ACANTHOSIS NIGRICANS.

By J. M. Melville
M. D., 1908
The word is derived from the Greek prickle. This was held to be an extremely suitable designation, for Pollitzer when describing the micro pathology was struck by the enormous increase of the cells of the prickle layer of the skin. This name remained in use until Radcliffe Crocker, to whom we owe most of our recent knowledge of this rare condition, adopted Kaposi’s appellation, and pointed out that the hypertrophy of the prickle layer was by no means the main feature of the histological examination. He considered that it was primarily a hypertrophy of the horny layer. Since we have adopted this name we have been able to classify it more satisfactorily, because it can be grouped with the other keratoses, although it is essentially different from all the other forms of this group. In fact, it is impossible to mistake it for any other condition that is to be met with clinically, with the exception of, perhaps, keratosis vegetans, also known as Darier’s disease, in which we get a general hypertrophy of the whole sebaceous system. Other synonyms /
synonyms used are Dystrophie papillaire et pigmentaire of Darier who published cases in 1893 and 1895. Later, in 1898, Hollopeau when publishing his case brought the two words together, Dystrophie papillo-pigmentaire, as if to show that the papillomatosis and the pigmentation were inseparable. This appears to be a very suitable description, for there is no doubt that in all the true cases of keratosi nigra-cans we have had described, we find a combination of these pathological processes. Notwithstanding this significant description, we are faced with the fact that if this appellation is the one that we decide to use, we have no clinical group into which it will naturally fall. It is, therefore, necessary to use the name which Kaposi used, and which gives us at the same time the pathological group to which the condition belongs - the keratoses.

It was my good fortune to discover the following case in May 1905. Since then I have followed the course of the disease very closely. The patient was in the Thompson Memorial Home, Lisburn, Ireland, and is still an inmate of that Institution.
Catherine W., agt. 42.

General History:

The illness commenced 18 months previous to admission to hospital with what seemed to be a very bad form of dyspepsia, and from the indications it was thought to be due to a hypersecretion of acid, for which she was treated with diet and the ordinary drugs. At this time she also noticed menstrual changes, the monthly discharges becoming more and more scanty, until at the end of a year it ceased altogether. At the same time a leucorrhoeal discharge appeared which was extremely offensive. This grew in amount until at the time of admission it was very considerable. At this time her hair became wiry and brittle, and began to drop out, but not to any great extent.

After six weeks a yellowish discolouration of the skin appeared; the tint was more akin to orange-brown than to the bronzing of Addison's disease. Nine months after the illness commenced, warts and warty cut-growths began to make their appearance all over the body, but were better marked in some parts than in others, the axillary region as well as the face and /
and hands being most affected. These went on growing for three months, when a large growth on the axilla began to discharge, and at the same time to decrease somewhat in size. The patient also noticed some roughness in her mouth, and also thought that her tongue was bigger.

The marked pigmentation of the skin did not show itself definitely until about a year after the commencement of the disease. It was noticed over the face, chin, neck and other parts normally exposed to light.

The patient's appetite has, as a rule, been good, except when the gastric symptoms were marked - at this time also she suffered from weakness and general debility. Up to the advent of the present condition, her health had been excellent. When 17 years of age she had a child, which is living.

**On Examination:**

One was struck with the extraordinary colour of the patient's face and skin. On first thoughts one felt that one was looking on the countenance of a middle-aged man, so rugged were the features.
Plate II

Early condition of face: accentuation of normal lines and coarsening of the hair
The normal lines and folds of skin were accentuated, and showed marked black pigmentation. This was also shown in patches elsewhere; otherwise the colouring was of a deep coffee hue, quite different from the bronzing of the typical Addison’s disease.

The warty condition was well marked on the face and scalp, - in these positions all the warts were single and sessile, and looked like enormously developed papillae. In parts of the face one was able to see a particularly large wart, about the size of a large pea.

The mouth showed some warts which were best seen over the tongue and soft palate, but otherwise no change, except for a deep orange colour of the mucous membrane.

The chest showed great blackening under the semipendulous breasts and also in the areolas. The outgrowths between the skin surfaces were somewhat like condylomata, though the surfaces were dry and scaly.

In the right axilla a large fungating mass was to be seen, something like a large cauliflower, only pink, which discharged an excessively fetid, straw-coloured
Plate III  Axillary growth, foaming ulcers and large related marks.
straw-coloured fluid. This showed no pigmentation except where it joined the normal skin surface, in which position it was surrounded by a slatey black circle of pigment. This growth at first might have been mistaken for an ulcerating scirrhus, but on closer examination it was seen to be in the skin and not glandular. The bend of the elbow showed a dark brown colour varying to slatey black, dry and scaly to the touch, much like potter's clay - but no great warts were visible. The warts were, however, very well seen on the hands, wrists, and fingers, whilst between the fingers was a dry scaliness which was very typical. To the touch the skin had a peculiar velvety feel, like the sensation obtained by running one's fingers over a plush cushion, or not quite so rough as the skin of a young dogfish. A few pedunculated warts were seen, but the majority were of the sessile variety. The nails are dry, uneven and brittle and cracked transversely. Between the fingers the skin is hypertrophied.

Abdomen and lower extremities:

The pigmentation in this region is not so well marked, though by no means absent. The pigmentation /
Plat. 144. Leukocyan, 2 to 3 years after removal.

Comparing of hair most marked from in plate II.
pigmentation is best seen near the umbilicus and in the dorso-lumbar region.

When, however, we come to the natal and gluteal folds, we have examples of the darkest pigmentation. In the natal fold we get good examples of the 'pseudo-condylomata', which are in reality non-pigmented warts. The colouration is seen over the patellae and front of the legs, while the hypertrophy and scaliness is seen behind the knees and on the soles of the feet. The nails and interdigital spaces are in much the same condition as the hands, although the number of the warts is not so great. There is no trace whatsoever of any abdominal cancer to be made out. On examination of the blood it was found to contain the ordinary cells, there being no eosinophilia. The differential count was as follows:

- Polymorpho nucleiars . . . 56%,
- Small Lymphocytes . . . . 36%,
- Large Mono-nuclears . . . 5%,
- Eosinophiles . . . . . . . 2%.

Thus there is some increase in the small lymphocytes and a corresponding decrease in the polymorpho nuclear cells.

Mucous /
Plate V  - Ridging and enlargement of the tongue.
Mucous Membranes:

Mouth and Naso-pharynx:

The patient during the initial stages of the disease complained of roughness and dryness of her tongue and lips; the tongue was large and rough and deeply furrowed; the mucous membrane of the tongue and soft palate was an orange tint and covered with out-growths, the average size of which was about the size of mustard seeds. The lips are deeply fissured and dry, and at the junction of the skin and mucous membrane there is a well-marked dark brown line. During the second year of the disease, she has noticed that the dryness has become very much less marked.

External auditory meati show no distinct warts, though the lining surfaces are much rougher than normal. The pigmentation is of a dark brown colour, and is distributed regularly through, except at the concha, where it is much darker.

The ears do not show any excessive warting, though there is a good deal of pigment present. The Hair is short and dry and extremely coarse, and is almost as stiff as the bristles on a boar's body. When /
When she first noticed the condition coming on, she was particularly struck with the fact that her hair was getting very coarse and beginning to fall out. Although the hair remains extremely coarse, it has ceased to fall cut, though it is much thinner than formerly. It is of an iron-grey colour, while formerly it was brown.

**Stomach:**

This organ does not show any signs of dilatation. At first there was a hyper-secretion of acid. The reaction to phloro-glucin and vanillin gave a very distinct pink colour - she has no sense of pain or discomfort, and no growth is palpable. These circumstances coupled with the fact that there is no progressive loss of weight nor appearance of cachexia, bear out the belief that no malignant condition of the stomach exists. Intestinal tract shows no abnormality; there is nothing to be felt per rectum except for a few small internal haemorrhoids. In the perianal region there are some pseudo-condylomata, or as Pollitzer describes them, warty condylomatoides. The stools are offensive.

**Vulva**
Vulva and Vagina:

The pubic hairs are scanty and much coarsened. There was during the initial stages of the disease a very profuse and fetid discharge, which required constant attention. It was controlled by douches of cyllin after about three months' constant treatment. The labia majora show no special change, but the smaller labia are markedly hypertrophied, pigmented and warty. The pigmentation is of an orange brown tint, and the warts are small and slightly coloured.

Haemopoietic system:

There is no enlargement of the lymphatic glands; the spleen, liver and kidneys are of normal dimensions. The kidneys are not tender, nor are they displaced. All the examinations of the blood have shown the same average figures.

Red blood corpuscles, 4,000,000 to 4,560,000 per cm.

White blood corpuscles, 7,800 - 8,300.

Haemoglobin, 80% - 84%, with a colour index of about .89.

The /
The differential counts average as follows:

- Polymorpho nuclear leucocytes. 58%,
- Small Lymphocytes. 35%,
- Large mono-nuclear lymphocytes. 6%,
- Eosinophiles. 2%.

No poikilocytosis and no nucleated red cells.

There was nothing abnormal in the urine and no pigment excreted by the kidneys.

**Treatment:**

Numerous drugs were used at first without avail, until at last a combination of

- Potass. Iodidi grs. x
- Syr. Trifolium (Parke Davis) 3ij.

was given thrice daily with evident good results. The dose was gradually increased up to 30 grs. of Iodide of Potassium and 3% of the Syrup Trifolium. There was a gradual decrease in the size of the growths. This was especially marked in the case of the axillary tumour. However, at the end of ten months, the improvement stopped, and a large cauliflower growth appeared in the left axilla, similar in size and appearance to that which was first observed in the right armpit - it was, however, much more darkly pigmented.

Last /
Last summer I used Calcium Iodate grs. xv, and Salol grs. x once daily, and every third morning half an ounce of Epsom salts with the idea of removing any fermentation from the intestinal canal. This appeared to bring about a cessation in the condition, but unfortunately no improvement can be recorded. The condition, however, appears to have become stationary, for there is no increase in the papillomatosis nor in the pigmentation.

ÆTIOLOGY /
Plate II. Dark segmentation of wrists and backs of hands. Not permanent but became lighter in colour.
AETIOLOGY:

Women appear to be more frequently attacked than men in the ratio of 10 to 3; Crocker believes that those over 46 years are more prone than those who are younger — for of the recorded cases only about one quarter are under 40 years. One case in America in 1898, the patient was 7 years of age when the condition was observed. Dyer, who published it, could not definitely state at what age the initial signs were noticed. In Crocker's first case, the disease commenced suddenly at the age of 13 without any previous indications of constitutional disturbance. Barkski had one child of 13 under his care for some time with a definite history that the disease commenced at 2 years, but the signs only became well marked at 10 years.

It will thus be seen that although persons of tender age may be attacked, yet those beyond the fourth decade are the ones who are most subject to this disfiguring condition. The oldest known case was that described by Pavlov, as a woman of 72 years.

In those early cases, there appear to be no predisposing causes, but when we come to consider the cases /
cases of later life, we have a different aspect of things.

Malcolm Morris considers that abdominal cancer is nearly always an associated factor, the primary seat of malignancy being either in the stomach or liver. Disease of the suprarenals in one case was mentioned, but this has not been borne out by other observers. Traumatism was given as the causal factor in a case which appeared in the British Journal of Dermatology in 1902. Some injury of the abdominal sympathetic system was believed to have taken place.

Exposure to extremes of heat and cold were the dominant factors in the cases of Janowski and Radcliffe Crocker. Hyperchlorhydria in my case was the only symptom which preceded the origin of the disease. Darier in his conclusions holds that the disease is always secondary to abdominal cancer, and that it should be classed with those maladies which depend on abdominal disease. In Morris' case, as also in mine, there were menstrual changes, but these cannot be defined as probable cause, since they were concurrent /
concurrent with the early stages of the disease.

It will be seen from the foregoing observations that we are totally unable to lay down any fixed statement as to the cause of this condition, because primarily, sufficient cases have not been met with for observers to place any definite lesions as the main cause for this strange manifestation.

SYMPTOMS:

We cannot say that there is any particular mode of onset, since there are but few cases in which we have similar features as regards the commencement of Keratosis Nigracans. In the case which I have described, obstinate dyspepsia and later menstrual disorder were the only prodromal symptoms before the pigmentation commenced. Nor can we group together any association of clinical changes which could be taken as pointing to the occurrence of the disease. In the case that Morris describes, there was undoubtedly a well-marked menorrhagia which gradually got less, until it ceased altogether. There was also some leucorrhoea, but this, though not great in amount, persisted. In one case (Crocker) a crop of /
Plate 74. Spurs across wrist, which are palpable. The breaking of the nails are still seen. There is also marked hypertrophy of the skin of the dorsum of the hand.
of warts first appeared on the fingers and backs of the hands. In my case, a yellowish discolouration and then warty outgrowths all over the body were the first indications of the general condition. Preceding this, however, there was marked coarsening of the hair, which also commenced to fall out. This was extremely well seen in the cases of Hollopeau and Morris. The pigmentation is different from that of the typical Addison’s disease, in that it varies from a coffee brown to a slatey blue, even going on to a jet black. As regards the mucous membranes, there can be no mistaking the dark orange brown, which, with the associated papillary overgrowth, must be held as almost pathognomonic. Darier states that the man whom he treated suffered from repeated vomiting and some dilatation of his stomach, which continued throughout the condition. The pigmentation, as well as the papillomatosis, is undoubtedly symmetrical, but certain parts of the body appear to be attacked more markedly than others.

As regards the chief sites of pigmentary changes, the neck, face, flexures of the elbows, hands,
hands, vulvae, perianal and umbilical regions appear to be the main sites of attack. Here the pigmentation reaches its darkest hue. In the elbows we get a peculiar slatey grey colour, which gives one the idea that a plaster of semi-dried potter's clay has been spread on the skin; there is transverse cracking of the skin surface, which corresponds to the folds of the skin. On the face and neck, the natural skin folds are greatly accentuated. In the axillae, the growth shows a peculiar appearance, as sometimes over the upper surface there is no deposit of pigment. We have, however, a raw pink mass, rather like a pink cauliflower - the base of the mass has a deposit of pigment around it, varying from a brownish hue to a definite black. The skin of the upper arms is roughened, though not to any marked extent, and here also we find but few warts, which are semi-pedunculated and more or less isolated. The hands and fingers show extraordinary changes. They are large and rough, both flexor and extensor surfaces occasionally being equally affected. The surfaces are a dark coffee colour, with /
with well marked blackening between the ridges of skin. In the interdigital spaces we get a greyish putty-like colour, and this, though not so well marked, can be seen on the flexor surfaces of the fingers. The nails show trophic changes in that they become brittle, and easily break off - there may be longitudinal or transverse ridges, and it is along these that we get the nail breaking. At the junction of the skin and nail, there is often a hypertrophy of the horny layer, which at times is enormous, and gives the appearance of a number of flat warts which have coalesced. It was at first thought that this was a warty condition of the nail fold, but recently it has been satisfactorily proved that it is an over-growth of the upper part of the stratum corneum. From this over-growth we occasionally get a serous discharge, which may have an unpleasant heavy odour, but this is by no means constant. The palmar surfaces show the most peculiar changes. There is an over-growth of the whole of the skin, which is perfectly regular and complete in its distribution. It has been likened to piled velvet, but it is more rough to the touch. It gives the sensation that /
that is felt when a cat licks the finger, and in
the later stages of the disease it may be as rough
as the skin of a dogfish. This hypertrophy may
not be seen in the earlier stages, but it is un-
doubtedly felt as the condition progresses. In
some cases the centre of the palm is not greatly af-
fected.

On the trunk the amount of pigmentation varies,
some cases shewing a great degree, while in others
it is comparatively slight. The warting also varies
as in the extremities, certain sites being more
prominently affected than others, but when the trunk
is taken as a whole and compared with the limbs and
head, the outgrowths are very few. Sessile and
pedunculated warts are visible; they are larger and
more isolated and generally darker than the surround-
ing skin. The upper half is seldom so darkly col-
cured as the lower half. The pigment generally shades
off from the neck, consequently the breasts may
show an orange tint. The areolae are deeply pig-
mented, and the nipples may be hard and tender and
surnounted with crusts. In those cases where the
breasts were pendulous and the skin surfaces in con-
tact /
contact, the pigmentation was not so deep — in fact the skin may be quite pale and sodden, giving the appearance of condylomata. Here also we may get a serous discharge.

Morris pointed out that the skin is generally bronzed and wrinkled, and in his first case there was a button-like growth at the umbilicus, circular, and about 1½ inches in diameter. It showed narrowing at its attachment to the surrounding surface, and encircled with a broad band of black skin. This growth appears to be similar to those which are found in the axillae.

In the lumbo-sacral region, types of the darkest colouration are found, in fact, it appears as if there was a deep deposit of soot. The external genitals are as a rule dark and near the orifices the surfaces are extremely moist and discharge a clear, fetid fluid. The hair of the genitalia is coarse and grey; in some cases it is white.

The femoral regions are brown, dry and rough, and are warted — the warts are as a rule pedunculated and dark. The prepatellar surfaces are ridged /
Plate X. General appearance after 2½ years.
ridged transversely and scaly, while in the popliteal spaces are found the same appearances as in the ante-cubital fossae. The front of the legs are rough and covered with short, coarse hair. The toes on their dorsal surfaces show the same condition of matters as the backs of the hands, but the exaggeration of the hypertrophy is much less apparent on the soles, which are as a rule non-pigmented. Over the joints of the dorsal surfaces of the toes, we get a good deal of ridging and some cracking of the skin, with an associated exudation. In this place we get a deep deposit of pigment.
Plate 6. Showing changes in face, tongue, lips and hair.
MUCOUS MEMBRANES:

Apparently all the visible mucous membranes may be affected, though, of course, it does not necessarily follow in all cases.

**Mouth:** The tongue is large and rough, and traversed by longitudinal and transverse ridges, the papillae are prominent, and the whole organ feels dry. This dryness may be the prominent feature; occasionally, however, the patient first complains that the tongue is too large for the mouth. The colour is a deep red, and it may have a covering of dark brown fur. There is seldom, if ever, a genuine deposit of pigment over the tongue. The inner surfaces of the cheeks are covered with small warts and are of an orange colour, and there is never any black pigment present. The hard and soft palates also show a warded surface associated with the orange coloured pigmentation. The lips are generally fissured with an associated desquamation of the mucous membrane. At the junction of the skin and mucous membrane, there may be a well-marked line of black pigment; this is more commonly seen on the lower lip. In one of the cases described, there were large semi-pedunculated growths at the angles of the mouth. There may /
Plate XI: Velvety appearance of the palmar surfaces. Very little pigmentation visible except at wrists and cubital fossae. One large desmosis wart on left forearm.
may be similar conditions in the orbital canthi, only
to a much less marked degree. The eyelashes are
coarse and scanty, and deposits of pigment may be
present around their bases - the lids are indurat-
ed and rough, and sometimes deep fissures are present,
which may have moist surfaces. Filiform outgrowths
were present in one of the cases published by
Darier and Janovski, while Couillaud indicated that
there was hypertrophy of the palpebral conjunctiva.
The conjunctivae are not pigmented. In the mouth
instead of an orange colour, we may have a greyish
white deposit. The vagina is as a rule abnormally
roughened, and gives a granular sensation when
touched - there is a slight orange tinge present.
A fetid serous discharge is usual, and the presence
of this may necessitate the isolation of the patient.
Around the anus we find a black ring. As regards
the auditory meati, we may get an enormous prolifera-
tion of the superficial layers, which diminishes
the lumen of the canal and causes deafness. To get
rid of the deafness, the administration of caustics
give the most beneficial results. This proliferation
is analogous to the papillomatosis, and even in this
part /
part we may get warts developing. There is sometimes a gelatinous fluid present rather like melted wax. The alae nasi may be encrusted and show condylomatosid growths with a prolongation of some parts of the lining mucous membrane. There is no case described in which a deposit of pigment on the nasal mucous membrane of the nose was found. In two cases there was some enlargement of the lymphatic glands, but this is rare - in one of these the inguinal glands were the ones affected, and here a foul vaginal discharge was found, which was semipurulent, shewing that the enlargement was due to an intercurrent condition.

Many cases have been described as keratosis nigracans which cannot be taken as examples of this disease. Crocker described a case that came on suddenly, and lasted for eight years. He held that it was due to exposure to extreme cold. Soft papillary outgrowths and some pigmentation appeared, but these were distinctly localised, the hands and mucous membranes being unaffected, whereas as a rule the hands show extreme changes. Du Castel, Pringle, Joseph and Leslie Roberts described cases which cannot be accepted as keratosis nigracans.

PATHOLOGY ;
PATHOLOGY:

One is quite unable to discuss the pathology of this extraordinary disease with any satisfactory result owing to the scantiness of literature, and also to the insufficient number of autopsies. A view has been advanced that it is due to a pathological condition of the abdominal sympathetic nervous system - the groundwork for this theory is based on the fact that one case arose as the result of a blow over the abdomen and also that in some of the cases disease of the viscera abdominales was present. As far as can be ascertained from the pathological reports on the subject, we get no change in this sympathetic system, either macroscopic or microscopic; this being so, one must regard this as a mere assumption without any sure foundation.

It has been suggested that there is either an atrophic or an irritative lesion in the trophic centres of the spinal cord, but since there are no other generalised symptoms, it is difficult even to imagine that so localised a change could exist in the anterior horn without some other association of symptoms. There is no appreciable pathogenic change in the blood to account for the deposit /
Fig A. H.P. Showing granules absent especially in Stratum Granulosum (a), horny material shedding (b), Corium (c), Stratum Corneum (d), follicle cells (e). Few granules of potassium added but no blue reaction obtained.

Signed: [signature]
deposit of pigment, for the red cells are well formed and contain a good percentage of haemoglobin.

When all the suggestions as to the pathology of this condition are carefully considered, observers must admit that there is no satisfactory explanation as to the origin of this disease.

It is just possible that an explanation might be found for the source of the pigment and the reason for its deposition on the superficial surfaces, but the reason why the hypertrophy of the skin should be present cannot be assigned to any internal change. Pollitzer made a most careful and minute examination of the outgrowths of his first case, and as a result of his observations he divided the warts into two groups, namely, those occurring on the hands, face, neck and feet, ichthyosoides, and those seen on the lips and mucous membranes the condylomatoides. Microscopically, the essential differences are as follows. In the ichthyosoides he found dilated blood and lymph vessels with a comparatively well-marked small cell infiltration. Among these small cells there were a great many mast cells and some which showed a deposit of pigment. The superficial horny layer was /
was brownish in colour, and undoubtedly hypertrophied.

The prickle layer was increased abnormally and traversed by wide lymph spaces which contained white blood corpuscles. The cells of this layer were pigmented. The stratum granulosum showed the above changes to a lesser degree, while the basal portion showed no abnormal change. Thus we see that from this description that ichthyosoid appearance is due to a thickening of the upper horny layers.

As regards the condylomatoid warts we have a much greater inflammatory deposit. There is a greater increase in the dilatation of the blood vessels with a corresponding increase in the number of the leucocytes, in fact, these spaces are packed with the white cells. Underneath the epidermis, there was distinct leucocytic infiltration. This may possibly explain the increased exudation which is so often present and found to exude from these regions. The enormous proliferation of the cells of the prickle layer is most evident here, sometimes four or five times greater than in the ichthyosoid warts. In acuminate condylomata the papillae in the centre of the hypertrophic /
hypertrophic ridges are reduced to fine needle-like structures, which reach high into the epidermis and may show a change like amoeboïd projections.

In the warts of the arm we get a further enlargement of the prickle layer which causes a flattening out of the papillary structures, and here we may get a number of masses of concentrically arranged bodies which are epithelial in type and not unlike nests of carcinomatous tissue. The cutis shews but little inflammation or inflammatory oedema and the apparent absence of hypertrophy of the horny layers is peculiar. There is only a slight inflammatory change in the cutis of these warts. Unna believes that there are many unclassified conditions allied to keratosis nigra-cans; in some of which there is an overgrowth of the prickle layer and also of the horny layer without pigmentation, while in others the prickle cells are increased without a corresponding hypertrophy of the horny structures, nor is there any inflammatory infiltration of the cutis. The result of the examination of the growth which was removed from Morris' case in 1894 shewed changes which /
which were in many ways similar, although unfortunately, only the one type of growth was examined. The following resume' indicates the main observations.

The corium was thickened and the venous radicles dilated with a distinct small-celled infiltration. This was best seen in the papillary region, which was hypertrophied and showed a formative growth of new capillaries. The sub-cutaneous tissue was normal, except for some greatly dilated vessels. The horny layer showed increase in size and in parts was partially detached. Otherwise there was nothing to note in the epidermis. No black pigment was observed, but in the protoplasm some brown granules were seen which were believed to be haematoidin crystals; after testing carefully with potassium ferrocyanide, a deposit of blue was given, but this was by no means constant, in fact it was quite the exception. At the same time Morris is inclined to believe that this pigment is really amorphous haematoidin derived from small intra-epidermal haemorrhages. Some small black granules were also seen which were opaque, angular, and irregular in form; these were got from the scrapings of the skin /
Figure 3 and 4. ken-Sion. Showing histological findings in skin. a) and b) are distinct graph phase; a) hard, b) tannic bogs. 

Section of head and neck region. 

R. P. Pigment not well seen under.
skin where the pigmentation was deepest, only one of these granules, however, gave the Prussian blue re-action.

However observers of late years are in agreement that the increase in the prickle layer is not the most prominent feature as was described by Pollitzer, because after careful examinations the horny substance was that which was most affected. The shedding of this layer is remarkable and shows practically no pigmentation. The pigmentation appears to be most marked in the stratum granulosum and in my case this was especially well borne out. The superficial prickle cells may have a deposit of pigment, but this is not a generalised pigmentation. The corium shows dilated spaces without pigment with slight leucocytic infiltration. The papillae as a rule show some hypertrophy; this is accentuated by the down-growth of the interpapillary processes. In one or two cases (Hollcopeau) an increase of the elastic tissue was observed, but on the other hand Borck found them diminished. The microscopical examination of my case showed a great increase of the horny substance with marked detachment and shedding. There was some very slight hypertrophy of the prickle layer and the cells nearest the stratum /
stratum granulosum were to a slight degree the seat of a small deposit of brownish pigment. Undoubtedly the granular layer showed the greatest pigmentation, which might almost be described as dense. The papillae are relatively enlarged and the corium shows some dilatation of the lymph spaces, but no enlargement. On staining the pigment with ferrocyanide of potassium, the Prussian blue reaction was negative.

DIAGNOSIS /
DIAGNOSIS:

The diagnosis of this disease cannot be regarded as difficult, except in so far as the rarity of the condition is concerned. The symmetrical pigmentation, the colour of the deposit, and the papillomatosis are characteristic, and to a minor degree the ridging of the tongue, the coarsening and falling out of the hair, and the peculiar appearance which is seen on the palmar surfaces of the fingers. In no other condition do we get this combination of phenomena. In Addison's disease there is the copper bronze colour and the profound anaemia with gastro-intestinal disorders, but no warting. In argyria, the colour is blue, but here again there is no verrucose change, and one is as a rule able to get a history of contamination with silver. In melanotic sarcoma the pigmentation is localised to the site of the tumour cells. The only condition for which keratosis nigricans might be mistaken is Darier's disease or keratosis vegetans. The sites of attack are similar. Innumerable small papules appear, often coming out in crops forming small papules which are reddish brown, varying from a pinhead to a pea in size; some are smooth /
smooth and dry and others are rough and greasy. In the larger sizes we may get a small crateriform erosion on the top. These papules when pulled away from the skin leave a funnel-shaped conical pit. If the base of the papules have their epidermis removed a little drop of pus or sebaceous fluid may be squeezed out. Sometimes there is an agglomeration of these papules about the umbilicus which may suppurate. It will thus be seen that these papules are quite different from the warts of keratosis nigracans. The pigmentation is darker in keratosis nigracans, the dryness of the skin is not found in Darier's disease, for here there is often a seborrhea; also it is commoner in males than in females, and it is a disease more commonly seen in early life.

PROGNOSIS:

The prognosis is bad. One or two cases have been reported as cured, but the great majority show no marked improvement, though occasionally an amelioration of the signs may occur. In my case during the last three months the patient shows signs of failure, her spirits are not so good, and the pigmentation is increasing.

TREATMENT /
TREATMENT:

Silver nitrate has been used for the warts as a local application, also Cannabis Indica, Salicylic Acid and Collodion. These applications in cases where the warts are multitudinous are of little avail and are contra-indicated. They may be used to remove the larger growths. Adrenalin Chloride was suggested, but as no change in the suprarenals has ever been noted, one must consider this treatment as empirical. Arsenic, Strychnine, Hydrobromic Acid, Calcium Iodate, the Iodides have all been tried without avail. In cases of fetid discharge, douching and scrupulous cleanliness are essential. If any other concurrent disorders are present, one's first object must be their treatment, as for instance, cancer will require operative treatment. Thus we acknowledge that we have no drug or combination of drugs on which we can depend for a cure. Hygienic principles with plenty of open air and attendance to the bowels are all that can be done.

LITERATURE/
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