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HYPERTRICHOSIS: A REPORT OF THREE CASES

BY

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Hypertrichosis is a fairly common complaint, especially in women, and, like the secondary sex characters, usually appears after puberty; but it may occur at any time of life. It seldom remains the only symptom for long, and becomes linked with alterations in somatic growth, sex function, or general metabolism. In children it follows the pattern of iso- or hetero-sexual precocity, which may be due to hypothalamic tumour or to adrenocortical hyper trophy or tumour. In virilism it may be pronounced, and mimic faithfully the male type. The hypertrichosis of Cushing's syndrome, whether of pituitary or of adrenal origin, is more downy. In anorexia nervosa the body is covered by fine down: amenorrhoea is invariably present and the hair disappears completely on recovery.

Hair in the male is of a much more stable character. The lack of it is generally associated with lesions of the testis. Profuse hair in men is occasionally seen in rare cases of adrenocortical carcinoma and in other men with tender nodules in the epididymides, or small testes, adiposity, and sexual disorders. It may be regarded as a type of feminism.

Danforth (1925) gives an interesting summary of some cases of hypertrichosis universalis in which the patients (either from birth or soon after) were covered with long fine silky hairs of the lanugo type. "The whole face, including the upper eyelids and nose, is covered with a thick coat of long soft hair. Likewise the pubic and axillary hairs are not present in the normal form, but replaced by the same 'exaggerated lanugo' that covers the rest of the body and limbs. These subjects are referred to as 'dog men' or 'ape men,' and several have been on exhibition. When the trait appears it is transmitted as a Mendelian dominant. The condition has been variously regarded as of 'arrested development' or 'atavism' or due to mutations. In some patients the teeth are deficient."

Danforth draws attention also to somewhat similar patients in whom the hair was coarser and "seems to represent an intermediate stage between a generalized covering of soft lanugo-like or transitional hair and localized hypertrichosis of the terminal hair."

The clinical histories only are recorded, and it would be interesting to subject patients of this type to detailed endocrine investigation. The various grades of hair run on closely similar lines to the various grades of intersexuality and their relation to prepubertal virilism. If we may regard the adrenal gland as an accessory sex organ, then clinically the emphasis is on hair in its hypertrichotic states, and on the lack of it in deficient states of the gonad.

Congenital Type: Case Report

This patient, a boy aged 9 months (Fig. 1), was born after a normal pregnancy, and is the youngest of five boys, the others being normal. So far as is known there is nothing abnormal in the family history. At birth he was covered with hair. The hair of his scalp extended down to his eyebrows; that on the limbs to his wrists and ankles; that on his trunk was abundant. His weight at birth was 6½ lb. (2.95 kg.), and he was breast-fed for three months. His lower incisors appeared at 7½ months, he could stand at 6 months, his epiphysial age corresponded to 2 to 3 years. He was precocious developmentally and also in behaviour. There were no other abnormal physical signs. His blood pressure was 130/70; his pituitary fossa was normal; his ketosteroid excretion was 1 mg. a day—normal for his age.

His head was covered by a mop of dark curly hair which reached to his eyebrows. The latter were heavy; the hairs of the inner half pointed upwards, and those at the outer canthus outwards and slightly downwards. The eyelashes were well formed and fanned outwards. The face, limbs, and body were smothered with fine downy hair of a lighter gingery colour, which was longer and denser in certain regions. On the back the hair converged upwards towards the occiput and towards the spine and then trickled caudally down the midline; over the sacrum it gathered and sloped downwards into a Pan-like tail. There were no whorls. In the region of the upper arms and shoulders the hairs converged in the form of a crest towards the line of contour, as if they had been combed both back and front in this direction.

In the mid-clavicular regions this crest passed across the back of the neck in a crescentic manner, like a necklace. This might have been due to the sweeping effect of the hairs from the back of the head. On the forearms the hairs swept towards the olecranon from the radial to the ulnar border. In front of the thighs they parted outwards and inwards, and behind the thighs they ran, obliquely downwards. The nose was broad and the mouth curiously pursed up by a narrow and prominent upper lip. The big toe lay apart from the others.

Sir Arthur Keith was interested in the

FIG. 1.—Child aged 9 months, showing atavistic hair tracts.

illustrations of this patient, and writes: "We look at present on the relatively nude condition of the human body as due to the assumption of the hair distribution, which is present in the late foetal stage of our anthropoidal ancestor. The hair distribution is not unlike that of the chimpanzee in the seventh-month foetal stage. I suppose the geneticist will explain the condition by calling it a mutation, as a hark back or a case of atavism."

Comment

Brandt (1940) gives an interesting account of the pre-natal development of hair tracts in primates, more especially in relation to homologous structures of the body. Of more immediate importance are his observations on the foetal arrangement in the gorilla and chimpanzee. The hair tracts of the head start from the eyebrows and sweep over the vertex of the skull in a backward or caudal direction down to the back of the neck, where they turn laterally on both sides and proceed forwards more or less transversely. On the back the hairs continue downwards. In both the gorilla and the chimpanzee foetus there is a parting which starts over the centre of the eyebrows and runs up the forehead to the vertex of the skull.

Gray (1934-5) noticed a similar arrangement on the forehead in 7% of Australian aborigines. He says: "Most of these are symmetrical, consisting of two streams that diverge from the midline as they ascend and then sweep laterally to mingle with the main stream flowing backwards." This condition conforms to the anthropoid type, which consists of a parting in combination with the primitive mammalian type.

In the gorilla foetus the arch of the eyebrows cannot be separated from the hairs of the scalp. In the lateral part of the eyebrows the hairs, instead of running upwards on the forehead, are directed outwards and downwards. The long lateral hairs of the scalp are continued on to the cheeks, sweeping downwards and obliquely forwards. On the forearm the hairs sweep obliquely from the radial to the ulnar border towards the tip of the olecranon, where a tuft or whorl may be present.

Wood Jones (1934-5) points out how baffling, both to Lamarckians and to geneticists alike, is the arrangement of hair tracts on the back, where in man they are a complete reversal of that found in the mammal. In the mammal the mid-dorsal line represents a watershed from which the flow of hair diverges towards the flanks, whereas man is unique in that the free tips of these hairs are convergent and point upwards towards the middle line of the spine. Particularly in the axilla and shoulders, the hairs slope more towards the occiput than do those of the loin. As these hairs reach the mid-vertebral line the stream is reversed, and they trickle caudally from the nuchal region to form a sacral tuft. In his studies of aborigines in Victoria, Wood Jones found this dorsal-cephalic trend marked and without exception, and he aptly stresses the fact that in this respect man is a mammal with his head where his tail should be.

In the region where the upward dorsal and the downward cervical streams meet—the area between the scapulae—there may or may not be present a whorl arranged in either a clockwise or a counterclockwise direction.

Comparing our illustration (Fig. 1) with that of an Australian aborigine published by Wood Jones, the dorsal hair tracts conform to a similar pattern, with the exception of an interscapular whorl which is absent in our case. From these general descriptions there arise interesting points of comparison, especially of human hair tracts showing reversions to those found in lower orders. As the clinical

evidence does not point to any obvious endocrine cause we must regard the condition as one of dysgenic origin.

Adrenal Type : Case Report

This case is presented because hair was the predominant symptom. A married woman aged 57 was admitted to Charing Cross Hospital on January 19, 1949 (Fig. 2). She had three

FIG. 2.—Case of hirsuties as a result of adrenocortical carcinoma, before and three months after operation.

children—a girl aged 24 and two boys aged 20 and 15. She passed through a normal menopause, and had been perfectly well until eight months ago, when she noticed hair growing on her face. It rapidly became worse and extended to her arms, but not to her body.

On admission a large mass which moved on respiration could be felt in the right hypochondrium. Her general condition was good. A plain radiograph showed a shadow in this region with elevation of the diaphragm, and an intravenous pyelogram revealed displacement of the right kidney downwards to the level of the pelvic brim, with kinking of the ureter. There was no evidence of any secondary deposits; the pituitary fossa was normal; and other investigations were within normal limits, except the ketosteroid excretion, which was considerably raised, ranging between 300 and 400 mg. a day (normal 7-14 mg.).

Laparotomy performed on January 21 revealed a huge suprarenal tumour on the right side, which was removed transabdominally. The tumour weighed 5½ lb. (2.5 kg.). Microscopical examination confirmed the diagnosis of an adrenocortical carcinoma, and staining with the Ponceau-fuchsin dye was moderate. Following a stormy convalescence, the patient made an excellent recovery. After operation the ketosteroid excretion fell to 4.8 and 6.4 mg. a day.

In another young woman, from whom a small adrenal adenoma was removed, the facial hair likewise completely disappeared. Her ketosteroid excretion fell from 62 mg. to 7.9 mg. a day.

Ovarian Type

Post-menopausal hirsutism is a common observation among old women in asylums. It has never been satisfactorily correlated with an ovarian lesion. Arrhenoblastoma of the ovary is a rare tumour which gives rise to virilism with hirsuties in younger women. Vines drew attention to the increased number of fuchsin cells in the stroma of the ovary at the menopause, and we have found colloid carcinoma of the ovary in hens undergoing varying degrees of sex reversal.

The following case is a most striking example of hirsuties associated with bilateral ovarian tumour.

Case Report

A married woman aged 70, with two normal daughters, was admitted to Three Counties Hospital, Arlesey, on August 10, 1945, under the care of Dr. F. Mackenzie Shattock and seen in consultation with Mr. Clement Shattock. Dr. N. McDiarmid has kindly allowed me to use the hospital records.

Three months previously, in May, 1945, 25 years after the menopause, hair began to grow on her face. It became bristly and developed into a coarse beard and moustache, and the eyebrows became bushy. There were a few coarse hairs on the chest, the axillary hair was scanty, and the pubic hair was female in distribution. The voice was unusually deep, the hands were large, and the breasts were represented by two folds of skin. She became morbid, depressed, and deeply conscious of her condition, to the point of entertaining delusions. She imagined she had a "cow face" or was "turning into a dog," and that horses kept looking through her window and laughing at her.

On admission her general condition was fairly good. She was rational but uncooperative. Her blood pressure was 150/80 mm. Hg. Apart from a small aneurysm of the right common carotid and a palpable right kidney, there were no physical signs. The only other interesting feature was a white cell count as low as 2,605 (with 66% small lymphocytes) on one occasion, and 4,685 with 71% lymphocytes on another.

An intravenous pyelogram showed depression of the right kidney with flattening of the upper calix, suggesting the presence of an adrenal tumour; ketosteroid estimations done at three different hospitals were within normal limits. Other investigations were normal also.

FIG. 3.—Case of hirsuties associated with bilateral ovarian tumour.

The photograph (Fig. 3) reveals an expression sad yet saintly, and a face which could hardly be surpassed as a model of martyrdom.

Laparotomy, which I performed with Mr. Clement Shattock, showed adrenal glands within normal limits, an enlarged spleen, and both ovaries large and cystic. As the condition of the ovaries suggested malignancy they were removed.

The following is the pathological report. "Large and small ovaries (6 cm. and 4 cm. in diameter). Both multilocular, with clear yellow fluid in cysts. One contains a calcified node. The small ovary has a portion of the fimbria tubae attached: slightly thickened oval calcified nodule removed from right tube near fimbria. Small papilliferous areas on both ovarian surfaces."

Microscopically, "section of both ovaries shows numerous old follicular cysts of varying size. The ovarian stroma between them is very fibrous, and there are numerous thick-walled vessels. One corpus albicans was seen. The papilliferous area on the surface of one ovary shows fibrous tissue with a covering of degenerate columnar epithelium. Section of one end of the Fallopian tubes shows that they are fibrous and congested, and the tiny epithelium is somewhat atrophic and degenerate."

The patient recovered satisfactorily. On discharge from hospital in October, 1946, she gained some insight into her condition, but she did not alter appreciably after the operation or react to her mental outlook; nor did she undergo epilation as one would expect in a case of adrenocortical tumour.

The patient died in April, 1949, at the age of 74 as a result of a second stroke. Her hair growth remained unchanged; she expressed no delusions after leaving hospital, and was less worried about her face than about financial matters.

Discussion

Although overgrowth of hair may at first be the only symptom, it seldom remains so for long. It is usually the prelude to secondary clinical manifestations, which appear to result from endocrine imbalance. It is difficult to assess the genetic determination of hair, but a few observations published elsewhere (Broster *et al.*, 1938) suggest an early interchange between genetic and endocrine control. According to our observations on intersexuality, based on a time-table of foetal endocrine integration between the seventh and fifteenth weeks, it would seem that the chromosomal phase is completed about the end of the ninth week. Before this the gonads can be recognized structurally, and after it the adrenal cortex of both sexes passes through a male phase and the cells of the pituitary gland appear. It seems probable that during this time genetic direction may become merged to a greater or less extent in endocrine control, at a time when the embryo is passing through its most plastic and formative stage. Such an assumption would account for the various grades of intersexuality where genetic direction has been overridden by endocrine control, resulting in the incomplete determination of sex. Indeed, some endocrine states seem to be latent, and when stimulated later in life by phases of physiological stress have the power to burst forth and inflict upon their victims monstrous and inhuman changes, from which neither age nor sex is immune.

An analysis of the three cases under review points to many of the problems we have mentioned.

In the genetic type, although hair was the predominant symptom, there were superadded signs of precocious somatic development and behaviour. The primary sexual characters were normal for the boy's age.

In the adrenal type the usual sequence is for hair to be followed by alterations in the secondary sex characters. There are also somatic changes and depression of sex function. The greater the severity and the earlier the onset of the adrenal lesion the more pronounced will these changes be. There are sometimes associated psychological changes—not surprising in a syndrome which affects appearance, libido, and marital relations. Moreover, by the removal of the adrenal lesion, and by a greater or smaller reduction of androgen production, amelioration of these changes has been noticed. That few of these changes, except overgrowth of hair, were present in our patient was due to the late onset of the lesion.

In the ovarian type the position is more obscure. There are relatively few secondary sex or somatic changes, although the general appearance is masculine. The only virilizing tumours of the ovary are the rare arrhenoblastomas; but correspondence on ovarian hilus cells (Shaw and Dastur, 1949a, 1949b; Shillitoe, 1949), which are attributed to Sternberg, suggests that they resemble the Leydig cells of the testis, and probably produce androgens with consequent masculinization. It is also to be noted that cystic degeneration of the ovaries is invariably found in the adrenogenital syndrome.

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ABOLITION OF PYLORIC SPASM BY ORALLY ADMINISTERED PROCAINE SOLUTIONS

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In the course of an investigation into the mechanism of the pyloric reflex it was found that "novocain" (procaine B.P.) given by mouth paralysed the pyloric sphincter. The technique used was the usual method of screening during and after the administration of barium sulphate suspension ("barium meal"). The type of pyloric activity observed in the large majority of healthy individuals, and therefore accepted as normal, was a slow "worm-like" opening and closure.

The investigation arose out of the observation that often when the first portion of contrast medium reached the pylorus the sphincter was patent and it passed into the duodenum without delay. Whether initially open or closed, the sphincter subsequently acted as follows: (1) it remained open; (2) it contracted and relaxed rhythmically in what has been called the "worm-like" movement; or (3) it closed abruptly—that is, went into spasm after the initial filling of the duodenal cap, and either remained closed or reopened only after prolonged deep massage of the epigastrium.

As the subsequent behaviour of the pyloric sphincter seemed to be unrelated to its initial state, the problem to be solved was, What determines whether the sphincter is originally open or closed?

We have observed that if the volume of contrast medium first entering the stomach is large enough to distend the pyloric antrum quickly (which can be achieved by inducing the patient to drink the suspension rapidly) the sphincter is nearly always found to be open. If, however, the barium suspension has been taken some time before screening (whatever the speed of swallowing), or if the contrast material is drunk slowly during the screening, the pylorus is nearly always found closed. The essential point of the latter circumstances seems to be the gradual filling of the pyloric antrum.

These facts suggested that the pylorus of an empty normal stomach under physiological conditions is open. Therefore, a series of cases was investigated in which it might reasonably have been suspected that the pyloric

sphincter was at first closed—for example, gastric ulcers, gastro-enteritis, carcinoma ventriculi, etc. It was noted that, even in some of these cases, if the contrast material was consumed rapidly it found the sphincter open. In these cases, after some barium had passed through, the sphincter went into spasm. From observations on several hundred cases over the course of almost four years it was deduced that under physiological conditions, in an empty stomach, the pyloric sphincter is open; it is closed only by some effect upon it of material passing from the stomach—whether nutrient or radio-opaque in character.

Holzknacht and Jonas (1909) have shown that in the empty stomach, although the walls of the pylorus are close together, the sphincter has a very low tonicity, so that material which does not act as a stimulus—for example, isotonic fluid at 37° C.—can pass it without hindrance. Hot or cold, hypertonic or solid materials cause a closure in most cases. This is in accordance with the observations mentioned, because the fine suspension of barium at body temperature, reaching the antrum at once, does not initiate this slow reflex mechanism, which is, however, put into action by the contrast material when this is drunk slowly.

Klee (1920) and Kestner (1924) found that the tonicity of the pylorus alters rhythmically and depends always on that of the stomach. Wheelon and Thomas (1921, 1922) proved with balloon experiments that the tonicity of the pylorus corresponds to that of the antrum. This was confirmed by Bárony and Hortobágyi (1924). The present work seems to confirm the suggestions that contrast material causing tonus in the stomach acts also as a stimulus to the closing of the pylorus.

However, there are indications that it is not only the tonicity of the stomach that determines the behaviour of the pylorus. As is known from the experiments of Cannon (1911), significant changes may occur in the tonicity without affecting a constantly closed or constantly open pylorus. These observations suggest that the pyloric reflex mechanism has extragastric components as well.

Probably the most important of the extragastric components is the autonomic nervous system. The vagus fibres end in the cells of the Auerbach plexus. However, consistent results are not obtained from their stimulation. McCrea and M'Swiney (1928) found that in the hypermotile stomach it initiates movements. It is generally accepted that the sympathetic nervous system relaxes and the vagus closes the pylorus as suggested by Thomas, Crider, and Morgan (1934).

Beattie and Sheehan (1934) stated that in the tuber cinereum there is a stimulating centre, while in the back of the hypothalamus an inhibiting centre is found. However, after total denervation of the stomach there occurs only a short pause in its movements. The vagus-compression experiments of Danielopolu *et al.* (1924) demonstrate mixed stimuli because the vagus itself is a mixed nerve.

The theory of the role of acid and base in the pyloric reflex is to-day regarded as doubtful. Van Liere and Sleeth (1940) stated that increase of acidity increased motility, but this was denied by other authors (McClure *et al.*, 1920; Baird, Campbell, and Hern, 1924; Bárony and Egan, 1925; McCann, 1929).

Experimental Findings

Statistical data were collected from barium-meal cases examined during the period 1940-6. The series consisted only of "normal" cases in which the barium-meal examination was done chiefly as a control and in which no specific

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