

ON A CONDITION OF MIXED PREMATURE AND IMMATURE DEVELOPMENT

BY

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(COMMUNICATED BY MR. JONATHAN HUTCHINSON)

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IN the 'Transactions' of the Royal Medical and Surgical Society for 1886 is a paper by Mr. Jonathan Hutchinson, entitled "Congenital Absence of Hair and Mammary Glands, with Atrophic Condition of the Skin and its Appendages, in a Boy."¹ Last year I brought to Mr. Hutchinson's notice a case in which a similar condition obtained in a youth of seventeen, who had been under my observation for nearly four years.

My patient died on December 15th, 1894, and as I had the good fortune to obtain a series of photographs of him at different ages, and was permitted to make an examination of the body after death, I am able to give a fairly complete history of his condition from beginning to end. Mr. Hutchinson has already written a short

¹ 'Med.-Chir. Trans.,' vol. lxi, p. 36.

description of this case in his 'Archives' for April, 1895. I am indebted to Mr. Hutchinson, not only for the light he has there thrown on the clinical features of the case, but for his permission to complete my account by the description of the present state of the patient he saw nearly twelve years ago. I have also to thank Dr. Jago, of Plymouth, for the very cordial way in which he both met my request to see his patient and helped me in my investigation of the case. I propose now to give a detailed description of my own case, and afterwards to add a short supplementary report of the present condition of Mr. Hutchinson's original case.

CASE 1.—*Family history*.—The grandfathers on both sides were subject to gout. The father and mother are well developed, and a little above the average height. There is no history of insanity, consumption, rheumatism, acromegaly, or syphilis. Of the four brothers and five sisters, all have been sound and well formed from birth, except one girl, who had rickets when a baby; she is now, however, in perfect health, and is without a trace of deformity.

A. R.— was the fifth child. There is not the slightest facial resemblance between him and the other members of his family, with one exception. I was shown the photograph of his paternal grandfather, taken when he was over seventy, and there certainly was in this instance a likeness between the two. But it was the likeness of one old face to another rather than that of two members of the same family. The resemblance lay in the shrivelled skin drawn over the wasted soft tissues and protuberant bone, in the aquiline nose, thin lips, white hair, and the general aspect of repose of old age.

Personal history.—His mother remarked no unusual circumstances while carrying him, except that she was nearly always "unwell." He was born at full time, and was a small and fretful child, but was in no other way remarkable during early infancy. He was never

of a bluish colour. His hair and nails were well grown, and though not fat, he was by no means emaciated. His mother attributes the commencement of the disease to teething. He began to cut his teeth when about six months old, and from that time his hair began to fall off, his nails to shrivel, and his fat to diminish. At the age of eighteen months, when his first photograph was taken, more than half his hair had thinned off, that running along the middle of the vertex of the head persisting longer than the rest. The shoulders were rounded, the chest narrow, and the cranium large in proportion to the face. The dropping of the head and consequent upward direction of the eyes, which in the photograph give a hydrocephalic look to the face, were said to be a characteristic feature at this period. But in the next likeness, which was taken at the age of seven, this furtive expression is quite absent, and though the hair is there as scanty as it was when I saw him, his hands and face look by no means devoid of fat. Indeed, the cheeks yet show evidence of the presence of the sucking pads of early childhood. He was a lively, good-tempered child, but was so easily fatigued that he could never run about with other children.

At the time of the third photograph (at the age of twelve) the face had assumed the sedate expression that it has in the last photograph of all, and the whole type of face and figure is that rather of an adult than of a child. His mother says these photographs are truthful representations of his appearance at these ages.

At the age of eighteen months he had an offensive mattery discharge from the nose, and afterwards from the left ear, which did not quite disappear until he was fifteen. He never snuffled in infancy, nor did he have rashes or sores round the mouth or on the bottom or cheeks. He was never double-jointed, nor did he at this time sweat unduly, and his limbs were always straight. He did not walk until nearly two years old, and was backward in learning to speak. Though he

began to cut his teeth at the age of six months, the process of dentition was very slow, and it is not known when the second dentition commenced. He had measles when about four years old, and at eleven became dangerously ill with broncho-pneumonia, from which he did not recover for seven weeks. He also suffered from attacks of flatulent dyspepsia from "as early as could be remembered." These were attended with epigastric pain, and occasionally with nausea or vomiting, and they became more frequent and persistent towards the end of his life.

From the time of the appearance of the first indication of his disease his breathing was difficult at times, and he could never hurry because he was so "short-winded." He told me that occasionally he could "hardly get his breath," but I myself never saw him in this condition. His mother confirmed his statement, but said the attacks never caused him to change colour, but were evidenced by the quickness of his breathing and by its asthmatic character. In the night he always lay with his mouth open, and his breathing was then sometimes so uneasy, and the noises he made so uncouth, that those who were with him feared he would be suffocated in his sleep.

Condition when first seen.—A. R.— was first brought to me in January, 1891, when he was a little over fourteen years old, but his appearance as he came into my room was suggestive either of a child of five or of a wizened and dwarfish old man. On the one hand, his size (height 1.04 m., weight 16.34 kilos.), manner of dress, and the fact that he was brought by his sister in a mail-cart, drove one at once to the conclusion that he was a child. On the other hand, had he come by himself in the clothes and other accessories of old age, I think there are few who would have detected the deception. This appearance of senility was occasioned not only by his baldness and by the wrinkled condition of his skin, but by the leanness of his figure and by the lack of that vivacity of carriage and expression which is one of the chief features of early

life. The thighs, moreover, were so thin as to give an appearance of undue width of the fork, and this, together with a slight stoop from the hips, a want of fulness in the buttocks, and a perceptible stiffness in gait, still further increased his resemblance to a decrepid old man. He was, however, neither tremulous nor tottering in his walk. The veins of the backs of the extremities, and of the neck, forehead, and scalp were large and very conspicuous, those in the last situation being readily seen from a distance of more than one hundred feet. They were asymmetrical, and consisted principally of a very large left temporal, which inosculated freely with a right frontal vein and with a few smaller branches of the right occipital. But what contributed more than all to his "old-mannish" appearance was the withered and juiceless look of his skin, the absence of colour in the scanty hairs on his scalp, and the piping tone of his voice. The eyelids and eyebrows, too, at first sight appeared devoid of hair, but on close inspection a few scattered and downy hairs were seen in both situations. A few were also to be seen on the backs of the hands and wrists, but on no other part of the body. The outlines of the cartilages of the nose could be seen with startling distinctness. They were slightly but unmistakably hypertrophied, so as to give an aquiline turn to that feature quite different from the shape of the nose of other members of the family. The cartilages of the ears were also large and well formed, but the lobules were absent. The nails of the fingers and toes were flat, ill-shaped, and membranous, and as short as though they had been bitten to the quick, though no nail-bed was visible. There was no vestige of mammary glands, and the nipples were unusually small. The umbilicus was a mere indentation in the skin, without folds. The skin was thin, soft, and pliable, and, though usually dry when I saw him, this was probably due to his very quiet habits, for on two occasions in hot weather I was able to detect the presence of sweat of normal reaction. He himself, and his mother, said that he often

sweated profusely. The colour of the skin was slightly brownish, with a tinge of red over the trunk, especially in front, where it was sprinkled thickly over with small non-pigmented spots as if he had been sprinkled with rain. This peculiarity was visible only on near inspection, except at the back and sides of the neck, where the colour was more pronounced. Tactile sensibility and the perception of heat and cold, as well as the senses of taste and smell, were fairly acute. He always felt extremes of heat and cold very severely, and on cold evenings in the winter was always carried up to bed wrapped in blankets. But while his body and limbs were cold, his head was generally hot, and even on cold days he would sometimes bathe it in cold water to relieve the feeling of heat. His temperature was always nearly normal when taken. Both superficial and deep reflexes were absent.

With the right ear he could hear the tick of a watch at ten inches, though the drum was represented by a mere ring. The only ear bone that could be seen was the incus, which was very large, and was exposed for nearly the whole of its extent. It should, however, be remembered that the ear bones do not grow after birth, and it was probably therefore only relatively large. On the left side there was a small perforation at the hinder and lower part of the drum. The membrane was tense, and the handle of the malleus very prominent. A watch could be heard on this side at a distance of twenty-one inches. The left Eustachian tube was patent, but no air could be got through the right.

The eyes seemed large and protuberant; but on comparison with those of another youth it was evident that this appearance was partly due to the narrowness of the palpebral aperture on the one hand, and the absence of surrounding fat on the other. There was no arcus senilis. The left eye showed an expansion of the semi-lunar fold into an imperfect nictitating membrane, which overlapped the cornea for about 3 mm. There was hypermetropia of both eyes, with slight astigmatism, which I

found was best suited with glasses of + 4·5 D. for the right eye, and + 2· D., with the addition of + ·5 D. in the vertical diameter, for the left eye. In other respects his eyes were normal.

His intelligence was uncommonly good, and though he was thrown much into the society of children his ideas were those of a man, and he could take his part in the small talk of adults with interest and intelligence. His memory was of average ability. He had had no schooling, but had taught himself to read easy sentences. He was quiet in manner and gentle in disposition, and his good nature and maturity of thought and judgment were shown in his consideration for others. Owing to his dread of rebuffs he was averse from the society of strangers, but was liked by those who knew him. When tired he often complained of headache, and then rested his head on his hands to relieve himself of its weight.

His muscles were not well developed, and were easily fatigued. He was unable to walk more than a mile at any time without feeling tired, but as a rule was drawn by his sister in a mail-cart.

In its more obvious aspects, his body was not badly proportioned ; for though his head was evidently large, it was not relatively disproportionate for one of his stature. For Sir G. M. Humphry¹ has pointed out that the heads of short people are naturally as large as, and may be even larger than the heads of those of ordinary height. In A. R.—'s case, however, the head was actually slightly smaller (16·5 cm. long, 14 cm. broad, 49·4 cm. in circumference) than that of the average adult (54 cm. in circumference).

The length of the limbs, too, was for a youth of his age not disproportionate, for the middle point of the total length was less than an inch above the symphysis pubis.

But in other respects he was not only stunted in growth but deformed. In the first place the right half of the

¹ 'The Human Skeleton,' p. 96.

cranium was smaller than the left, the latter projecting nearly 2 cm. behind the former, but being level in front. The forehead was not overhanging, and the orbital plates of the frontal bone were horizontal. There were also no bosses on either of the parietal bones, and both they and the occipital showed no wasted areas. The anterior fontanelle was, however, open to the extent of about 5 mm., and the pulsations of the brain were easily seen. The margins were not thickened, and the lines of the sutures could not be distinguished. In the next place the shoulders were rounded, and the chest narrowed by the smallness of the clavicles, which were so puny as to remind one of the "merry thought" of a chicken. Each measured no more than 6 cm. in length. The scapulæ were also small.

Lastly, while the shafts of the long bones of the limbs were decidedly thin, the ends were relatively thick. Thus on comparing his hands and feet with those of another emaciated boy, it was manifest that not only were the knuckles conspicuous by the absence of fat, but they were also enlarged. Some epiphyses were large in proportion to others. This, as Mr. Hutchinson had pointed out, was the case with the lower ends of the humeri and the upper ends of the radii. But the lower epiphyses of the femora were still more disproportionate in size. While the limit of its articular surface projected well beyond the level of the edge of the articular surface of the tibia behind, in front the effect of the undue prominence of the condyles gave an appearance to the tibia of being partially dislocated backwards. It also gave rise to an exaggerated prominence of the large patella, and caused its ligament to be set into its tubercle at an angle of 135° with the shaft. It was perhaps, some corresponding disproportion in the size of its articular surfaces that caused the hip-joint to be stiff. He could not bend downwards sufficiently to lace his left boot, though he could just manage the right. I was unable to ascertain whether this explanation was correct, nor could I be sure whether

a similar cause accounted for his inability to fully open his mouth.

His lips were thin and compressed, and formed with the mouth a conspicuous exception to the senile type of his other features. Instead of falling in so as to give the well-known crab-claw aspect to this part of the face, the alveolar portion of both jaws was unusually prominent. The effect of this was as if he were wearing a set of artificial teeth too large for his mouth. It also gave to the face, to a slight extent, the shape of a hatchet. The jaw could not be opened widely enough to permit of an examination of the fauces. The frænum of the tongue was so short that he could hardly project it beyond the teeth. The tongue itself was small, and not so thick on the right side as on the left, and was smooth and almost glazed on its surface, owing apparently to a deficient development of papillæ. It was never furred. Both maxillæ were contracted, and the two sides of the palate were convex downwards from side to side so as to meet at an angle and form a furrow along the middle line. The teeth were few in number, and very irregular both in level and shape, though the sockets of the milk teeth were raised to the same level as those of the permanent. They were crowded and erratic in situation, and variable in size. Many were decayed, and some were not fully cut. The two upper central incisors, the molars, and the left first bicuspid were unusually large. They were arranged in two disorderly ranks, the upper teeth being set within the lower. There were ten in the upper jaw, of which two were left temporary molars, while the other eight belonged to the permanent set, six being greatly crowded canines and incisors and two right-sided bicuspids. The second bicuspid was much rotated and displaced. In the lower jaw there were thirteen teeth, of which six were much decayed milk teeth, viz. two central incisors, two last molar roots, one right anterior molar, and one left canine root. The roots of the lower milk incisors were abnormal in that they were little if at all absorbed

in spite of their successors being in place. Of the seven permanent teeth there were two greatly decayed anterior molars, three incisors, two canines, and one large bicuspid (on the left side).

His appetite was indifferent, and he ate little as a rule, preferring such soft foods as sweetbreads, milk puddings, and eggs; but this choice of diet was partly owing to the fact that his digestion was not good. He disliked fat, and when he forced himself to eat it, soon became "bilious" and had to give it up. He was also soon nauseated by cod-liver oil. His abdomen measured 45·8 cm. round at the level of the navel. The protuberance of the abdomen was probably in great part due to the size of the liver, which extended from the level of the seventh rib above to nearly halfway between the ribs and the navel below. The bowels were opened regularly every morning and evening.

No splenic dulness could be detected. His thyroid gland could be easily felt, and was in no way unusual either in shape, size, or consistency. There were no enlarged lymphatic glands, and no swelling could be felt at the root of the neck.

He soon became short-winded on exertion, though, as a rule, he respired through his nose at the rate of sixteen per minute in the sitting position. The chest measured 42·6 cm. round the line of the nipples on deep expiration, and 48·4 cm. on deep inspiration. On percussion over the chest, dulness was evident over a triangular area of which the base was situated about 1 cm. to the right of the sternum for nearly its whole length, while the apex was 2·2 cm. beneath and 1 cm. outside the left nipple. At this last spot a soft indistinct systolic murmur could be heard traceable into the axilla. At the base another bruit was distinguishable over the aorta, also systolic in rhythm, though less soft and of a more permanent character than that at the apex. The pulse was small, and varied in rate from 112 to 120 per minute. The temporal artery felt tortuous and thickened. On counting the number of red

discs in ten cells of a hæmocytometer, they were found to be of the usual size and shape, and to number 106·9 per cent. of the normal. A number of small granular masses were also present, but no nucleated red discs were to be seen. The white corpuscles were in the proportion of 1 to 346 red, and were of average size and appearance. The blood was examined on a warmed stage, and also diluted with neutral solution of sulphate of soda, and again with the acidified solution.

The rugæ of the scrotum were present, but were not so distinct as usual, giving the latter a smooth appearance at a little distance. The testicles were descended, and were of medium size. The usual sensation was experienced when they were squeezed. His urine varied greatly in character. Some specimens that he brought me were of average density, and some were pale and clear, and of a sp. gr. of from 1002 to 1006. The sp. gr. never exceeded 1025. The result of a careful observation continued for seven days in the spring of 1893 gave a daily mean of 396 c.c. in the twenty-four hours, a sp. gr. of 1019, and 12·6 grammes of urea. It was faintly acid, and contained neither albumen nor sugar. A specimen of sp. gr. 1008 allowed to stand for three months became dark in colour and aromatic, but did not decompose.

Subsequent history.—From the time that I first saw him in 1891, A. R— grew in height at the almost uniform rate of 2·5 cm. a year. The measurements of his head and abdomen were, however, always the same, while the girth of his chest increased by nearly 5·0 cm. The last measurement was made in October, 1894, when he was found to be 1·13 m. high. He seemed to age rapidly. His features became manifestly more shrivelled, and as he grew older he became still older in his ideas, and impatient of being treated as a child. When he had passed the age of sixteen there was evidence of sexual maturity. He occasionally had “wet dreams,” and on one of these occasions I was able to detect the presence of spermatozoa. The cartilages of the larynx, however, did not enlarge, and

there was no alteration in the peculiar tone of the voice. Neither was there any other sign of sexual maturity. He at this time began to suffer from rheumatic pains in his joints.

In the early part of the winter of 1893 I attended him during an attack of lobar pneumonia of the right base. The lung was consolidated from the base to an inch above the level of the lower angle of the scapula. His temperature at its highest was 103° . There was no sign of embarrassment of the heart, and notwithstanding great enlargement of the lymphatic glands of the neck the constitutional disturbance was slight. The crisis set in on the fourth day, and a gland over the left mylohyoid suppurating and breaking about five days afterwards, he speedily got well.

In the autumn of 1894 he became dispirited, more easily tired after exertion, more grave and subdued in manner, and less inclined for society. He was also more frequently ailing. His digestive trouble increased, and he sometimes complained of sharp pains in the left breast which shot down the arm. At the beginning of the winter he had a troublesome dry hacking cough.

On December 8th his last illness set in with diarrhoea and vomiting, and his usual pain and tenderness at the epigastrium. He was also unable to lie down on account of a choking sensation in his chest, which became worse when he was in the recumbent position. The breathing was slightly laboured and stridulous, though it was not distressingly difficult. No abnormal lung sounds could be heard. The pulse was 134, small and weak, and slightly irregular. No murmur could be heard at the cardiac apex, and the sounds were very indistinct. There was no oedema of the feet. The temperature was 101.4° . Liver dulness was increased, but there was no tenderness. The area of stomach resonance was manifestly extended, and he attributed much of his distress to "wind." Bismuth was given in half-drachm doses, with strophanthus and carminatives, and

these soon relieved the diarrhœa and sickness. The next day he was better, but on the morning of the third day he had a slight return of diarrhœa and was sick once, though his breathing was more natural. Later on, however, I received an urgent message to visit him, and when I arrived, found that while his mother was downstairs she had heard a noise from his room, and on running up had found him slightly livid, and sitting up in bed with his eyes and mouth open, trying to get breath. She took him in her lap, where he died quietly in a few minutes.

Post-mortem examination.—This was made two days after death. Rigor mortis was well marked.

On cutting through the skin it was at once evident that the subcutaneous fat was not entirely absent, though it was so scanty that it did not form a continuous layer. It was present over both the chest and abdomen, and was not thicker at the lower part of the abdomen. Fat was also present in still less amount in the mesentery and great omentum, where it was dotted here and there in the membrane, and was in meagre quantity behind the kidneys. There were no appendices epiploicæ.

The anterior fontanelle was closed, and the bone appeared to be of almost the same thickness there as elsewhere on the head, though pulsation had been evident less than three months before. The skull resembled in thickness and structure that of a child of a year old. It had an almost uniform thickness of about 2 mm., and there was no differentiation into compact bone and diploë. Neither the frontal sinuses nor the sella turcica were deepened, and the appearance of the base was otherwise normal. The ribs and their cartilages were of usual development, and the segments of the sternum were fully ossified, and all but the manubrium were united. The left clavicle was removed, and was with its cartilages 5.5 cm. in length.¹ It contained the beginning of a

¹ I find that the clavicle of a child of fifteen months old measures exactly 5.5 cm. without its cartilages. It should be remembered that "its mode of ossification is intermediate between that of a true cartilage bone and a membrane bone."

medullary canal. There was no centre of ossification at the sternal end, but the cartilaginous cap was very large.

The brain was normal in every respect. The convolutions were well formed and not flattened, and there was neither excess nor deficiency of fluid in the ventricles and subdural space. Neither the pineal nor the pituitary bodies were either larger or smaller than usual, and both were of healthy appearance.

On opening the thorax, a persistent and hypertrophied thymus came into view. Its lobes were nearly equal, and extended from about 2 cm. above the level of the manubrium to the junction of the fifth rib with the sternum below, overlapping the pericardium. They were of the usual shape, and when removed from the body the right lobe had a length of 7·2 cm., a breadth of 4·8 cm. at its widest, and a thickness of 2·3 cm., while the left was a little smaller. The two weighed 48·3 grammes together. The trachea was slightly flattened, but was far from being occluded by the pressure of the gland. The veins from the neck were not specially full. There was no ecchymosis. A microscopical examination was afterwards made, but owing to the thymus having been left too long exposed, no details of its structure could be made out, except a considerable increase in the amount of its fibrous tissue.

The thyroid gland was of relatively normal size and appearance, and microscopic examination revealed nothing amiss.

The lungs were quite healthy, but a few old pleuritic adhesions were present near the right base.

The heart weighed 121·0 grammes. There was no evidence of old pericarditis, and the muscle was firm and healthy. Both ventricles contained blood. The mitral orifice was not stenosed, but both valves were atheromatous. That half of the anterior valve which was attached to the ventricular wall was thickened with a large calcareous plate, but the free half of the valve was much less affected. The posterior valve was rolled up at its edge and incompetent. The bases of the aortic valves were studded with

cauliflower-like calcareous excrescences, almost surrounding the orifice. Above the right posterior valve was a large irregular patch, which extended for a height of 23 mm. up the aorta, and was composed principally of one unbroken plate continuous with that on the anterior mitral. Both coronary arteries were completely blocked, the right at its commencement and the left in the substance of the ventricle, where it felt like a bone in the muscular wall. Soft atheromatous patches occurred here and there over the whole of the aortic arch, especially along its convexity. On its concavity, opposite the origin of the left subclavian artery, was a large patch of calcareous material. Atheroma also extended into the branches, and a collection of organised fibrin almost blocked the origin of the right subclavian from the innominate artery. No trace of a ductus arteriosus was visible, and the coronary valve was quite closed. The tricuspid and pulmonary valves were healthy.

The spleen weighed 42·0 grammes; its capsule was thickened on its convex surface to the extent of from 1 to 2 mm., and was of cartilaginous hardness and consistence. On the concave surface the capsule was of little more than usual thickness. Its structure was normal.

The kidneys together weighed 130·0 grammes, and were neither hard nor congested. The capsules were slightly adherent. The supra-renal bodies were both of perfectly healthy appearance. The microscopical appearance of both kidneys and capsules was like that which occurs in the fibrous organs of the aged.

The stomach was dilated, and its mucous membrane markedly congested. The muscular and epithelial elements of both stomach and intestine were thin, and Peyer's patches were so atrophied as to be distinguished with difficulty. The liver was not congested: its structure appeared to be perfectly healthy; its edge extended to about halfway between the umbilicus and the edge of the ribs.

I was unable to weigh the brain and liver, and in some

other respects the examination had to be curtailed in deference to the wishes of the friends.

CASE 2.—The descriptive part of Mr. Hutchinson's original paper on this case is as follows, viz.:

“Congenital absence of hair and mammary glands with atrophic condition of the skin and its appendages in a boy whose mother had been almost wholly bald from alopecia areata from the age of six.”

“The subject of this case, a boy aged $3\frac{1}{2}$, presented a very peculiar withered or old-mannish look, all his features being thin and pinched. His fingers were shrivelled and dusky, and their nails, which also were remarkably thin, were curved backwards so as to present more or less of hollow in the middle. His head was large and the anterior fontanelle not quite closed; the scalp was exceedingly thin, and with the exception of a quantity of down, was quite bald. It looked semi-transparent and tight, and the veins coursing in it were everywhere conspicuous. The veins were probably larger than natural. A large trunk came down the forehead on each side of the eyebrows and communicated by a transverse branch at the root of the nose. The inosculations across the middle line of the scalp were many. There was a peculiar blue tinge about the lips; it involved the skin, and not the prolabium only. At first I thought that this was due to accidental staining, but after he had been half an hour in my room it much diminished, as did also the turgescence of the veins of his scalp. His lips were exceedingly thin. His teeth were all cut and were tolerably regular; but his incisors did not stand quite straight, most of them had some slight inclination into the mouth. On his shoulders he was so thin that his coracoids and the outlines of his acromion processes could be easily seen, the skin over them being not much thicker than brown paper. The tightness of skin was nowhere very conspicuous excepting on the scalp; thus, on the abdomen, arms, and thighs the integument was

quite loose, but everywhere very thin. His muscular development was slight in all parts excepting the thighs, which felt hard and had muscles quite out of proportion to the rest of his body (this remark does not apply to the buttocks). His genitals presented a very remarkable contrast to the rest of his body. The parts above the pubes and upper part of the scrotum were so full and plump that a suggestion occurred that he must have double hernia. This, however, was not borne out by examination, and I believe the simple fact was that the scrotum and adjacent parts of the skin were in the state of those of a normally stout child, while everywhere else the skin, subcutaneous cellular tissue, and panniculus adiposus were almost absent. The true scrotum was small, naturally corrugated, and occupied only the lowest part of the genital pouch which I have described. I do not think that there was anything very unusual in this state in a child, but must admit that possibly there was some excess of subcutaneous development about the pubes and root of penis. His testes were well placed and of normal size. His penis, except that there was phimosis, was quite natural. His toes and their nails were in the same condition as his fingers. He did not walk quite perfectly, always keeping his knees a little bent, but I could not make out any definite muscular defect. One other remarkable feature remains to be mentioned: he had no nipples, and their sites were occupied by little patches of scar. These scars were exceedingly superficial and slightly marked, but I am sure that they were there. Nothing like a mammary gland could be traced.

“The history which the mother gave me of the child was that he had had no ailments since his birth, was of cheerful disposition, and very intelligent. It had been necessary from cross-presentation to turn during delivery, and for some days after birth he had been very blue, probably in a state of partial cyanosis. He was still liable to vary very much in blueness in connection with

the temperature and states of excitement, but never now presented anything approaching a cyanotic condition."

Dr. Jago described his condition when he was fourteen years old in the following letter to Mr. Hutchinson:¹

"Plymouth, July 5th, 1894.

"DEAR SIR,—I am pleased to reply to your letter received this morning. Master B— was fourteen years old in April last, is 43 inches in height, and I guess his weight to be about 55 or 60 lbs. He presents the old man—even aged man—in his countenance. His voice is fairly good, but has a very peculiar piping sound. There is no want of intellect, and his fondness for study is more than usual among lads of his age. His general health is good, and he is very active. When an infant he had cyanosis, which gradually lessened as he got older. At present the veins are seen distended and remarkably distinct all over his limbs; but over the back, chest, and belly the veins assume the look of a network of coarse capillaries. The veins all over the skull are very distinct, and remind one of an anatomical plate, coloured. The fontanelle, which when he was an infant was very large, is not even yet quite closed, and pulsation is still visible in it. The sutures of the head seem normal, and the skull is normally hard. There is not a particle of fat anywhere in the whole of his body.

"The joints are large, but look disproportionate because of the exceeding leanness of his body. The outer condyles of the arm and thigh bones are, however, abnormally large. The movements of the fingers and toes are free enough, but the wrists have a very limited flexion in any direction.

"When an infant up to about two years of age, the head was thinly covered with pale, weak hair. At that time I did all I could to make it grow. I thought I had found parasitic growth on and in the hair, but I suppose now that I must have been mistaken, for there is no sign

¹ 'Archives,' April, 1895.

of hair to be seen on the scalp or on the body, except the very faintest growth of the external ends of the eyebrows. Even lanugo is utterly absent. Not a trace of eyelash.

“His mother has been bald, I understand, ever since she was a girl, and has worn a wig for many years.

“The sisters of this boy are well grown, and have very good hair. One of them had splendid hair,—thick, black, and long. Suddenly her hair began to fall off, leaving large, perfectly bare patches, fortunately cured by Ung. Acid. Carbolico., and the hair is excellent again.

“The nails of the feet and hands are very little developed, just visible.

“The teeth are abnormal in number, none are decayed nor have any been lost or extracted. The canine, bicuspids, and incisors are normal, but somewhat irregular, but there are no molars.

“I have written all I can think of. Should there be anything more, I shall be glad to write you.

“I am, yours truly,

“FRED. W. P. JAGO.”

When Mr. Hutchinson so courteously permitted me to see this patient he was twelve years older than when this account was written, and had attained a height of 1·096 m., and a weight of 17·25 kilos.

I had been prepared to see a strong likeness between this case and the one which I have described, but I was amazed at the striking personal resemblance of one youth to the other. This doubtless was because the features of the disease and of the person are to some extent identical. Thus in S. B— there was not only the tight scalp and large and prominent veins, the old-looking, lustreless skin, and extremely emaciated face of A. R—; but the same beaked nose, thin lips, protruding eyes, and ill-developed irregular lower jaw. In fact, while neither had the remotest facial resemblance to any of the other members of his respective family (with the one exception I have referred to), and while those families were themselves very unlike,

yet they closely resembled each other. In other respects, too, the likeness was equally remarkable. S. B— came into the room with the same straddling walk, and spoke in the same piping voice as his prototype. His judgment and intelligence were of the same adult character. He was good-natured, quiet, and self-contained in demeanour, sensitive to the opinion of others, and keenly alive to his own personal defects. Like A. R—, he was much affected by extremes of heat and cold. He, too, sometimes sweated profusely from slight causes, and was taken out by his sister in a mail-cart, because he so soon became tired. He was, however, not so short-winded as A. R—, and only on one occasion could he remember being short of breath when not exerting himself, and then he had had to sit up the greater part of the night. He could also take cod-liver oil, though he disliked fat as a rule. His appetite was poor, but he seldom had indigestion. Measles was the only disease with which he was ever laid up.

He also was growing at the rate of about 2·5 cm. a year, his height in June, 1886, being ·907 m., in May, 1894, 1·072 m., and in September, 1895, 1·096 m. His head was 50·8 cm. in circumference, while he measured only 53·4 cm. round the chest on deep inspiration, 45·8 on deep expiration, and 56 cm. round the abdomen at the navel.

The anterior fontanelle was only half closed, and the pulsations of the brain could be easily distinguished, but quite as conspicuous pulsations were also visible on other parts of the vertex. One of these spots was situated on the posterior superior angle of the right parietal bone, close to the lambdoid suture; another was in the corresponding angle of the left parietal, almost in the situation of the posterior fontanelle; and two others were to be seen between this and the anterior fontanelle about 1·8 cm. to the left of the middle line. These four areas were between 2 and 3 mm. in diameter, and the three to the left of the middle line were connected by a curved line of indistinct pulsation, running into the anterior fontanelle.

The pulsations were in a distinct excavation in the bone, and could not be stopped by pressure with the fingers on any one point. The position of the closed lambdoid and coronary sutures could not be detected by touch. There were no bosses of bone, nor wasted areas on the occipital bone.

The scapula was small and the clavicle diminutive. But it was both my own opinion and Dr. Jago's that the head of the radius, though large, was not then disproportionate in size when compared with the other epiphyses, and this was subsequently confirmed on taking a "shadow" photograph of the part. The lower end of the humerus was, however, still relatively large, and the patellæ and both condyles of the femur were conspicuously hypertrophied. The long bones, as a rule, were thin and straight, but each femur had its natural curve exaggerated. Both lower extremities were of the same length, and so too were the upper extremities, which were not so long in proportion as A. R—'s. The backbone also had its natural curve as in A. R—'s case.

On close inspection a feeble growth of colourless hair was found to be present on the backs of the hands and wrists as well as on the head. The trunk and back and sides of the neck were also spotted and pigmented of the same reddish-brown hue, and of the like relative depth, as in the other case. But the colour was deeper, and the face was bronzed and freckled. This last condition I was told was partly due to his having recently gone away for change of air, but was also in part usual with him. The pads of fat near the genitals and at the root of the neck, noticed by Mr. Hutchinson twelve years before, had disappeared.

There was the same inability to fully open the jaw, and the same condition of the tongue as was seen in A. R—. The palate was, however, not abnormal in shape, and the teeth were all of good size and in fair condition, and, though crowded, were by no means so irregular. There were no milk teeth. The alveolar portion of the jaw was

enlarged for their reception, but this not so marked as in my patient.

The meatus of each ear was too swollen to permit of an examination of the drums. With the left ear he heard a watch 25 cm., and with the right 72 cm. away. The right had discharged more or less since he was "quite young."

The palpebral aperture was not narrowed. The right eye showed slight hypermetropic astigmatism in the oblique diameter, and there was hypermetropia of about 2 D. of the left. The optic discs were a little red and their outlines were blurred, but no other abnormal condition was present.

Like A. R—, when he runs he feels a pain beneath the middle of the sternum, but there was no dulness on percussion over the bone. On the contrary, nearly the whole of the chest area was hyper-resonant, and only a little less so over the situation of the heart; the apex beat was best heard 12 mm. outside the nipple line in the fifth space, where there was a soft systolic murmur traceable to the angle of the scapula. A less soft but more distinct systolic bruit could be heard over the aortic area. From this it will be seen that his heart was apparently also in the same condition as in the other case.

In the blood, too, the red discs were too numerous by over 8 per cent., but were not otherwise abnormal. A few minute granular masses could be seen. The white corpuscles were in the proportion of 1 to 236 red. The thyroid gland was easily felt, and was of average size relative to that of the rest of the body. The patellar reflexes were diminished, and no cutaneous reflexes could be obtained. The lymphatic glands could not be felt. The bowels were at one time habitually constipated, but of late they have been relieved regularly. The urine, which was kindly analysed for me by Mr. Hopkins, was found to be normal in every particular.

Remarks.—It should be noticed that in the second of these cases, while some of the symptoms rather suggested

such a cause, there was no direct evidence of persistency of the thymus. In the first it is questionable whether death resulted from thymic or from cardiac asthma. I believe that his habitual dyspnoea was partly the result of pressure of the thymus on the trachea or on the adjacent nerves, for though the thymus was not greatly enlarged relatively to the size of the body¹ it must be remembered that the tiny size of the clavicles greatly narrowed the space between the sternum and the spine. It is my opinion, however, judging from the appearance of the parts after death, that he died of cardiac and not thymic asthma, though a temporary engorgement of the thymus may have acted as a contributory cause. But still more important, probably, was the catarrh and consequent inflation of the stomach, which I attributed to influenza.

His death was singularly like that of many old cardiac cases. It was preceded by a slow general decrease of vigour, by rheumatism, and by the onset of anginal pains, and was precipitated by influenza; and after death there was found extensive atheromatous degeneration of the mitral and aortic orifices with obliteration of the lumina of the coronary arteries. In short, I think there is good evidence in favour of the view that A. R— died of senile decay at the age of seventeen. It is, however, noteworthy that while the heart and blood-vessels were prematurely old, the lungs, if we may judge from the way in which they were affected by disease, were quite the reverse. Thus, they were affected with the infantile disease broncho-pneumonia at the unusually late age of eleven, and it is remarkable that he should have recovered at all from a disease of which the prognosis is so grave in weakly children. But it is probable that the heart mischief had not by that time developed, for the doctor

¹ Triesethau ('Die Thymusdrüse in norm. u. path. Beziehung') has published a list of cases which show that the hypertrophied gland may be larger than this at the age of eight months, while in the sixth year it may be nearly double the size.

who attended him has no recollection of it. Then again the lobar pneumonia, which he had at the age of sixteen, showed in its rapid and benign course (in spite of the grave complication of atheromatous degeneration of the valves of the heart) that the lungs possessed the recuperative powers of those of a child.

On glancing over the main clinical features of these two cases and of the description of the appearances that were found after death, it is evident that they may all be grouped under two heads. They are indications either of defective growth on the one hand, or of relative increase of growth on the other. The changes which terminate in old age and decay are in abeyance in some parts, while they are accelerated in others.

Evidences of slow or of arrested development were shown in the condition of the bones, especially of the skull, clavicle, and lower jaw, and in the enlargement of the knuckles, but in a lesser degree in nearly all the bones of the body.

There were signs of too rapid development or maturity of the skin, mucous membrane of the tongue and intestines, hair, and nails, and of the brain, liver, and of the blood vascular system. It is noteworthy too that, in testing his sight, dilatation with atropine revealed no concealed visual defect, though he was both hypermetropic and astigmatic.

But it is not only in different tissues or organs that this inequality of nutrition was shown. It was also to be seen in different parts of the same tissue. Thus, while the shafts of the humeri and of the femora were of defective growth, the lower epiphyses were grown quite out of their relative proportion. Indeed, it may be said of the femur that the shaft was the shaft of a young child while the condyles were those of a youth. This feature is also well shown in the case of the teeth in A. R—. In the same jaws were unshed milk teeth crowded alongside average-sized or unusually large permanent teeth. The tongue, too, was more developed on one side than on

the other, and one half of the skull was larger than the other half. In one ear of A. R.— it was interesting to see an incus of adult size taking up so much room in the ear of a child. In the hypertrophied thymus, again, we have an instance of arrested development of an infantile structure and its hypertrophy in the same part.

These are, so far as I am aware, the only two cases of this affection which have hitherto been described. But the condition is so singular, the life-history of one case so complete, and that of the other so evidently of the same species, that there can, I think, be little hesitation in regarding it either as a distinct disease, or such a striking variation from some known disease as almost to merit a name of its own. I will venture, for the purposes of this paper, to give it the provisional name of micromegaly. I am fully aware of the objection to a word which is made up of two adjectives, but the fact that those two adjectives express the opposite qualities of smallness and largeness is, in my opinion, a point greatly in its favour instead of the reverse, for the disease manifests itself in these two directions. It connotes in one word the two great features of the collection of changes and symptoms which together constitute the disease. Above all it serves to indicate its connection with a disease to which it is apparently closely allied. I allude to acromegaly. At first it may appear that there can hardly be two diseases which are more widely different. Indeed, in some respects the features of the one disease are the exact contrary to those of the other. Thus the patient with acromegaly has thick lips, a large tongue, and heavy jaws, while these micromegalics have thin lips, small tongues, and ill-developed jaws. In acromegaly the collar-bone is often hypertrophied, while here its development is arrested. In acromegaly the hair is abundant, and the skin is thick (pachydermatous), and becomes loose, yellow, or brown, and scaly; in these cases of micromegaly both the skin and its appendages are atrophied almost from the beginning. In acromegaly there is both atrophy and hypertrophy of the sexual

organs ; in these cases they are apparently unaffected. In acromegaly the intelligence may become childish while the body takes on the proportions of a giant ; in these instances the reverse is the case, the mind may be precocious while the body is stunted. But these differences are not indications of a want of connection between the two diseases. On the contrary, they show their relationship—that the one is in some way complementary to the other.

In the above comparison the widely different effect of each disease on the same parts has been shown. In other respects, though the same parts are not affected, the method of the disease may also be shown to be the same, *e. g.* while in acromegaly it is the lower ends of the radii and tibiæ which are enlarged, in these cases it is the lower ends of the humeri and femora. Here, too, an associated cause is apparently at work in the two diseases, though the effects are different. Both are trophic diseases. In both there is relative over-development, on the one hand, going on side by side with arrested development on the other.

Another factor of importance to be taken into consideration in estimating the relations between the two diseases is the variation that occurs in the symptoms of acromegaly in different cases. The same parts are not always affected, and atrophy in one case may be hypertrophy in another. For example, the muscles are wasted, as a rule, and correspondingly feeble, but sometimes they are quite Herculean in their proportions and strength. For this reason, also, too much importance ought not to be attached to the hypertrophy of the pituitary body in the one disease and not in the other, for it has been shown that in more than 20 per cent. of the autopsies that have been made on acromegalics, no such condition was present. It is not an essential part of the disease.

It can also be shown that a few of the symptoms of the two diseases are alike, and some of these are of importance in their bearing on their mutual relations.

One of the first names that was given to acromegaly was "exophthalmic cachexia" in recognition of the prominence of the eyeballs that is one of the features of the disease, and of the debility, which is another. Both of these symptoms were also present in each of the two cases of micromegaly that have just been reported. Much of the weakness of which acromegalics complain is due to the emaciation of the muscles; and the same feeble muscular power, with wasting, is also present as a symptom of micromegaly. The marked pigmentation of the skin so often met with in the former disease reminds one of that pigmentation which was present in both cases of the latter disease. One of the features of these two cases of micromegaly is the large size of the cartilages of the nose. This corresponds with the hypertrophy of the same tissue in acromegaly. The alteration in the tone of the voice, the atrophy of the mammary glands and nipples, the increase of perspiration, the flattening and atrophy of the nails, the diminution or absence of patellar and skin reflexes, are also common to both diseases. A condition of the blood-vessels is sometimes present in acromegaly, which is suggestive of early atheroma, while the heart is enlarged. In other cases the thymus has been found hypertrophied. Both these conditions are present in these instances of micromegaly. In short, in acromegaly as in micromegaly, the clinical features of the disease are hypertrophy and atrophy, irregular development, and premature decay.

Is it possible that micromegaly is acromegaly modified by age? Do they bear the same relation that congenital syphilis does to acquired syphilis; or are they opposed as cretinism is opposed to exophthalmic goitre? *A priori* it seems reasonable that a trophic disease will show very different manifestations when it appears respectively in infancy, at puberty, or when the body is fully developed. In an interesting article by Dr. Woods Hutchinson giving the account of the autopsy of a giantess of about eighteen, who was 6 feet $7\frac{3}{4}$ inches high, some of the features of the disease were wasting of the mammæ,

sparseness of hair, extreme emaciation, and debility ending in death. A reproduction of a photograph of this giantess is printed with the article. In it she is represented as standing beside her two sisters, one of whom appears to be a full-grown woman, while the other, to judge by her size, is a child of less than twelve years old. Nothing is said of this girl in the paper, but elsewhere I have found that she was in reality the eldest of the three, and that she was thirty-two years of age when the photograph was taken. Now there is nothing in this dwarf to remind one of the above cases, with the important exception of her hands, which show an enlargement of the knuckles similar to that which obtained in both Mr. Hutchinson's case and my own. But surely it cannot be due to mere chance that two such rare conditions as true gigantism and true dwarfism should occur in the same family. The gigantism in this case was due to acromegaly. Acromegaly shows hereditary tendencies. Is it not probable that the dwarf also owes her condition to the same disease? ¹

Does acromegaly of infancy tend to produce dwarfism, and of puberty gigantism?

Are all dwarfs of the "Tom Thumb" type micromegalics? A few years ago I saw the Mongolian giant Chang when he was being shown in company with a dwarf. Is it possible that both the giant Chang and the feeble little midget who stood on his hand were instances of the same disease?

As a final speculation it may be asked, is micromegaly in its slight or less marked forms, more prevalent than is supposed. Mr. Hutchinson has done much to call attention to the great utility of the study of rare diseases in view of their commoner occurrence in slight or atypical forms, and of the light they throw on other diseases. I call to remembrance a case of a child of eight years of age who died from the results of middle ear disease while under my care. Though well cared for, she was thin, weakly,

¹ I have not yet been able to obtain confirmation of this relationship.

and puny, and of very feeble muscular development, but mentally she was unusually sharp for her age. Was this an instance of micromegaly of aberrant type, and if so, are there many such cases of mild or partial forms of the disease that have hitherto been unrecognised?

(For Report of the Discussion on this paper, see 'Proceedings of the Royal Medical and Chirurgical Society,' Third Series, vol. ix, p. 4.)

DESCRIPTION OF PLATE V.

On a Condition of Mixed Premature and Immature Development
(HASTINGS GILFORD).

A. R—, at different stages of disease, showing rapid and progressive general maturity.

Age one and a half years.



Allard, imp.

DESCRIPTION OF PLATE VI.

**On a Condition of Mixed Premature and Immature Development
(HASTINGS GILFORD).**

Age seven years.



Ailard, imp.

DESCRIPTION OF PLATE VII.

**On a Condition of Mixed Premature and Immature Development
(HASTINGS GILFORD).**

Age twelve years.



Adlard, imp.

DESCRIPTION OF PLATE VIII.

**On a Condition of Mixed Premature and Immature Development
(HASTINGS GILFORD).**

Age fifteen years.

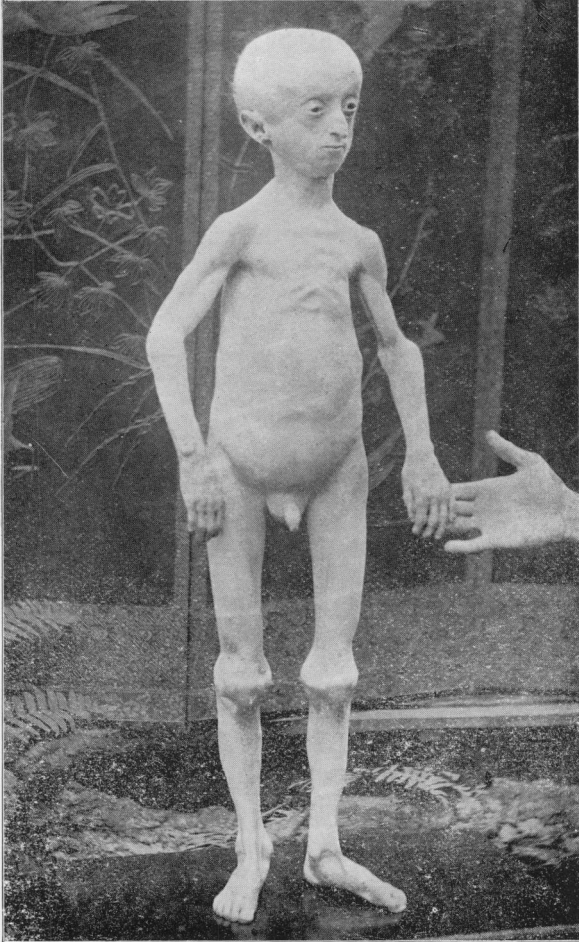


Allard, imp.

DESCRIPTION OF PLATE IX.

**On a Condition of Mixed Premature and Immature Development
(HASTINGS GILFORD).**

**Age seventeen years. Normal hand introduced to show
relative size.**

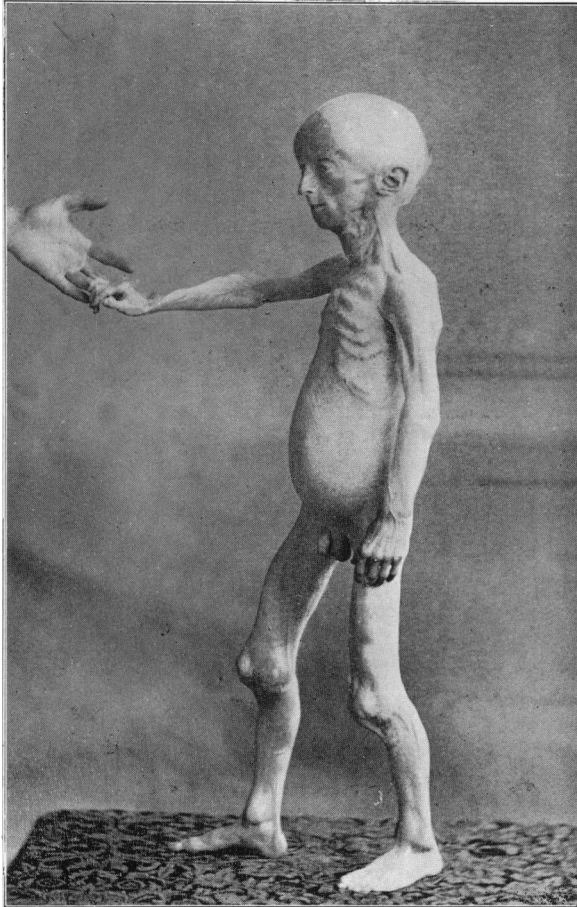


DESCRIPTION OF PLATE X.

**On a Condition of Mixed Premature and Immature Development
(HASTINGS GILFORD).**

**Mr. Hutchinson's case. S. B.— Age fifteen and a half years.
Normal hand introduced to show relative size.**

Side view.



DESCRIPTION OF PLATE XI.

**On a Condition of Mixed Premature and Immature Development
(HASTINGS GILFORD).**

**Mr. Hutchinson's case, S. B—. Age fifteen and a half years.
Normal hand introduced to show relative size.**

Front view.

