# A HEREDITARY ECTODERMAL DYSTROPHY*

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THOUGH extraordinarily rare, according to medical literature, the form of hereditary dystrophy of the hair and nails about to be described, is comparatively a commonplace in this part of Canada, where it is peculiarly associated with the French race. In fact all the cases reported on the American continent have been of French Canadian origin. The only other families referred to in the literature are not only from France but from that section whence came the early settlers to Canada. One can infer a common familial and individual source at some time more than 170 years ago (previous to the Battle of The Plains of Abraham in 1759) That it is not a racial but a familial trait is shown by the fact that the defect readily carries over into German, Anglo-Saxon and West Indian admixtures. The group reported from Buffalo, N.Y., by Jacobsen[1] is a direct branch of our family. Including his cases with ours we have not only the largest family group described (119), but considerably more than all others combined. Of the family about to be reported upon, 40 have been inspected, some closely and some casually. This, also, is a larger number than the combined total of cases seen by all the other writers.

The supposed rarity of the condition seems most astonishing to those of us who recognize it. I know of at least three other family groups which between them would add another hundred or more cases. A study of Chart I shows that on the average each affected individual passed on the defect to three others. A simple calculation would indicate that there are at least six thousand in America, (three to the eighth power).

Constant features are heredity and nail dystrophy.

## HEREDITY

Through unusual circumstances I have seen members of five generations. Two who are great-grandfathers have been examined. These, can give information about their grandmother who was the most remote sufferer from the defect about whom we can obtain a history. She had five children with the dystrophy. One daughter is the ancestress of Jacobsen's group. One son is the head of the group which I can check and cross-check closely, having seen more than half of them. On another son only partial information is readily available, but such as it is, it has been included in the chart. I have excellent reasons for believing that the remaining son and daughter are represented by two groups about which I have some information, but, lacking complete identification, they are not included in any way.

There are 118 descendants of the original woman shown by the incomplete chart to have had the dystrophy.

| *Sex of Cases* | | *Parent Affected* | |
|---|---|---|---|
| Males | Females | Father | Mother |
| 57 | 61 | 60 | 58 |

*Children in Groups A, B, C. only*

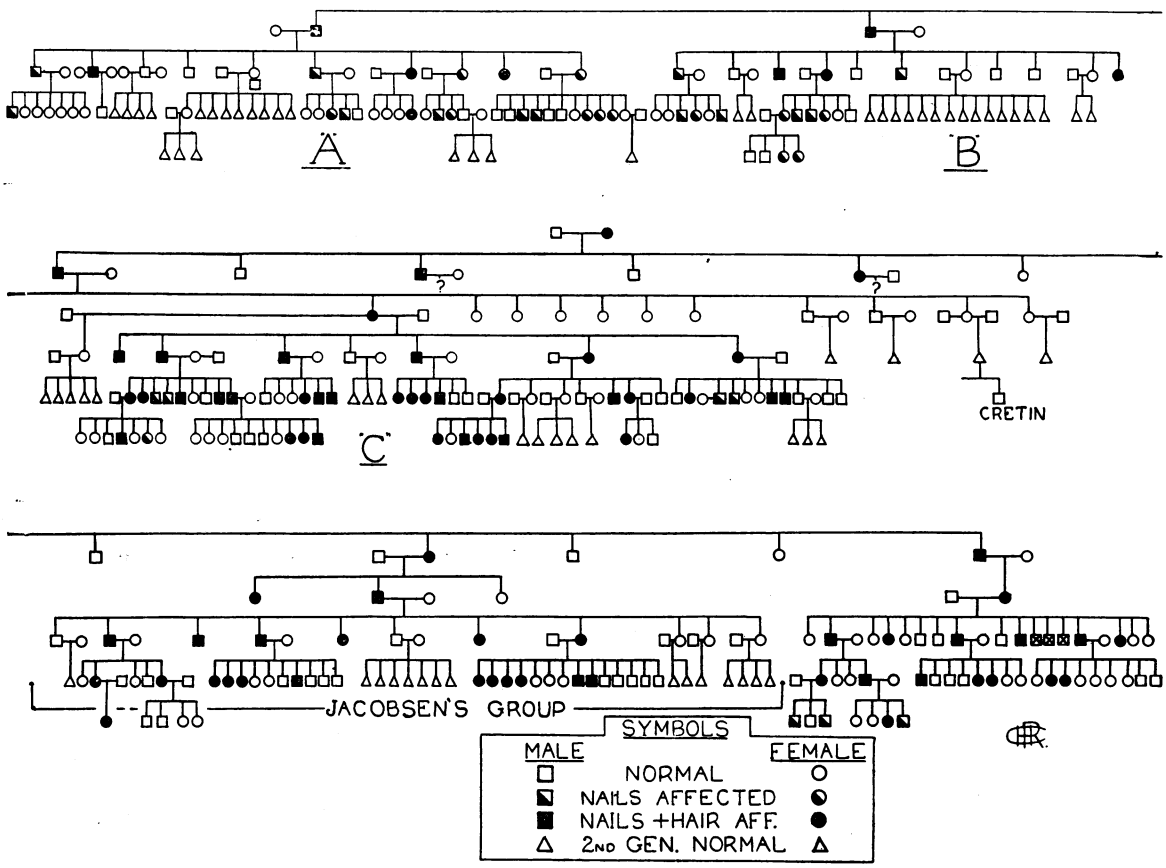
| Defective Fathers | Defective Mothers |
|---|---|
| 83 children | 82 children |
| 38 defective | 41 defective |

In other words males and females are equally affected; males and females transmit it equally; and one-half of the children of defectives are defective. It therefore follows the law of a Mendelian hybrid, not sex linked, the defect being a dominant.

Practically always the mating of an affected person with a normal gives a mixed progeny. The apparent exceptions present no difficulty to the students of chance and probability. If a child escapes the defect, he and his heirs are free forever. It never jumps a generation. Moreover, even where the normal child of an affected parent marries the normal child or normal grandchild of an affected person the dystrophy does not return. Neither does it increase the dystrophy in the children when the affected person marries a normal who is de-

* Read before the Montreal Medico-Chirurgical Society November 17, 1928, and the General Session of The Canadian Medical Association, June 21, 1929.

CHART I




The three sections fitted together from left to right form a single family tree. No attempt has been made to chart any normal line after the 2nd generation, and in some instances the single triangle represents a whole family of normals. In no case has the dystrophy occurred in the family of "normals".

scended from a defective. We have instances illustrating all three. As a dominant it is either visibly present or wholly cast out.

White[2] has reported a group in which it was said that there was one instance where the normal child of an affected parent was the father of a defective child. Thompson,[3] in the case of a familial nail dystrophy, also reports an alleged instance of reappearance of the defect. Neither White nor Thompson were able to confirm this personally. We also ran across an alleged instance, only to find on inquiry that a wife had given misinformation about her husband. A learned and philosophical member of the affected group, who had made some study of the family, laid it down as a law that normal parents never begat defective children, and if it appeared to be so, there was evidently "a cuckoo in the nest."

There is a belief among them that the condition tends to die out, both as to the number affected and its severity. There is much evidence to support this in the case of some groups. On the other hand there are at least three instances where the children have a more severe grade than the parents. There are also cases in the sixth generation in which the dystrophy is nearly as severe as it ever was, and families where the proportion is just as great or greater. (See group "C").

The condition is not wholly characterized by any fixed signs or symptoms, and the difference in the clinical findings noted by the various reporters seems partly due to their scarcity of clinical material, and partly to the great variety of forms in which the interplay of many factors permits them to be expressed. One sees every degree of defect. They themselves divide the afflicted ones into two groups, *viz.*, (1) those with "bad nails and bad hair", and (2) those with "bad nails only". On close examination of a large number this is seen to be inaccurate. Members of the family will disagree on the classification of certain border line cases, and actually

there is every grade of the condition to be found. The individual who admits that he is in the first class either wears a wig or other head covering constantly, except when in bed. A few have the moral courage to disregard this custom.

We shall take up the subjects under separate headings, as The Nails, The Hair, The Eyebrows, etc.

## THE NAILS

No case has been counted among the dystrophic ones unless the nails were involved. The toe nails are always affected when the finger nails are. As Nicolle and Hallipré[4] noted, the nail defect is more persistent than that of the hair. This suggests that certain familial nail dystrophies may really be milder expressions of the same condition. (*e.g.*, Thompson's cases were found to be of French origin).

Microscopic examination of scrapings has proved negative for mycoses in our cases as well as in all others recorded. Moreover, the distinctive condition can be recognized in the newborn child.

The nail defect varies enormously and several degrees of dystrophy are frequently found on the same hand. As might be expected in an hereditary condition there is a tendency towards a symmetrical arrangement. In the mildest condition noted the nails were merely thickened and slightly discoloured, striated longitudinally, and, if long, were bent forward at the finger-tip like a beginning claw. The appearance is little different from the condition seen on the hands of those whose nails are subject to trauma, but the growth, if any, is extremely slow. It is common to find one or more of this grade even in the severest cases. In only one case were they all of this class.

A second grade shows a concave free edge behind the normal line and great convexity from side to side. In infancy the nail may be milky white and thick, as though watersoaked. In early childhood the surface layers of the nail seem to be more concentrated and normal, but bulged from beneath by imperfect horn. If the nail is long it will be found that it is really separated from the nail bed for at least the forward one-third and for varying distances farther back as the condition is more severe. Some of those affected state that this forward bayonet-like projection naturally tends to accumulate dirt, and that it is liable to catch on things and be torn backward, with resultant infection. They say that they keep their nails trimmed back to the nail bed. Trimming is very seldom necessary. The forward part may seem to dry and wither and show a distinct line of demarcation from side to side. (This is possibly the result of the action of soap, water, the elements, and trauma on both sides of a nail which is growing extremely slowly). In a seven year old boy a crack appeared along this line and the withered portion fell off. The sharper border then tends to wear off and may result as shown in Fig. 1.

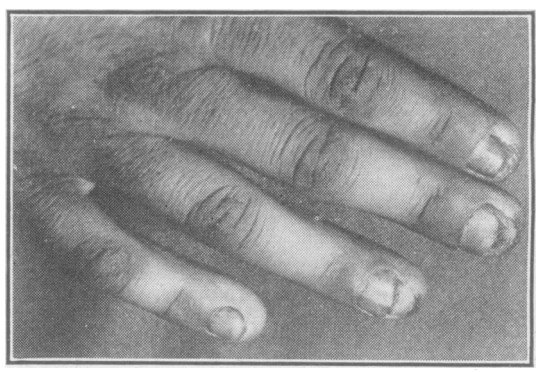


FIG. 1.—Mild form of nail dystrophy associated with good hair.

In a more severe grade there is a central ridge which runs forward and upward. The nail may be split along this ridge, as seen in Fig. 2. In some cases the underlying debris seems to have escaped and the divided portions lie flatter. If the separate pieces grow they may curve forward in opposite directions, or, if they do not, there may be only short tags of nail at the root. Some of these defective nails are very deeply pigmented.

A still worse grade shows only a pigmented fringe of nail bed around the nail grooves, or there may be only cicatricial tissue where the nail should be. (Fig. 3).

Defective nutrition, becoming progressively worse the greater the distance from the lateral vessels, might explain the slower central growth and the consequent concave free edge and also the central splitting. Defective nutrition is also displayed in the proneness to sub-ungual inflammation as the result of slight trauma. This condition is very slow in healing. Nicolle and Hallipré were greatly impressed by the vile stink which is a constant feature of this suppuration.

The victim can readily agree with Lady Macbeth that "All the perfumes of Arabia will not sweeten this little hand." As a means of fighting the Devil with fire, iodoform is preferred by some, but thymol iodide, etc., are very useful. There is a persistent belief among these families that about puberty there is a change from the nails of childhood towards the condition which they will assume for the rest of life. They say that there is more inflammation about this period and that the nails come off, break off, or split, etc. Observation tends to confirm this statement. This may be due to the increased liability to injury as the older children begin to work. If however the condition has an endocrine association, as some believe, this may have some significance. Inflammation is much less frequent after the age of twenty-five than before it. Wholly unconfirmed is the idea held by some of their fellow citizens that the attacks correspond with some phase of the moon or menstrual cycle.

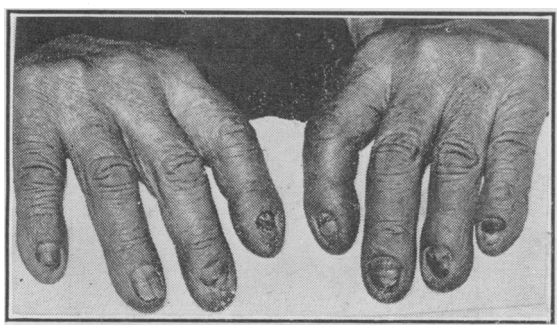


FIG. 2.—Note the clubbing of ring-finger.

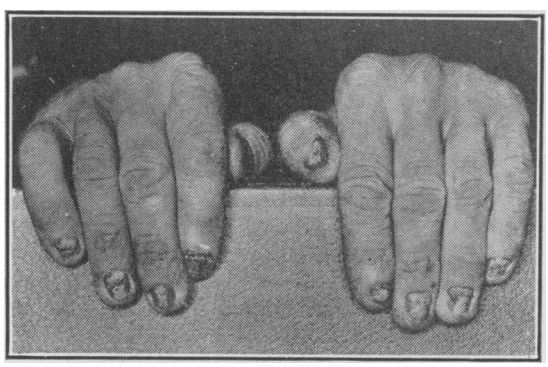


FIG. 3.—Severe grade. Note the absence of nails on some fingers.

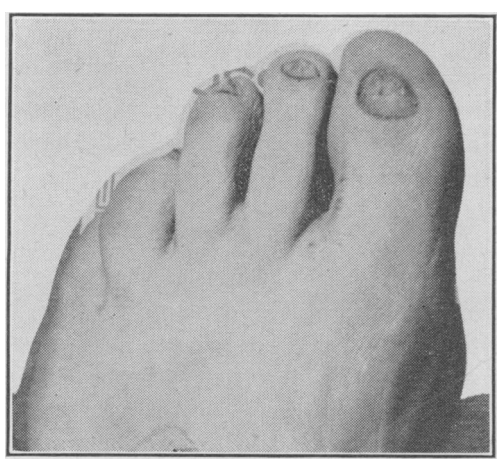


FIG. 4.—The toenails are always affected when the fingernails are.

## THE HAIR

According to their own classification of themselves (largely followed on the chart), about one-half of the patients have good hair. They are nearly half right. About 20 per cent of those inspected showed no discernable dystrophy of the hair. They range in age from 3 months to 16 years. It is worthy of note that in those inspected no individual over sixteen years of age who had dystrophy of the nails failed to show some of the hair also. It is quite possible that some of those now considered normal will not be so classed as they grow older. On the other hand, it gives support to the belief that there are some forces at work tending to make the condition "run out." They say that their hair does not wear well. The growth at best is very slow, and when the destruction due to wear overtakes the replacement power the defect appears. In the mildest condition the hair, though fine in texture, seems normal on the top, the front, and the sides, but somewhat shorter, finer and more lifeless from the occiput down the back of the neck. To girls of this grade the modern method of hair dressing known as the "Boyish Bob" was a godsend. The short hairs could be equalized and the use of certain lotions would make the hair appear more normal. In a more severe grade there may be a bald spot from the occiput downward, with the edges passing gradually into more or less normal hair. Presumably this is just where the head touches the pillow. Practically always one can account for any patchiness by friction and wear. Where a complete wig is worn, the distribution of the short, sparse hair is often remarkably uniform.

There are successive gradations in which the hair is shorter and shorter and more sparse, until there is only a slight lanugo-like growth which may not be apparent a few feet away.

In a few cases there was no hair of any kind. These are older people. They will usually give a history of "fever," or insist that the wearing of the wig is responsible for the complete baldness. It is to be understood of course that one grade does not necessarily pass into another, except as the hair may deteriorate in normal people and for the same reasons. The youngest child may be almost completely hairless and remain so, as shown in the family history, for 113 years.

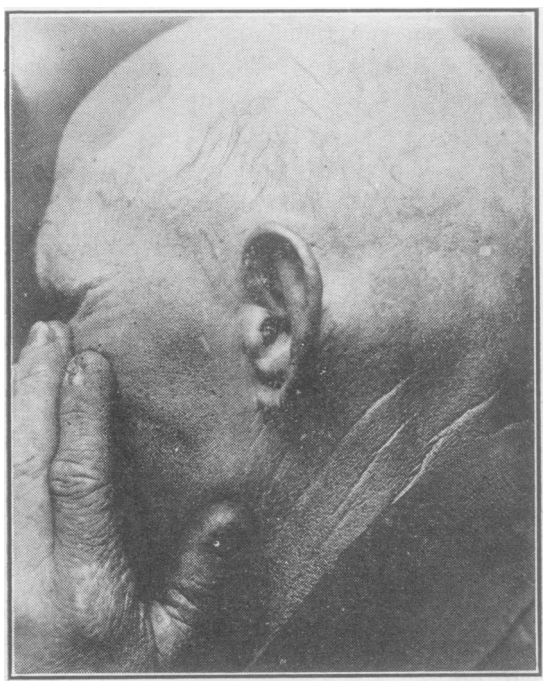


FIG. 5.—A common hair condition.

French Canadians as a rule are dark haired people, although there is also a blond strain, derived probably from the Norse vikings who swept Northern France and mingled there with the dark haired Franks. In this family there is an unusually large proportion of blonds, as was true also of the cases of Nicolle and Halipré of Rouen. This blondness, when present, accentuates the apparent amount of the dystrophy—the blond fine short lanugo-like hair being almost invisible (Fig. 6). It is not an essential part of the dystrophy, however, as is shown by the fact that there are some good heads of golden hair in children showing the nail defect, and also by the fact that some of the most marked cases have dark pigment in the lanugo-like hair. Indeed, in some instances, the scalp of a victim would be absolutely interchangeable with the skin from the leg of a normal brunette. It is a blondness and not an albinism.

The hair is very fine and is rather dry and brittle. Microscopic examination shows only a fine hair, otherwise normal. Some writers have found that the hair pulls out very readily. This is not a feature of my cases. There is also the statement that the hair falls out at eight or nine months and never returns. Experience with this family would indicate that this is merely a shedding of embryonic hair which occurs frequently in normal babies as a normal process. Many of this family have the extreme form of dystrophy from birth.

FIG. 6.—A boy of the sixth generation.

### THE EYEBROWS

The eyebrow condition is perhaps the most striking feature of the dystrophy. The head may be hidden by a wig or hat. The nails are so instinctively hidden that those in close contact with the sufferers may never see their deformities. But the eyebrows proclaim to the initiated not only the condition but the extent thereof. In hyperthyroidism the eyebrow is

frequently thinned in the outer third. In this condition, with extremely rare exceptions, it is thinned in the outer two-thirds. Usually this section is thinned so much that it appears absent at a short distance and often is missing altogether. The condition of the inner third indicates with fair accuracy the amount of hair on the head. When there is hair, the dividing line between the inner and the outer two-thirds is usually quite abrupt (see Fig. 7). This line

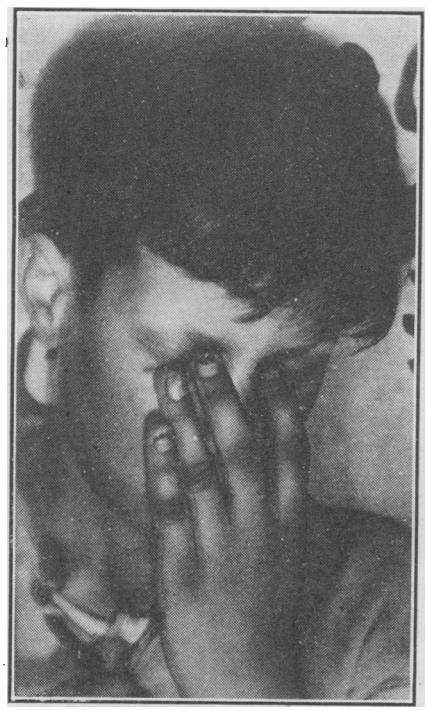


FIG. 7.—The eyebrow sign. The eyebrow stops abruptly at the supra-orbital notch. Note the pigmentation of the knuckles.

corresponds to the supraorbital notch which carries the artery, vein, and nerve, and is presumably an embryological division. Eisenstaedt's pictures show this division, but no writer seems to have noted the exact line.

The eyelashes are small and few in number, corresponding to the general condition. Sometimes they are entirely absent.

The pubic hair holds its normal proportion to that of the head. It is sometimes entirely missing. When present, is usually of the female type of distribution—confined to the mons—and may be compared to that of normal youths at the beginning of the pubescent changes. Axillary hair is present or lacking according to the condition of the rest of the body. On other parts of the body there is extremely little if any growth. Occasionally a man with a quite severe type of the dystrophy shows a fair amount of hair on the chest, but ordinarily the lanugo hair is as conspicuously affected as the rest. In one case there was a thin moustache.

## THE SKIN

Since the hair and nails are only appendages of the epidermis, one might expect to find further epidermal dystrophy. Since the one constant factor is the dystrophy of the nails and since the nails are merely thickened stratum lucidum, one would look for signs of it in those spots where the stratum lucidum is present, *i.e.*, the palms of the hands, soles of the feet, etc. In very few cases was it entirely lacking. This condition, like all the others, varies so greatly, and the milder grades shade into the normal so gently, that the observer must know what he seeks and where to find it. Tobias[5] noted some thickening of the skin on the distal phalanges and the verrucous condition at the free borders of the nails. Eisenstaedt[6] also noted this and an increase in volume of the same phalanges. He also noted a papillary hypertrophy and pigmentation in the axillary region and the anterior surfaces of the knees which was suggestive of acanthosis nigricans. None of the writers on the familial type of this dystrophy seem to have noted the very striking condition of many of the hands. Sutton remarks on the hyperkeratosis sometimes accompanying dystrophy of the nails and Gottheil,[7] discussing Eisenstaedt's cases, says that it is evidently closely related to the hereditary type of hyperkeratosis of the palms and soles.

Nearly always there is a papilliform hypertrophy on the lateral and posterior surfaces of the phalangeal and metacarpo-phalangeal joints and the free edge of the nail. This also occurs sometimes on the elbows and knees. Frequently the whole palm and sole have an extraordinary appearance (Fig. 8). The natural lines are much accentuated. The furrows and ridges, when definable at all, are much coarser than normal and have some tendency to intercommunications, "like the bark of an elm tree." Over the remainder it would appear that the ridges were divided irregularly at right angles. When the papillary projections so formed are fine they resemble

the "pile" of a carpet and can be parted in the same way so that one can look down into the base. In the coarser forms the result is an irregular mosaic. Usually there is not the hard consistency about the surface which one would expect from the thickening. In one case with the severest dystrophy, in a man who was engaged in heavy manual labour, there was the appearance that the projections had worn off the bearing surfaces of the palms. It was present on the lateral and posterior surfaces

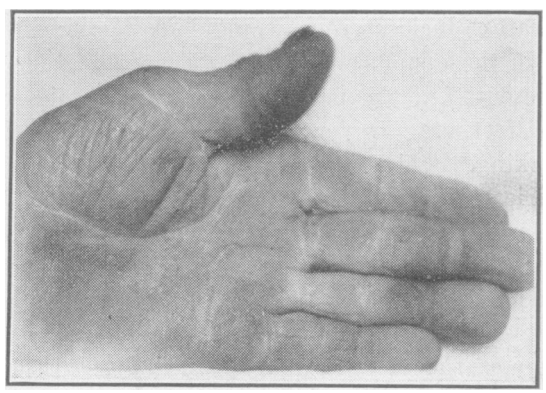


FIG. 8.—Hyperkertosis; pigmentation; clubbing of fingers.

of the phalangeal joints. The resultant surface was abnormally smooth and the palms were curved forward as though by the contraction of scar tissue. There was the history of a cracking of the skin with infection.

The degree of skin alteration does not run absolutely parallel with the severity of the hair and nail dystrophy. It is more marked in the males than in the females and more in the adult than in the child. In the lightest case recognized as one of the dystrophic ones the hair was good (the eyebrows met across the forehead), yet the palmar condition was very marked. It is evident that here is the link between this dystrophy and the condition known as keratosis palmaris et plantaris.

It has not been possible to obtain a piece of the whole skin from these parts for microscopic examination, but in one case the surface layers were lifted from the sole of the foot of a boy by a large pustular bulla. The new soft skin underneath seemed nearly normal, and the change from normal to abnormal seemed to have occurred in the surface layer. In this separated piece the openings of the sweat glands were very large and appeared to be the factor which divided the ridges into papillæ. The papillæ on the surface, therefore, do not represent the papillæ of the corium which are much smaller. "A ridge is composed of two or more rows of papillæ and the ducts of the sweat glands emerge between rows of papillæ and open on the curved surfce ridges." Gray's Anatomy).

Apart from the skin of the palms, soles, phalanges, and occasionally the elbows and knees, there was no roughening elsewhere.

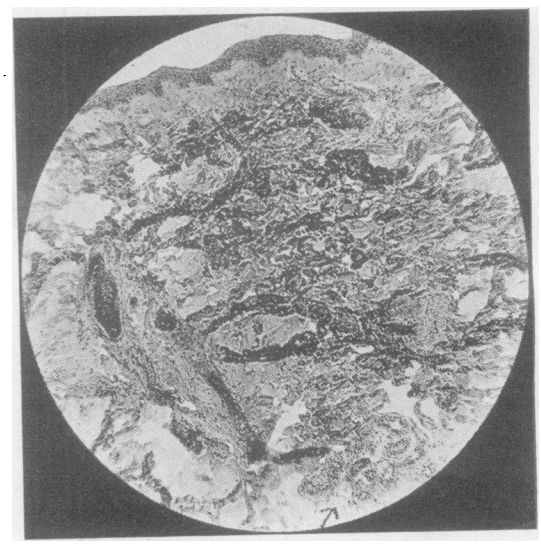


FIG. 9.—Microscopic section. Note the sweat gland which differentiates the condition from the MacKee-Andrews defect.

Indeed before middle age the skin seems to be of very fine texture. Its striking smoothness apparently is due to the absence of hair and follicles.

Clinically the sweat glands are very active. The female mammæ (which are modified sweat glands) are unusually excellent. Some of the mothers nurse their babies for two years and more as a contraceptive measure.

It is difficult to judge the condition of the sebaceous glands macroscopically. The skin is dry. The hair is rather dry. Both sexes seem to be comparatively free from acne.

Through the courtesy of Dr. J. F. Burgess, a microphotograph of a section of the skin of the scalp is reproduced. The patient was a female, seven years of age, and a member of the sixth generation of this family. The section is from the mid vertex and shows the sparseness of the hair follicles and their small size. No sebaceous glands were found in any part of the specimen removed, but occasionally

there were clumps of cells in the appropriate position which might represent them in a rudimentary state. The sweat glands are relatively few in number, but definitely present and normal. The derma is thin and somewhat atrophic. There is absolutely no suggestion of myxœdema.

MacKee and Andrews[8] have described and photographed a "Congenital ectodermal defect" which shows an astonishing number of similar characteristics, but there are also equally striking differences. In their cases there are no sweat glands and no sweating. In the dystrophy described here there is free sweating. The section shows a sweat gland (Fig. 9). Their cases have different racial origins, do not follow definite Mendelian laws in heredity, have papular skin on the face, and invariably have saddle-backed noses. In my cases there are smooth skins and there are some well marked Roman noses.

In this family a nail defect is constant and the tooth anomalies are relatively slight. In the other type the nail deficiencies are of a less severe form and are not constant, but the teeth are very markedly affected both in numbers and in conformation. Weech,[18] in an article which was published since this paper was first read, calls the other type the anhidrotic form of ectodermal dysplasia).

### PIGMENTATION

A characteristic often remarked upon is a colouring which suggests the orientals. This is not intense enough to attract great attention among people who work much out of doors, but certainly they tan readily with a peculiar tinge. In addition there is often increased pigmentation over the phalangeal joints and sometimes on the knees and elbows (Fig. 8) The nipple areola is usually relatively dark. There is frequently pigmentation in the axillæ and about the genitals. In one patient a certain black appearance of the palms was subjected to washing with soap and water, gasoline, ether, and alcohol without effect. It seemed to be pigment. He also showed a roughness and deep pigmentation over the tuberosities of the ischium. Some cases show pigmented spots on the skin in other places and in one instance the only trace of an alleged burn was a yellowish patch about three by five inches. One case showed pigmentation of the mucous membrane of the mouth. Many of the nails are coloured deeply. In many cases the teeth are poor and pigmented. There are some notable exceptions to this, however. Another striking feature in some cases is the extreme depth of colour of the iris. This is sometimes so marked that the pupil cannot be distinguished at a short distance.

### THE TEETH

As a whole they have poor teeth, but there are some with the severest form of dystrophy whose teeth are very good. In one case there is dependable history of several of the second teeth failing to erupt. Occasionally there is wide spacing. In a year old baby which has been under observation since birth the teeth are erupting normally and there is seldom any history in other children of marked delay.

### BODY CONTOUR

The majority of the victims are rather short in stature and light in weight, but they are not marked out in that respect from their normal brothers and sisters. In a few cases they are over the average in height. In less than 10 per cent is there anything suggestive of hypothyroidism.

Frequently there is a relative enlargement of the distal phalanges, both in length and breadth, even in children. This is most marked in the middle and ring fingers. In the adult, especially the male, this may become a definite clubbing and there is an increase in breadth, though the hands are usually small. In one man the hands might almost be said to show gigantism. In another the metacarpals and phalanges are disproportionately long (see Fig. 11). Kyphosis in the older males seems much more common than usual.

### NERVOUS AND MENTAL CONDITION

In this, as in every other feature, there is enormous variation. Among those showing the severest dystrophy there is to be found a highly respected city clergyman, a nurse who served in France, the mayor of a village, a manager of a "go-getter" sales force for a large corporation, and a states trooper on the border patrol. It is scarcely necessary to point out that neither

religion nor learning, neither business nor political acumen, necessarily exempts one from the defects of an inherently weak nervous system nor the effect of endocrine imbalance. On two occasions an outstanding member of the group has required institutional treatment for a "nervous breakdown." On the other hand, in groups A, B, and C (80 cases) there are 7 frankly mental defective (9 per cent). One of these is an idiot. This is a female, who is short and thin, with small bones and a small head and practically hairless. Before being sent to an institution, at about forty years of age, she had never allowed shoes or stockings on her feet. She walked upon the toes and front part of her foot with her heels some inches from the ground. She would not sleep on a bed but curled up on the floor. She carried on a spiteful, senseless chattering. The other mental defectives as a whole are small, and seem to have a mental and physical asthenia.

Two of the mental defectives have strabismus. Strabismus was found 4 times in 80 in the group (5 per cent). In Jacobsen's group there were several who stammered. This has been noted once in this branch of the same family. Epilepsy is present in one case. Nicolle and Hallipré recorded these conditions and state that "they seem to indicate that the dystrophy of the hair and nails is not the sole stigma of decadence in this family of degenerates."

Barrett[9] found a very high proportion of delinquency in his cases and also many neurological defects in members of the family who were free from the dystrophy of the hair and nails. The group that I have studied, on the contrary, is a particularly mild and harmless lot of citizens. Behaviour abnormalities in the normals are no more frequent than in the surrounding population. There is one mental defective and one cretin among the normals, but nothing like the conditions found in Barrett's cases. His photographs do not look like mine. He found a high proportion of myxœdema in his family. Employers of labour state that as a whole these people are under average for their purposes. Even here there is the exception who is better than the average.

To what extent the mental condition is due to the innate and hereditary ectodermic defect, and how much to the oppression on the part of the rest of the human race, is a nice question to decide. One of the first anxious questions after birth is whether it is like the father or the mother. The pregnant neighbour woman turns from them for fear of marking her child. The young savages of the human species with exquisite cruelty chant nicknames and derisive rhymes. School boards sometimes require certificates that they are not diseased. The nail suppuration at times ostracises them from their own social groups. Imagine the mental effect of keeping the nails constantly in hiding. Strange workmen object to them being included in the gang, for fear of syphilis. Remember that their matrimonial opportunities tend to be restricted to those whose opportunities are also limited or to the more broad minded. It is difficult to calculate the effect of this selective breeding for generations. It is obvious that these people have not received a fair deal from man, and they wonder plaintively why God allowed them to come into the world "like that." They do best in occupations which do not call for too great exertion of any kind.

### HEALTH CONDITIONS

Their infantile death rate is normal. They seem fairly resistant to infections, and they live to fine old ages. One woman is said to have been proved by birth certificate to have reached the age of 113. Two men, brothers, are 87 and 85. The former splits much of his own wood and is quite active generally. Their father died at 90.

There is absolutely no indication of syphilis and Wassermann tests have been negative.

### ENDOCRINE GLANDS

Most writers suggest an endocrine origin. As there has been no histological or pathological work done, we here enter the realm of pure speculation, but an investigation of the evidence so far secured yields interesting, and hitherto unsuspected results. The various glands will be considered individually.

### THE GONADS

1. *Female.*—Menstruation is said to have begun at 11 in one of the severest cases and also in one of the milder ones. Another mild case began at 16. No significant relationship could be made out between the amount of dystrophy

and the earliness or lateness of menstruation. The female form and the breasts develop normally. The desire for personal adornment is quite as great as among their normal sisters, and all the "flapper" instincts are quite as fully manifested. At least one was married before 15 years of age. Pregnancies are normal, and abortion or miscarriage is very rare.

2. *Male.*—In the male there are the regular voice changes and there is, sometimes, a slight growth of hair on the face and chest. The amount of hair which appears on the pubes is proportionate to that on the rest of the body, but it shows a tendency to assume the female type of distribution. One gains the impression that among the males there is some retardation

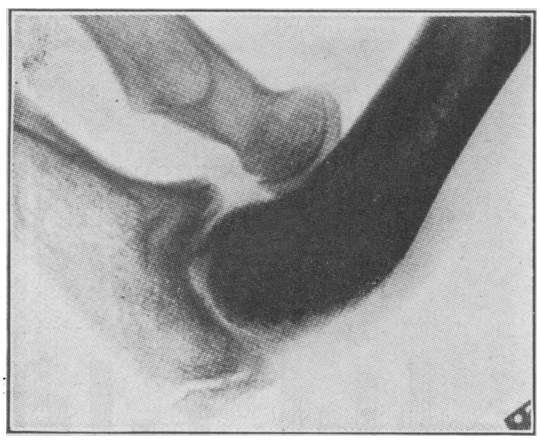


FIG. 10.—Ununited epiphyses in a boy in his 17th year. The dislocation of the radius is congenital.

of maturity. There is support for this idea in the x-ray examination of the hands of two boys in their seventeenth year. The epiphyses are abnormally widely separated. Films of the elbows of one of them show that the epiphyses of the radius and ulna are still ununited. (The radius should unite at puberty and the ulna in the sixteenth year.) Both elbows showed the same condition. The congenital dislocation of the radius which was present in this case permits a better view of the radius than is usual (Fig. 10).

They also tend to marry later than other males in their station. Once matured, a high proportion of them marry, and, if reproduction of the race is any test, it is evident that both sexes are adequate. Furthermore neither castration nor any known form of infantilism produces such nail and hair changes as are here recorded.

### THYROID

Some writers have suggested that the condition is basically a thyroid deficiency. Barrett diagnosed myxœdema in some of his cases and proved it by biopsy. Ten per cent of our cases had an appearance suggesting hypothyroidism. However, it is to be remembered that these people and their ancestors have lived in a goitre district, and there seems quite as much thyroid affection in the normal inhabitants as in the affected group. While congenital hypothyroidism or cretinism is well known there has never been found any nail or hair condition to compare with this one. Indeed there is a case of true, and extremely marked, cretinism appearing on the chart as "a normal."

A comparison with our cases shows the following points.

TABLE I.

| | *Cretin* | *This Dystrophy* |
|---|---|---|
| When suspected. | Not for months. | At birth. |
| Dentition. | Delayed. | Mostly normal. |
| Teeth. | Poor. | May be good. |
| Skeleton. | Stunted (less than 4'7") | Some over average. |
| Epiphyses unite. | Late. | Late. |
| Nose. | Depressed bridge. | Some Roman. |
| Body. | Thick "pot belly". | Normal. |
| Legs. | Bowed. | Normal. |
| Sweating. | Never. | Normal. |
| Hair. | Coarse. | Very fine. |
| Eyebrows thinned | Outer third. | At least two-thirds. |
| Nails. | Thin brittle. | Short thick. |
| Skin. | Thick, white. | Thin, often pigmented. |
| Sexually. | Sterile. | Fertile. |
| Mammæ. | Poor. | Good. |
| Mentality. | Always dull. | Sometimes bright |
| Lips. | Thick. | Normal. |
| Metabolism. | Low. | Varied. |
| Pulse. | Slow. | Normal. |
| Hands. | Broad in youth. | Broad in age. |
| Life. | Usually short. | Often long. |

The basal metabolic rate has only been taken twice. Jacobsen found a plus 23 on a child; but points out the unreliability of rates in children. In the only in which it was taken in our group, it was minus 14 in a man of 67. He was 5 feet 6 inches tall and weighed 222 pounds. Unfortunately he is the only male in

those inspected who showed obvious overweight. (It should not be forgotten that hypothyroidism is not the sole cause of a low basal rate.) A well marked case was in the Royal Victoria Hospital, Montreal, with a compound fracture of the tibia and fibula. A report on him says "At that time he did not show any signs of hypothyroidism." He left the hospital after six weeks and in a few months there was no discernable disability. There is no defect in the healing power.

Hypothyroidism undoubtedly is present at some stage in some of the cases, but it is not an essential part of the dystrophy and, as will be seen later, it would appear to be secondary to affections of other glands in the endocrine chain, rather than primary and causative.

### SUPRARENAL GLANDS

Eisenstaedt noted a condition suggesting acanthosis nigricans. Such an appearance was present over the tuberosities of the ischium in one of my cases. Acanthosis nigricans is believed to be due to some disturbance of the chromaffin tissue of the abdominal sympathetics, which in turn is similar to that of the adrenal medulla. The pigmentations already noted on the knuckles, knees, elbows, axillæ, nipples and genitals, the exposed parts, etc., may to some extent be explained by the hyperkeratoid condition of the skin. However, in distribution they are suggestive of the earlier stages of Addison's disease.

Blood pressure readings were taken in 14 cases.

TABLE II.—BLOOD PRESSURE READINGS

| *Case No.* | *Sex* | *Age* | *Diastolic* | *Systolic* | *Dystrophy* |
|---|---|---|---|---|---|
| 10 | M | 16 | 60 | 92 | Slight |
| 30 | M | 16 | 60 | 110 | Marked |
| 29 | M | 25 | 60 | 110 | Marked |
| 33 | F (4 para) | 30 | 75 | 122 | Slight |
| 5 | F | 31 | 65 | 90 | Severe |
| 17 | F (7 para) | 34 | 64 | 108 | Severe |
| 24 | M | 36 | 65 | 95 | Severe |
| 24 | M | 36 | 70 | 106 | Severe |
| 1 | M | 43 | 90 | 118 | Marked |
| 11 | F (11 para) | 45 | 65 | 108 | Marked |
| 21 | M | 50 | 62 | 112 | Severe |
| 20 | F (6 para) | 49 | 78 | 120 | Severe |
| 35 | M | 84 | 70 | 130 | Marked |
| 6 | M | 87 | 80 | 180 | Severe |

Case 10 is shown in Fig. 8. Pigmentation is a feature.

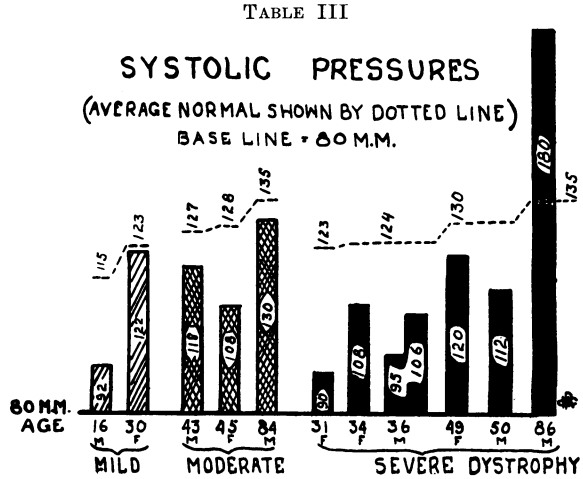
Case 5 died after years of periodic attacks of a condition in which there was great psychic and physical asthenia, and gastric and abdominal disturbances so severe that peritonitis was well simulated. There were very low blood pressures. Pigmentation was not more marked than in other cases.

Case 24 has had two attacks of abdominal distress associated with great muscular weakness and blood pressures of 70-106 and 65-95.

Case 21 has complained for many months of fatiguability and has a blood pressure of 62-112.

In Case 6, a man of 87, there is sufficient arteriosclerosis to show the vessels very distinctly in a skiagram of the hand. If we exclude this case it is seen (Table III) that no other pressure reaches the normal average systolic for the age, nd that the lower pressures show a tendency to accompany the severer dystrophies.

TABLE III




As a whole these people sweat easily.

Altogether, there is considerable evidence of suprarenal dysfunction.

It is interesting to note that the two structures most strikingly involved (*i.e.*, the hair and nails) differ in chemical composition from the rest of the skin chiefly in their greater content of sulphur. Swingle and Wenner,[10] and also Loeper, Decourt and Garcin,[11] find the adrenals to be greatly concerned in the metabolism of sulphur. The medulla of the adrenal is derived from the ectoderm.

In the family groups which show a diminishing severity of the dystrophy there has been a coincident amelioration of living conditions.

In the group showing an increase in numbers and severity there has been an appalling degree of under-privilege. One man tells of a Canadian winter fifty years ago when their sole diet was cornmeal cooked in a frying-pan with candle grease as a lubricant. The profound effect which is produced on the adrenals by starvation or lack of vitamin B may be significant.

### THE PITUITARY

If this dystrophy is ectodermal, and if there is any endocrine association, one might look for signs of involvement of the anterior lobe of the pituitary, which is derived directly from the ectoderm. We shall divide the signs and symptoms present in these cases into two main groups.

A. *Symptoms usually attributed to decreased function.*—(1) Late maturity. (2) Delayed union of epiphyses. (3) Thin smooth skin (in youth). (4) Scanty growth of hair of axillæ and beard. (5) Feminine distribution of the scant pubic hair. (6) Sexual hypoplasia. (7) Small sella turcica in all five cases examined.

B. *Symptoms usually attributed to increased function.*—(1) Two cases in which the bones of the hand are disproportionately long (increase before epiphyses united). (2) "Sausage fingers" or clubbed fingers (Figs. 2 and 8. (3) Accentuated normal lines of the skin (after middle life). (4) Kyphosis common in older men. (5) Thickened calvarium, heavy occipital protuberances and enlarged frontal sinuses, which were present in all the skulls x-rayed. (6) Marked tufting of the bones of the terminal phalanges. (7) Broadening of hands.

On this tufting great stress is laid by Cushing[12] and also by Bell[13] as a sign of acromegaly. Towne[14] says that "The characteristic changes" (of acromegaly) "are exostoses of the phalanges, which may be an early radiographic sign of the disease." Dock,[15] in Osler and McCrae's Modern Medicine, says "The tufting of the terminal phalanges is a *unique and diagnostic sign* of acromegaly." Acromegaly is of course ascribed to dysfunction or hyperfunction of the anterior portion of the pituitary body. This tufting of the terminal phalanges was present in every x-ray which has been made of the hands of any adult male. (7 cases, see Fig. 11). However, as this tufting is often associated with some clubbing, two other suggested explanations may

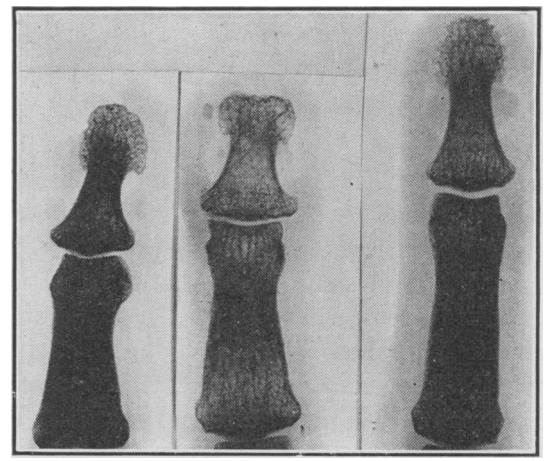


FIG. 11.—These are all from different cases. Note the tufting and the great length of the phalanges of the case on the right.

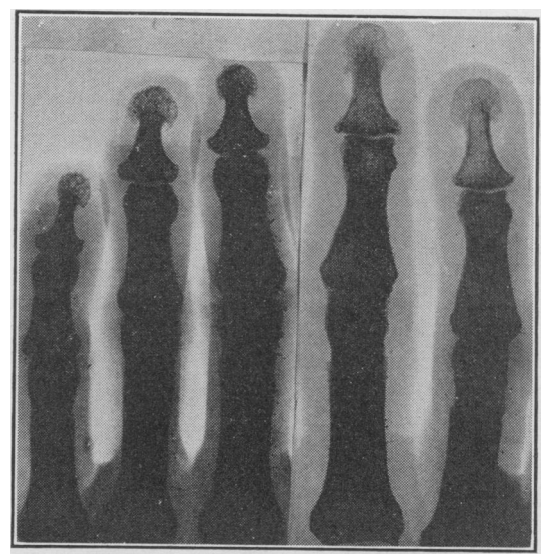


FIG. 12.—Two other cases showing a tufting of the terminal phalanges which is similar to that found in acromegaly.

be considered. It has been asked whether the clubbing and tufting are due to frequent subungual inflammation with its congestion, *etc.* This seems improbable because the tufting does not appear at the ages when the inflammation is frequent, but only later, when the inflammation has become largely a memory. Furthermore, the bony changes are not confined to the terminal phalanges.

Again it may be objected that the changes are those of secondary (or pulmonary) hypertrophic osteo-arthropathy. Locke,[16] whose authority on this subject seems to be accepted, concludes that hypertrophic pulmonary osteo-arthropathy is always secondary, and that simple clubbing of the fingers and secondary hypertrophic osteo-arthro-

pathy should be regarded as identical, the former representing an early stage of the latter. He also says of the osseous changes that they closely resemble, or are even identical with, the appearances seen in cases of acromegaly. In this dystrophy there are none of the conditions which are commonly found to be the precursors of secondary hypertrophic osteo-arthropathy. But even if we should accept that as the true explanation of the clubbing, *etc.*, it would not exonerate the anterior part of the pituitary body. Dock in summing up hypertrophic osteo-arthropathy holds that "An endocrine origin seems strongly probable." In that event one naturally suspects that gland which is known to be capable of producing those changes which "closely resemble, or are even identical with it," (*i.e.*, the anterior pituitary body).

X-ray films of the sella turcica in five cases show this cavity to be under, rather than over, the average in size, but in the oldest cases the

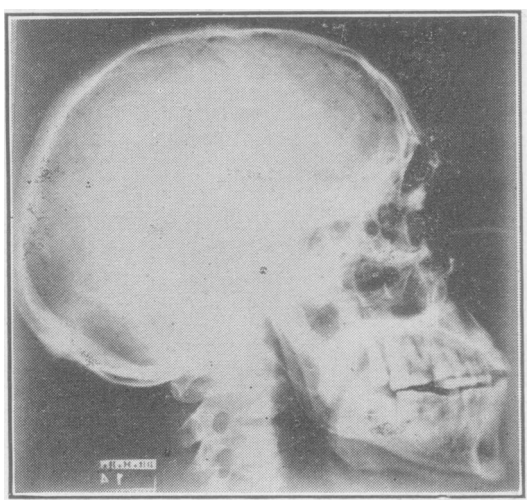


FIG. 13.—Thickened tables of skull; large frontal sinus; heavy occipital protuberance; prominent jaw.

clinoid processes are small and wide open. It is, however, well recognized that acromegaly may occur from hyperfunction or dysfunction of the anterior lobe of the pituitary body without enlargement. There is some support in these cases for the theory of Walter Timme[17] that sometimes the anterior lobe of the pituitary body attempts to compensate for a deficient adrenal, and that this physiological and self-limited response produces certain features of acromegaly.

No symptoms attributed to involvement of the posterior lobe were noted, unless the low blood pressures, and an irregular polyuria or enuresis, which was found occasionally only, can be so explained.

### THE PINEAL BODY

Of the pineal gland very little is known, but it is conjectured that it is related to:—

1. The rate of sexual development.
2. Pigmentation.
3. Certain muscular dystrophies.

It will be seen that our dystrophy might establish contact with the pineal gland under two of the three headings. To advance anything further would be the quintessence of futile speculation.

### CONCLUSIONS

Notwithstanding the interesting evidence for endocrine involvement, it would seem, in the ordinary sense, that this is a result of the participation in the general dystrophy of the ectoderm, rather than the cause of the whole condition. The deficiency on the part of the sebaceous glands is not merely a suppression of secretion, or a degeneration, but a failure of development, which dates back to before the third month of fœtal life. The eyebrow division is an embryological one.

Equally important is the fact that the cardinal features are present (or absent) at birth. How can one explain on an endocrine basis the fact that the defective mother produces normal and defective children in equal numbers, and likewise that the normal mother also produces normals and defectives in the same equal numbers? There is no difference between the defectives born of normal or defective women, and the normals are equally "normal." Some of the very worst cases have drawn their prenatal and postnatal nourishment from normal mothers, and both grandmothers have been normal. The male germ plasm has carried the defect through two generations of normal women without any change. The condition is as fundamental as the germ plasm itself.

### TREATMENT

Treatment must be divided into that of the individual and that of the family. In the individual there may be some slight improvement in the hair conditions by the well known methods of stimulation of the elements already present, but there is no indication that any form of therapy will cause the formation of a pilo-

sebaceous system where it does not exist, even if it could be applied, as would be necessary, before the third month of fetal life. If no effect is produced on the fetus by the internal secretions of a normal mother, it is obviously unreasonable to expect much effect from endocrine preparations from another source which must survive preparation and absorption.

Are these people, then, "compelled to sorrow as those that are without hope?" Not at all. Are Mendelian characteristics immutable? Not at all. In recent times sex itself (a Mendelian characteristic) has been shown to be reversible by the action of the adrenals and the thyroid. But whether it conformed to theory or not, there is the experience of this family itself that the dystrophy is diminishing. We can see every phase in transition in those studied. It is absurd to suppose that there are not less than 6,000 easily recognized cases in America; and less than a score in the literature actually reported as seen. The condition, therefore, *is* disappearing before our very eyes, *and the improvement runs parallel with the improvement in the living conditions of the ancestors.* Help these people by the recognition that the dystrophy is only a pitiable deformity and not a loathsome disease. Remove the economic and social conditions which make for improper nutrition, and in a few generations the condition will be only a curious memory.

## SUMMARY

1. This is an analysis of 119 cases in 6 generations of a well marked and easily recognized condition, usually known in the literature as hereditary or familial dystrophy of the hair and nails. Forty cases were inspected.

2. The dystrophy follows the law of Mendelian hybrids, not sex-linked; the defect a dominant. It is estimated that there are more than 6,000 cases in America.

3. The dystrophy involves the epidermis itself, the nails, the hair, sebaceous glands, and to some extent the sweat glands.

4. Clinical evidence is presented that it involves other ectodermal tissues, *e.g.*, the teeth, the nervous system, and the glands of internal secretion of ectodermal origin.

5. Dystrophy of the nails is adopted as the constant factor.

6. The hair condition is a true and general hypotrichosis from birth. It is a failure of the pilo-sebaceous system to develop.

7. The dystrophy tends to diminish in succeeding generations, both as to incidence and severity, and every stage in transition is seen. The improvement seems to coincide with improved living conditions of the ancestors.

8. Familial dystrophy of the nails alone, in some cases, is merely a mild expression of the same condition.

9. Hereditary keratosis plantaris et palmaris, in certain cases, is probably another residual form of the disappearing dystrophy.

10. Involvement of the adrenal medulla is suspected because of symptoms resembling those of Addison's disease in its earlier stages.

11. Involvement of the anterior lobe of the pituitary is held to be responsible for certain features suggestive of those found in acromegaly.

12. Since the condition is as fundamental as the germ plasm, the treatment is familial rather than individual.

I have to thank Dr. L. J. Rhea for much help as well as kindness and patience; Dr. Edward Chandler, who traced out one family group; Dr. Burgess, who supplied the skin section; Dr. Rabinowitch, for the basal metabolism work; and many others on the staff of the Montreal hospitals.

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