1884.

have depended upon dilatation and loss of tone, of the vessel walls, and that hypertrophies dependent upon hyperaemia do occur was shown by Stirling[1] who, as we have seen, when experimenting on young rabbits and puppies found that after excision of a portion of the cervical sympathetic system on one side there was hyperaemia and hypertrophy of the corresponding ear.

Other cases in which the growth changes were typically acromegalic, but in which there was an undoubted failure of nerve control have been published by Holschewnikoff[2]; by Bier (as acromegaly,) by Fischer[3] (same case, as syringomyelia;) and by Peterson[4].

Sternberg in his work on Acromegaly has attempted to exclude all such cases. Undoubtedly in origin they are different from those in which the pituitary is enlarged, but, so far as growth changes are concerned, if a complete loss of vascular tone be established after obliteration of the epiphyseal plates, the areas most affected must be the phylogenetically and ontogenetically more youthful, and, so far as the precocious/

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(1) Stirling, Journal of Anatomy and Phys. Vol. X. p.511, 1876.
(2) Holschewnikoff, Virchow's Archiv, CXIX.S.10, 1890.
(3) Fischer: Beitrag der Casuistik der Akromegalic Syringomyelic, Kiel, 1891.
(4). Peterson: The Medical Record, Vol.XLIV.p.391.1893.

precocious senility is concerned, the spinal curvatures and so-called rheumatoid changes are developed just as in those cases which are hypothetically dependent upon failure of the exogenous metabolism. There, therefore, seems to be no greater impropriety in describing all such growth manifestations under the generic title "acromegalic gigantism" than there is in using the word jaundice to describe the yellow staining of the skin dependent upon the biliary retention of catarrhal or malignant obstruction, or of gross mechanical blockage of the bile duct.

In including such cases I do not desire to differ from Sternberg as to their essential dissimilarity to the larger group which are marked by enlargement of the pituitary, but I see no advantage in calling a symptom by one name at one time and by another, at another.

It is hypothetically necessary that there should exist a large number of cases in series with these in which hypertrophy is limited to the area of distribution of an artery, great or small. Records of such cases exist in plenty, but probably the most interesting from the present stand-point is that described/

described by Dr. Douglas Webster (1) under the title "A Case of Unilateral Cerebral Hyperplasia with co-existent "Acromegaly" of the Feet and a Slight Degree of Unilateral Gigantism." In this case the hyperplasia affected, especially, those parts of the brain which are supplied by the left internal carotid artery and to a less degree the left half of the body. He concludes that the cause of this may have been a vaso-motor derangement affecting slightly all the arteries of the left side and to a greater degree the left internal carotid and its branches. The most interesting point in this interesting case is the growth of the brain which microscopically was found to be associated with a high degree of vascularity.

In this case, as in others of vaso-motor origin, there was no enlargement of the pituitary and it is round enlargement of the pituitary that the hottest discussions upon the etiology and pathogeny of acromegalic-gigantism have raged. I devote the next section to a discussion of this interesting topic.

SECTION IV. THE SIGNIFICANCE OF ENLARGEMENT OF THE PITUITARY IN ACROMEGALIC-GIGANTISM.

Tumours/

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(1) Webster:--The Journal of Pathology and Bacteriology, January, 1908.

Tumours of the pituitary are never present in cases of acromegalic-gigantism which depend for their pathogenesis upon loss of vascular control whereas they are apparently invariably present in cases of acromegaly where there is no loss of vascular control. The easy assumption from this would be that the growth changes are dependent upon some perversion of the internal secretion of the pituitary. There is no evidence to support this view. As the result of a somewhat extended search through the literature I am of opinion that tumours of the pituitary are just as frequently not associated with symptoms of acromegalic-gigantism as with them.(1) This seems to me definitely to negative the vague idea that the growth changes are a syndrome of pituitary enlargement and to suggest that growth of the pituitary and growth of the body may both be symptoms, but not necessarily homologous symptoms of the underlying cause which I believe to be nutritive overloading.

Of the nature of the pituitary enlargement in cases/

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(1) References to some of the older papers are given by Sternberg in his work on Acromegaly and Cagnetto has published a useful paper dealing with this in the "Archivio per le Scienze Mediche." Vol.XXXI. No.1.p.80, 1907.

cases of acromegalic-gigantism little can be said; the tumour has been described as a "pulpy mass of embryonic tissue," "hypertrophy (adenoma?) of the gland," "sarcoma with embryonic cells" "furious glandular hypertrophy," "growth of the normal cells." "cystic degeneration of the nervous portion -- exaggerated development of the buccal portion," but such descriptions convey no very definite idea of what the condition of the gland was. I have, however, examined most carefully drawings and micro-photographs that have been published under such titles as sarcoma of the pituitary and adenoma of the pituitary and have failed to discover in what respect the microscopic structure portrayed differs from that normally found in elderly persons.

In view, however, of the extreme recency of much of the knowledge of the histology of the pituitary and of the extreme difficulty of interpreting its structure there is little wonder that many of the older records are unsatisfactory.

My idea is that the first stage of the pituitary enlargement is due to a true functional hypertrophy, and that later there are appearances which it is difficult or impossible to distinguish from adenoma and still later appearances suggestive of angio-sarcoma; while/

while sometimes at a very late stage the whole gland degenerates into a semi-fluid blood stained mass. This conjecture is founded partly upon hypothetical considerations, partly upon experimental and partly upon pathological evidence.

1. PATHOLOGICAL EVIDENCE

The pathological evidence I have drawn more particularly from papers published by Cagnetto[1] and by Tamburini.[2]

In one of Cagnetto's cases the anterior lobe of the pituitary showed all stages of transition from the normal to the apparently angio-sarcomatous condition, the posterior lobe remaining unaffected as appears invariably to be the case in acromegalic-gigantism.

Tamburini is of opinion that in virtue of their pituitary structures cases of acromegalic-gigantism may be arranged in the following way. First, those in which there is true hypertrophy of the gland; second/

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(1) Cagnetto, Virchow's Archiv. Beit. CLXXXVII.S.197, 1907, and loc. cit.
(2) Tamburini, Revue Neurologique, Novembre 1897.

second, those in which there is an adenomatous change, as in the case of Claus and Van der Stricht,(1) third, those in which there is "sarcoma" as in Dallemagne's(2) first case or cystic degeneration, as in his second and third cases.

2. PHYSIOLOGICAL EVIDENCE:--

The physiological evidence I have drawn from Gaetano Fichera.(3) His work has been directed towards establishing the effects of castration upon the pituitary and he most conclusively shows that after castration the pituitary hypertrophies and that it shows, microscopically, clear signs of great functional activity.

From this I conclude that in cases of reduced nutritive demand and, therefore, of increased nutritive concentration the hypophysis undergoes a true functional hypertrophy.

Also in these cases of reduced nutritive demand/

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(1) Claus and Van der Stricht: Ann. Soc. de Méd. de Gand, Vol. LXXII, p.71, 1893.
(2) Dallemagne: Archiv. de Méd. Exp. et d' Anat. Path. Vol. VII, p.589, 1895.
(3) Fichera, Article reprinted from Policlinico VII, C.1905.

demand the thymus remains large and the lymphatic tissue does not show its usual diminution with age.

This is of interest in connection with the well-known occasional persistence of the thymus and with the hyperplasia of the lymphatic tissue so often found in the bodies of acromegalic-gigants.(1)

3. HYPOTHETICAL CONSIDERATIONS:--

The hypothetical considerations are more widely based.

It is necessary to consider, first, the effects of excessive food supply upon the functional activity of the brain; and the structural changes which it induces throughout the whole central nervous system; second, the known physiological effects of intravascular injection of extract of the infundibular portion, or more probably of the necessarily coincident injection of extract of the intermediate portion of the pituitary, and, third, the known facts with regard to pituitary enlargement in cases of acromegalic-gigantism.

I. CEREBRAL EFFECTS OF NUTRITIVE OVERLOADING.

The effects of food supply to excess upon the functional activity of the brain are very marked; the somnolence/

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(1) See Fritsche und Klebs, op.cit. or Ballet and Laignel-Lavastine, N. Iconog.de la Salpêtrière, tome XVIII. p.176, 1905.

somnolence of surfeited animals and the keen mental activity which is within certain limits associated with hunger have already been referred to. With this must be considered the development of the practically functionless connective and supporting tissues which occurs in the central nervous system in cases of nutritive overloading.

From these facts I conclude that it is disadvantageous for an individual to have too great a supply of nutriment delivered to his brain. It therefore seems to me hypothetically reasonable to suppose that there is some mechanism in the body which in normal circumstances has the power of stimulating secretion should there be a tendency for the nutritive value of the body fluids to increase to excess and which, therefore, in cases of diminished nutritive demand upon the body fluids and in cases of increased nutritive concentration in the body fluids will show signs of increased activity of function.

The last desideratum is certainly true of the pituitary, and, further, it undergoes what is apparently a functional hypertrophy after removal of the thyroid, when it is known that the body has great difficulty in performing its metabolic functions and when, apparently,/

apparently, secretion is deficient.(1)

II. PHYSIOLOGICAL EVIDENCE.

The posterior lobe of the pituitary produces an extremely active stimulant to renal excretion. The anterior lobe of the pituitary has as yet had no definite function assigned to it by physiologists. Professor Schäfer and Dr.Herring have, however, conjectured that in it the material which is to furnish the active agent of secretion found in the infundibular portion passes through certain stages of its formation and that its production is merely completed in the neuro-ectodermic part, in which part alone the full activity of the secretion is acquired. In formulating this guess these observers were influenced by the similar anatomical association in the suprarenal body of a highly vascular epithelium, possessing no discovered function, with a neuro-ectodermic portion which yields a highly active substance. This is certainly the most reasonable of all the guesses that have been made with regard to the pituitary's function and probably it is right up to a certain point. The anterior lobe of the pituitary may have this function along with others as yet/

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(1). Cimoroni Sulla ipertrofia dell'ipofisi cerebrale megli animali stiroidati Archivio di Biologia normal et patol. Anno LXI., Fasc.1.II.,1907.

yet undreamed of. Were this proved to be so it would strongly support the guess which I have made with regard to the rôle of the pituitary in the animal economy. I imagine that whenever the body fluids of an individual become more nutritive than is good for the central nervous system the anterior lobe of the pituitary is stimulated to activity, and that by providing for the neuro-ectodermal part, the raw material of a hormone of renal secretion it attempts to save the brain from the excessive development of non-functioning elements and the consequent lowering of the psychical potentialities of the individual.

It is, I think, obvious from what was written in Part I. with regard to the growth of cartilage that so long as there are many active chondroblasts in the body there will be no necessity for this activity of the pituitary to be induced; for the cartilage cells in virtue of their great absorptive power will do much to reduce the nutritive concentration to a normal level.

III. SOME KNOWN FACTS WITH REGARD TO THE ENLARGEMENT OF THE PITUITARY IN CASES OF ACROMEGALIC GIGANTISM.

So far as I have been able to discover from the/

the records of the giants, symptoms of pituitary enlargement are never found until the close of active macroplasia. This, again, fits in with my conjecture.

Further, were the conjecture proved to be correct it would be hypothetically right to expect that in the cartilaginous fishes the pituitary would not possess excretory functions. I have been informed that the unpublished results of experiments with the pituitaries of elasmobranchs suggest that this is so. This also fits in with my guess as to the function of the pituitary. A word of warning is, however, necessary here. Nothing that I have written presupposes that the cartilaginous fishes should be able to grow to unlimited size. All that is implied is that in the event of failure of their exogenous metabolism, or in the event of a long continued surfeit their possession of cartilage cells in large numbers renders it unnecessary for them to possess any further mechanism destined to save their central nervous system from the effects of excessive nutritional supply. Normally their size is sharply defined and doubtless it is limited, as in other animals, by the balance struck between intestinal absorption and activity of exogenous metabolism on the one hand and total body bulk on the other. All that the hypothesis, were it established/

established, would demand is that they should not possess a special mechanism, an inner line of defence, as it were, to save their nervous system from the destructive effects of a too great food supply, because they already possess in their cartilaginous skeletons a sure weapon against any accidental excess of nutritive supply.

I therefore think that it is not unreasonable to conjecture that the excretory function of the pituitary has been developed by bony animals as a means of defence of their nervous tissue against the damaging effects of nutritional excess, and that the enlargement of the pituitary met with in cases of acromegalic gigantism dependent upon nutritive overloading is primarily a functional hypertrophy directed towards saving the nervous system. The other changes sometimes found I regard as purely secondary and degenerative.

This conjecture is merely a slight elaboration of Cagnetto's hypothesis that the growth changes and pituitary enlargement met with in cases of acromegaly are wholly independent results of an underlying metabolic disturbance.

There remains for discussion the mechanism of the establishment of the nutritive overloading which

I/

I believe undoubtedly to exist.

SECTION V. THE MECHANISM OF NUTRITIVE OVERLOADING.

Upon this subject I have little to say: it is my desire merely to raise certain questions and to leave them to be answered in the future.

1. Nutritive Overloading Consequent Upon Excessive Food Absorption.

Hypothetically, nutritive overloading might be dependent upon abnormal activity of intestinal absorptive power or upon an abnormal development of intestinal absorbing surface. The former is a purely conjectural condition; the latter is not infrequently met with, for example, it was present both in E.A.S. 79 and in E.A.S. 07.

2. Nutritive Overloading Consequent Upon Failure of the Exogenous Metabolism.

The liver is believed by Folin and Noël Paton to be the principal seat of the activities which determine the exogenous metabolism. Hypothetically, therefore, it might be the seat of changes determinant of metabolic failure. It is interesting to note that in E.A.S. 07 the liver was markedly diseased.

Hypothetically, for aught that is known, failure of any one or of any group of the ductless glands/

glands might be the cause of nutritive overloading. In Acromegalic-Gigantism all or any of the ductless glands may be diseased.

Freund has suggested that the prime lesion is to be looked for in the ovaries or testicles, but this view is apparently insufficient to explain the facts.

Lorand thinks that the thyroid is primarily affected and has most clearly distinguished between exophthalmic and myxoedematous types of the condition.

The suprarenals are frequently affected as in Ballet and Laignet Lavastine's case.

The parathyroids are sometimes hyperactive as in E.A.S. 07. This condition was noted by Erdheim in his case published in 1903.

The pineal has been found enlarged and the spleen gigantic.

The thymus and the lymphatic glands are frequently enlarged.

Amid such a welter of conflicting post-mortem discoveries judgment is difficult and certainty impossible, but I am inclined to think that the condition essential for the establishment of nutritive overloading is not simple and that nutritive overloading is itself but a symptom of still deeper lying glandular/

glandular failures and hyperactivities.

There are many cases on record in which the onset of the growth manifestations almost immediately succeeded an attack of typhoid fever, and I should in no way be surprised if ultimately it were shown that, in some persons, the liver subjected to the action of the toxins of the typhoid bacillus lost its power of satisfactorily carrying on the exogenous metabolism, but I should be surprised were this to be proved to be the only cause of the nutritive overloading which is the most important factor in the development of Acromegalic-Gigantism.

From my present stand-point and with my present knowledge this review of the problems of giant growth has reached the limits of its conceivable usefulness. In the next chapter I give in summary the views which I hold and the reasons which have led me to adopt them.

CHAPTER XXIV.

A SUMMARY, THE CONCLUSIONS AND THE END.

SECTION I. GENERAL SUMMARY.

Long ago, in the prehistoric days of physiology, John Hunter showed that the growth of a part of an organism was influenced by the amount of blood that it received. Thirty years ago Stirling, experimenting on young rabbits and puppies found that if the walls of the blood vessels were deprived of their nervous control they dilated and the blood flowed through them more rapidly and that as a result there was abnormal growth. From these experimental results and from the known effects of grafting I conclude that the stimulus to growth is food supply.

This law holds throughout the animal and vegetable kingdoms. In the vegetable kingdom growth must be in some measure limited by food shortage at the/

the point of growth or the triumphs of grafting would be unthinkable: in the animal kingdom, although locally the amount of growth is limited by food shortage, the amount of food made available for the tissues is limited by some mechanism of control, the mechanism of the exogenous metabolism which is situated primarily in the liver, but is probably governed by the secretions of the ductless glands. This mechanism occasionally breaks down and the tissues receive an altogether abnormal supply of food with the result that growth is not checked at its normal limits.

But in addition to being actively overloaded with food stuffs the body fluids may become passively congested with them, owing to a reduction in the amount required by the various tissues of the body. This takes place when the testicles are removed.

It is possible that in both these cases the essential element in the overloading which stimulates to growth is nitrogen, for there is reason to believe that cases exist in which the overloading is purely carbohydrate and that in them there is a condition of altogether abnormal fatness.

In some cases of Acromegalic-Gigantism the composition of the body fluids is normal but the vascular tone is abnormal, and in these, as in Stirling's rabbits/

rabbits with their cervical sympathetic nervous system destroyed, abnormal growth occurs as the result of local excess of food supply.

The histology of growth is interesting; more especially that of cartilage. In conditions of excessive nutritive supply the chondroblasts become rapidly surfeited to death, and the greater the amount of food in the body fluids, the greater is the tendency to surfeit and the more rapid is the proliferation of the cells.

Associated with this hyperanabolic growth of the skeleton are delay or suppression of sexual maturity, and a peculiarly incomplete mental development. These three symptoms together form a group indicative of an abnormally excessive supply of food to the cell protoplasm.

Such rapid proliferation of the epiphyseal cartilages leads to an abnormal development of body bulk. If now there be no reserve, if everything that the intestine can absorb be given to the tissues, the result is precocious senility: for the anabolic power of the somatic cells steadily declines with age, and this means that unless there be a safety margin of nutrition maintained in youth, starvation of the body must result in maturity.

As/

As starvation makes itself felt, the bones and cartilages become weakened; unusual strains are thrown on ligaments; local increases of blood supply and therefore local increases of food supply result, and irregular bosses and buttresses of bone are formed.

As the food shortage begins to develop the epiphyseal cartilages tend to disappear and the more absorptive fat fibrous tissue and bone cells of the youthful areas of the body are, as a rule, alone capable of continuing to grow.

Exceptionally, however, some other of the body areas may be more absorptive than usual as is evidenced by the facts of partial physiological giantism. But, apart from abnormal variations of this nature, the rule is that the tissues of the body axis are the least absorptive, and that from the axis to the tips of the body processes the anabolic power of the cells steadily increases. Thus all the tissues formed in the ventral median line and the extremities of the limbs have relatively a great anabolic power. But in addition to these ontogenetically youthful areas there are certain phylogenetically youthful areas, such as the great toe and the inner column of the tarsus in which anabolic power, apparently, is maximised.

If now excessive nutritive supply to the cells be/

be established in early life, hypermacroplasia results because of the great absorptive power of the cartilage cells, but if it be established after the epiphyseal cartilages have disappeared, or if it persist after the disappearance of the epiphyseal cartilages, hypereuryplasia results, and the hypereuryplasia is specialised and affects the phylogenetically and ontogenetically most youthful areas of the body.

If, however, the nutritive overloading is essentially a passive congestion of nutritive material in the body fluids, the result of a diminished nutritive demand, growth continues to the limits of support and thereafter the mechanism of the exogenous metabolism is able to supplement in the normal way, though at a slight disadvantage, the food supply to the body cells and thus prevents the development of an acute food shortage and its attendant precocious senility.

But if the nutritive overloading be the result of complete failure of the mechanism controlling the exogenous metabolism, growth continues to the limit of intestinal support and then, as the anabolic power of the somatic cells diminishes, nothing can prevent the development of the most acute food shortage and its attendant precocious senility.

Thus, old eunuchs are tall and thin and stupid, but/

but old giants are unknown, unless the onset of the nutritive overloading occurred after maturity when the bowed and prematurely senile Acromegalic-gigant with his large hands and feet, enormous mandible and creaky rheumatoid joints is the result.

Among the acromegalic-gigants there are two classes; first, those in whom there is no enlargement of the pituitary; second, those in whom there is enlargement of the pituitary.

The first class is, as yet, clinically, wholly indistinguishable from the second, but post-mortem they can be distinguished by the presence of somewhat syringomyelic changes in their spinal cords and it seems probable that in them the body fluids were of normal composition, but that the supply to the tissues was in some way abnormal in amount due to loss of nerve control of the vessel walls. Be that as it may, the existence of such cases definitely and permanently negatives the ideas that the pituitary functioning excessively or inefficiently or pervertedly is the essential cause of acromegalic-gigantism.

There is no evidence to support these widely accepted ideas; on the contrary, the fact that pituitary enlargement is a late symptom of the true giantism of nutritive overloading is absolutely certain evidence that/

that pituitary enlargement is not the cause of nutritive overloading.

It seems to me most probable that the pituitary is a blood testing station which samples the blood delivered to the brain, and that when the blood is too nutritious the pituitary is stimulated to produce in greater amounts some internal secretion which, either by breaking up the food stuffs or by stimulating renal excretion or by both, frees the body, if it can, from the obnoxious presence of too much food and saves the central nervous system from surfeit and from injury dependent upon an excessive increase of cells which possess no active function.

It is likely that there is some such mechanism in the body for the brain functions poorly in the presence of much nutritive material and, if the excessive supply be prolonged, growth changes which are not to its advantage occur.

According to this view the growth of the pituitary found in these cases is primarily a true hypertrophy, and the degenerations which it so frequently shows are secondary phenomena. The less active growth of the pituitary during the period of rapid hypermacroplasia is to be explained by the fact that the chondroblasts are extraordinarily actively absorbent/

absorbent cells, and it seems not impossible that they extract from the body fluids a great deal of nutriment and reduce even excessively overloaded fluids to a condition of practically normal concentration.

The enlargement of the pituitary in castrated animals is certainly in favour of the idea that the pituitary enlarges whenever the body fluids are unusually nutritious.

SECTION II. GENERAL CONCLUSIONS:—

1. Acromegaly and the Giantism of Nutritive Overloading are one, and are dependent for their different lines of evolution upon differences in the constitution of the body which, in turn, is dependent upon the age of the whole body or of parts of the body or of inborn differences of the body cells.

2. Nutritive overloading is either systemic and dependent upon failure of the exogenous metabolism or local to the tissues and dependent upon failure of the vascular control.

3. Failure of the exogenous metabolism may be the result:—

A. Of an undue and altogether excessive strain being thrown upon its mechanism as the result of an abnormally great intestinal absorptive power.

B./

B. Of changes in the liver which may be secondary to typhoid fever or some other acute infectious disease.

C. Of changes in the ductless glands which govern the metabolism of the liver. In some cases these are of unknown origin, in others, they appear to be secondary to some acute disease, still in others to some profound nervous disturbance whatever the intimate meaning of that may be.

4. Enlargement of the pituitary occurs in all those cases in which there is systemic nutritive overloading and is to be regarded as a functional, compensatory hypertrophy, frequently carried to excess and frequently associated with secondary degenerative changes.

5. Enlargement of the pituitary does not occur in cases in which there is no systemic nutritive overloading.

6. Acromegaly and the Giantism of nutritive overloading are best classed together under the title Acromegalic-Gigantism.

7. Acromegalic-Gigantism is a symptom of excessive nutritive supply to the somatic cells.

8. The growth changes of Acromegalic-Gigantism affect most markedly the most absorptive cell areas of/

of the body which are found, first, in the epiphyseal cartilages, second, comparing each tissue with tissues of its own kind in the ontogenetically and phylogenetically more youthful areas of the body.

9. Acromegalic-Gigantism is inevitably associated with the development of a precocious senility which, unlike true senility, is of environmental, and not of protoplasmic, origin. There is, therefore, always a chance of rejuvenescence in the presence of increased blood supply. This almost invariably occurs and bossing and buttressing of the bones results.

10. Acromegalic-Gigantism superficially resembles Eunuchoid Gigantism and Physiological Giantism, but is essentially different from both in origin and result. In origin because in them there is no loss of metabolic control; in result because they do not carry with them the inevitable doom of a precocious senility and an early death.

SECTION III. CONCLUSION.

My hypothesis is completed: it is based upon the certain fact that protoplasm cannot create matter. Of that I am certain, for the rest I have striven to see and to understand and to test my bricks as I used them./

them. But though, for the present, I have finished, the task is incomplete. Without buttresses on all sides my fabric cannot stand; that material for many of these supports is forthcoming I now know, though I did not know it when I started to build. Whether or not more will be forthcoming in the future time will show. That modifications of my beliefs will be necessary before the work is done I feel sure, and so, not in the spirit of one who has proved anything, but in the hope that the work which I have done will aid some fellow-toiler to find the right or to avoid the wrong, I leave my hypothesis to the consideration of its judges.

END OF THE THESIS

entitled

ACROMEGALIC-GIGANTISM

Written

by

A. CAMPBELL GEDDES M.B., CH.B.

and

submitted by him for consideration for

the degree of M.D.