APPENDIX.

ALTERATIONS OF THE SKIN IN ADDISON'S DISEASE.

This disease is likewise accompanied by a great increase of the pigment of the skin, but the pigment hypertrophy is merely an isolated symptom among a whole series of others.

Although this alteration in the color of the skin yields in importance to the other symptoms of Addison's disease, it still is a very significant symptom, inasmuch as it often appears as the first conspicuous sign of the affection. With the progress of the affection the dark pigmentation of the skin likewise increases apace, until it finally becomes deep bronze-brown, the color of a mulatto. This pigmentation, however, is generally not uniform, but a particularly dark tint is exhibited by all those parts of the body which normally possess a deeper pigmentation than the rest of the skin: the face, neck and hands, nipples, and genitals; furthermore there occur, as a rule, besides the general coloring scattered over the entire surface of the body, darker spots here and there which are not sharply demarcated, but gradually blend with their surroundings.

The nail-beds and conjunctivæ always remain uncolored, which of course produces a conspicuous effect by contrast.

On the other hand, the mucous membrane of the mouth and pharynx often participates in the discoloration, grayish spots being formed which occasionally exhibit a slight bluish tint. These spots, as a rule, develop by preference at points indented by the teeth.

This affection of the mucous membranes and the scattered occurrence of darkly pigmented spots on the skin, of course aside from the general symptoms, would furnish a differential diagnostic landmark from the diffuse increase of the cutaneous pigment which sometimes occurs in otherwise healthy persons, and which likewise occasionally produces an intense brown pigmentation of the whole surface of the body.

The anatomical examination of the skin has shown a very great augmentation of the epidermal pigment, and in the more pronounced cases also numerous aggregations of pigment granules in the cutis, especially in the papillary body. Otherwise no changes have been found in the skin

MACULÆ CÆRULEÆ.

Clinicians have long been acquainted with a peculiar exanthem described under the name of tâches bleues, ombrées, or as pelioma typhosum, by Trousseau and Griesinger,[1] and which had usually been interpreted as a symptom of typhoid fever. Lewin ascertained that this exanthem stood in no relation with syphilis, as had originally been believed.

In 1868, Falot and his pupils Guiol, Jaquemin, and Moursou, discovered the connection of these peculiar spots with the presence of phthirii; this discovery has since been confirmed by numerous observations, as for instance by O. Simon,[2] but especially by Duguet,[3] who succeeded in producing this exanthem experimentally.

These maculæ cæruleæ appear as roundish or oval spots, ranging in size from a lentil to a quarter dollar and often larger, of a reddish-blue or peculiar dull, dark-blue color; they are not elevated and do not disappear on pressure. They are confined usually to

[1] Comp. also Liebermeister, this Cyclopedia, Vol. ii.

[2] Brest. ärztl. Ztschr., 1881, No. 14.

[3] Annal. de Derm., 1880, p. 544; 1881, p. 357, and Comptes rend. des Séanc. de la Soc. de Biol., 1882, p. 617.

certain regions, particularly to the anterior and lateral parts of the abdomen, the sides of the thorax, the anterior and inner surface of the thigh, the nates, more rarely the back, the arms, and legs. In no case in which these spots are present will the search for crab-lice be in vain, or the history will demonstrate that the patient has removed the pediculi previous to the examination. The arrangement of the spots, too, around the localities forming the usual habitat of the phthirii points to the above-mentioned causal connection. This becomes still more evident by the fact that the spots remain exactly on the roads the pediculi travel from one favorite locality to the other; *e. g.*, on the anterior and lateral portions of the trunk between the inguinal region and the axilla. Still more convincing is the observation that in persons having phthirii in one axilla only, maculæ cæruleæ are present on the corresponding side of the thorax alone. Positive proof has been furnished by Duguet (l. c.), by rubbing some crab-lice to a paste with water, charging a lancet with this, and puncturing the skin of different persons. On these places there appeared most promptly—not earlier than six hours—maculæ cæruleæ which differed from the natural ones in nothing but the small excoriation in the centre caused by the puncture.

Inoculations with ova were always negative, and the last experiments of Duguet have shown that the coloring principle is most probably contained in the salivary glands situated in the segment of the body of the animal bearing the second pair of legs.

Although it is absolutely certain, therefore, that the maculæ cæruleæ are due to the presence of phthirii on the skin, and most probably to the bite of the animals, still the real nature of the process is by no means clear. It is certain that the spots are not simple hyperæmias or hemorrhages, because they behave altogether differently from the changes wrought by those processes. A certain predisposition seems to be necessary to their occurrence, inasmuch as they are not exhibited by all persons infested with crab-lice. Duguet's inoculations, too, succeeded in all cases only with persons who had maculæ cæruleæ before the inoculation. In such as had no crab-lice, and of course no maculæ, the inoculation succeeded only in isolated cases. The former, therefore, were predisposed and if invaded by phthirii would have been the only ones to show maculæ. As a general rule, blond persons with delicate skin usually exhibit this symptom.

I have been induced to give this detailed description because in none of the textbooks have I found a correct explanation of this subject. Finally I must guard against being accused of interpreting this affection as an alteration of the real pigment of the skin. For the present, we are still completely in the dark as regards the actual pathological process, and it is considered in an appendix to pigment hypertrophy merely as a temporary make-shift.

PIGMENT ATROPHY.

Pigment atrophies, of course, are most conspicuous in the colored races, and most of the earlier descriptions refer to them; until recent times even the occurrence of partial pigment atrophies in the white races has been totally denied by some authors. In Germany v. Bärensprung[1] first classified them in the manner still prevailing at the present day. The latter erects three groups—albinismus universalis partialis and vitiligo; the former two comprising the congenital, the latter the acquired pigment atrophies. It must be added, however, that the morbid pictures on which Bärensprung bases this classification do not fully accord with what we understand nowadays by these terms. For the cases

[1] "Ueber Vitiligo und Albinismus partialis." Deutsche Klinik, 1855.

described by him as albinismus partialis are most probably cases of vitiligo in the present acceptation, and his cases of vitiligo were cases of that very rare cutaneous disease known as morphea, or sclérodermie en plaques.

For the present, therefore, we distinguish two groups, congenital and acquired pigment atrophies; the former of which is again subdivided into two classes, according as the pigment atrophy implicates the entire surface of the body or merely circumscribed portions of the skin—leucopathia congenita s. albinismus universalis and partialis, and leucopathia acquisita s. vitiligo.

The best known of these three anomalies is albinismus universalis; if for no other reason, because those affected with it present a most striking appearance even to the laity. Those affected with this anomaly are altogether free from pigment, their skin is perfectly white (albinoes), only here and there it acquires a reddish tint from the more or less perceptible blood-vessels. All the functions of the skin are quite intact; it seems that even other diseases of the skin run the very same course as in normal persons.

The hairs likewise are either white or have a peculiar light whitish-yellow color, with a silky lustre, and are usually of remarkable fineness. The iris is colorless, appearing red in consequence of the visible blood-vessels. Still not very rarely the iris appears blue, but even then only in side view; but if the albino's eye meets the eye of the observer, the blood-vessels gleaming through impart a red color to the iris. However, the blue color of the iris is not due to pigment, but is nothing but a phenomenon of interference of light. The lack of pigment of the iris in albinoes induces photophobia and nystagmus.

The majority of albinoes are of a weakly constitution, but this rule is by no means without exception.

The anatomical examination of the skin shows no alterations except an absolute absence of pigment, which has been demonstrated in the skin, in the choroid, and in the pigment layer of the retina.

We know of but a single etiological factor—heredity. Direct inheritance, however, seems to be very rare, for in the majority of observations we find it particularly emphasized that the parents of the albino were normally pigmented. Schlegel[1] cites a case in which this anomaly was transmitted from the grandfather to the grandchild. Another fact, however, proves quite indubitably that the infantile organism is affected by an anomaly of the progenitors, which indeed is still unknown to us—namely, the fact that brothers and sisters are albinotic with extraordinary frequency; nay, more, that the occurrence of but a single albino among many children of the same parents must be called strictly exceptional. I know of a family in which six children are albinotic, and one normal. Moreover, the statement that albinism prevails endemically in certain localities, as in Loango and Lower Guinea,[2] might have to be taken into consideration here, should it be confirmed; for in a disease which is not contagious and not caused by external influences, its endemic occurrence, of course, can be explained in no other way than by hereditary transmission.

[1] "Ein Beitrag zur näheren Kenntniss der Albinos." Meiningen, 1824.
[2] Eble: "Die Lehre von den Haaren." Vienna, 1831, p. 167.

Partial Albinism.

It is generally conceded that this is met with in the colored races, but its occurrence in Europeans is denied by many. However, there is no doubt that this congenital partial lack of pigment in whites is by no means very rare, though we do not intend to deny that this anomaly may perhaps be more frequent in the colored than in the white races.

We have to deal now with that congenital lack of pigment of isolated parts of the skin which presents itself in the form of white spots, generally with irregular border, the skin of which is otherwise perfectly normal. They are limited either by normally pigmented skin, or else they are surrounded by a zone containing less than the normal amount of pigment, so that the transition is gradual. In no case is the skin immediately adjoining the white patches more strongly pigmented than normal. In short, partial albinism forms in every respect a perfect analogue—the "reverse side," as Kaposi happily expresses it—of the congenital flat pigment moles. Indeed, to complete this analogy still more, we even know of cases in which the congenital pigment atrophy, exactly like the pigment hypertrophy in nævi of the nerves, accurately corresponds with the distribution of some nerve. I subjoin here the description and illustration of a very pronounced case of this nature.

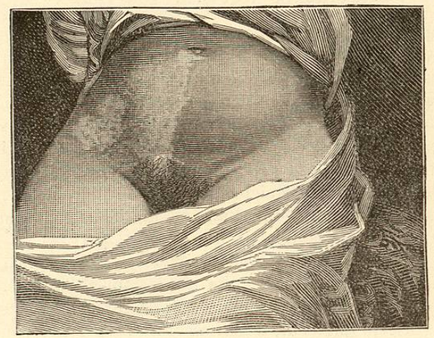

FIG. 35.

Anna K——, æt. 19, came under treatment for soft chancre. The wood-cut renders any further description of the pigment atrophy unnecessary. It corresponded exactly to the distribution of the hypogastric branch of the ileo-hypogastric nerve.[1] Corresponding to the conditions prevailing in herpes zoster and the nævi of the nerves, the whole region of the nerve is not unpigmented, but within it are portions of normally pigmented skin, especially on the outer side. The transition into the normally pigmented skin is not quite abrupt, but a more faintly pigmented zone everywhere surrounds the non-pigmented spots. Besides, the patient presented a second pigment atrophy on the right side of the neck, in the shape of a triangle, the base of which corresponded to the line between chin and jugulum, and its apex about to the middle of the sterno-cleido-mastoid, where the skin, though not altogether unpigmented, was still evidently less strongly pigmented than the surrounding parts. This latter spot corresponds to the distribution of the N. subcutaneus colli med. et inf. derived from the third cervical nerve. Both alterations existed from birth.

In the case of a girl dead of phthisis, who had a similar congenital pigment atrophy on the right side of the abdomen, I have been enabled to examine the skin anatomically,

[1] v. Bärensprung: "Die Gürtelkrankheit," p. 88.

and to demonstrate complete absence of pigment only in the central portions, while at the periphery there was a gradual transition into the normally pigmented skin.

Special attention should also be given to the color change of the hair. Very frequently, though not always, the hairs on the unpigmented spots are likewise white. Thus, in the above-mentioned case, the hairs on the non-pigmented skin of the right half of the mons Veneris were white. But cases are by no means rare in which some bunches of hair are white from birth, while the skin bearing them shows no noticeable lack of pigment. Of course, the capillitium at these points appears somewhat lighter as compared with the portions set with darker hairs.

This phenomenon has been frequently described as poliosis circumscripta, and unquestionable cases of inheritance of this pigment anomaly have been observed. Thus, Seligsohn[1] describes a white ringlet on the anterior part of the head of four brothers. Still more important is the communication by Stricker,[2] according to which a white lock on the forehead was inherited in one family through six generations. In this instance direct inheritance only was observed, reversion of the defect of the grand-parents not occurring in the children of healthy parents. Sex made no difference as regards the transmission.

LEUCOPATHIA ACQUISITA S. VITILIGO.

The term vitiligo is now applied merely to acquired pigment atrophy.

The disease occurs mostly in middle age, and manifests itself first in the shape of small, regularly round, white spots. These white patches gradually increase in size and lose some of their regularity of outline. They become more oval, and irregular white figures arise particularly by the confluence of such spots. But even in the case of large spots due to the confluence of several circles or ovals, this mode of origin can generally be demonstrated with great distinctness. For the limiting lines are always convex toward the outside, while the skin remaining pigmented is accordingly bounded by concave lines. In this way, finally a large portion of the skin, and in the most advanced cases almost the entire skin, may lose its pigment.

Now, while the partial pigment atrophy is evidently the original pathological process, still the surrounding parts exhibit quite noteworthy alterations, which sometimes are even more conspicuous than the former. In the surroundings of the white spots there ensues an increase of pigment, which becomes progressively more intense as the white patches enlarge. The impression conveyed is exactly as if there were a continuous displacement of the pigmeut in a centrifugal direction.

Of course, by this pigment accumulation at the periphery, the contrast between the non-pigmented and the pigmented places is correspondingly intensified as the former enlarge, and finally, when the entire pigment, as it were, is crowded into isolated small islets, these small spots appear deep brown in color, while the rest of the body is white. Sometimes these pigmented islands are situated at the most peripheral parts of the body—in the face, at the hands and feet. It is these cases especially which have given rise to the very natural mistake that the brown places are really the abnormal ones—a mistake which is rendered impossible by the observation of many cases in the different stages, or by the observation of the progressive development in a single case.

Another very remarkable phenomenon is this, that the decolored patches usually

[1] Eulenburg, "Realencyclopädie," Bd. i., p. 162.
[2] Virchow's Arch., Bd. 73, p. 623.

occur symmetrically. In this way are produced quite peculiar markings, as appears most clearly in the adjoining illustration.

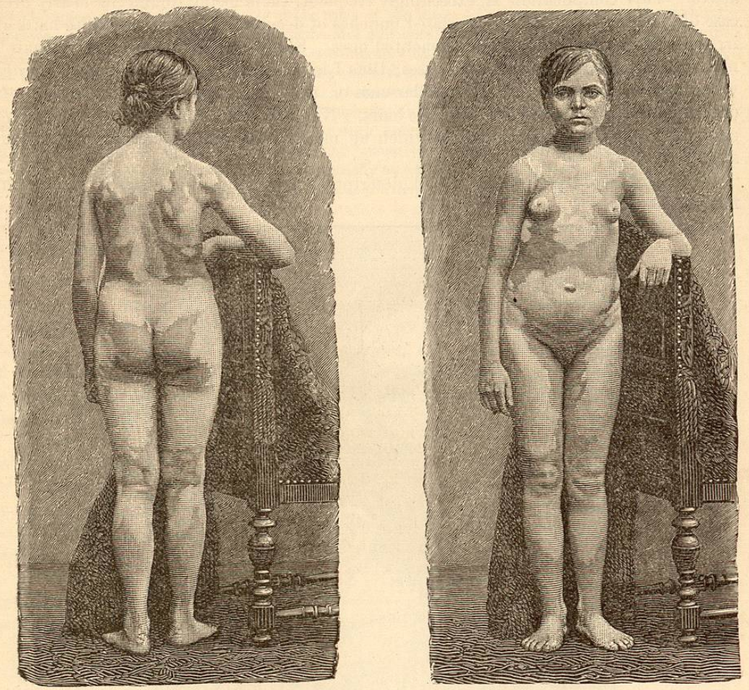

Fig. 36.

Ida P——, æt. 16, was admitted to the clinic with syphilis. More than a year ago the patient had an attack of remittent fever. Soon after, the decoloration commenced with a white spot at the nucha. Till that time the patient had a light-colored skin, while from that period forward the not decolored portions became even darker, some of them at present being deep brown. The almost exactly symmetrical arrangement of the decolored places is evident in the illustration. The limits everywhere are quite sharp, the darkest pigmentation of the colored parts is exactly at the border. At the occiput is a bunch of white hair about one centimetre in diameter.

I call to mind here the fact that, in a large number of cutaneous diseases, the efflorescences appear symmetrically arranged, and that this peculiarity is due pre-eminently to the circumstance that the anatomical relations of the skin—by no means uniform throughout this organ as a whole—are perfectly equal on symmetrical regions, and hence, of course, afford an equal basis to any morbid process affecting them. It is most reasonable to ascribe to this fact also the symmetrical spread of the unpigmented spots in vitiligo, and not to connect them with the distribution of the nerves.

No other disturbance in the cutaneous activity takes place.

The participation of the hairs in the process of decolorarion has been mentioned above. This complication is exceedingly frequent, there being found in nearly every case of extensive vitiligo either isolated bunches of decolored hair, or else white hairs are irregularly scattered among the pigmented ones. Sometimes decoloration of the hair is met with also in slightly advanced cases; thus I have observed a case having but a single white spot on the trunk, several smaller ones on the hands, and one, about the size of a dollar, on the head, covered with white hairs. Now and then, however, the leucopathy is confined to the hairs, an occurrence which we might term poliosis circumscripta acquisita.

I append here the illustration and description of a most characteristic case of this nature.[1]

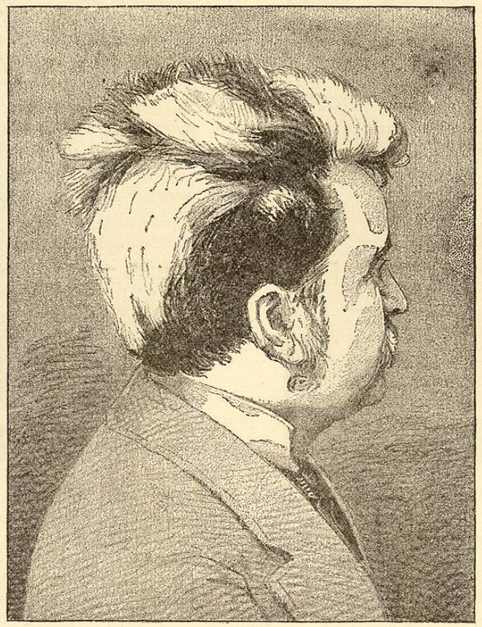

Fig. 37.

M——, barrister, æt. 23. In the family of both parents there is stated to be congenital canities præmatura. Some white hairs have been observed in patient even in childhood. In the fifteenth year, after a grave attack of scarlet fever, the hair fell out to a great extent. The succeeding growth of hair is stated to have been throughout lighter in color and fissured at the points. Soon afterward, a bunch of white hairs appeared on the occiput. In the succeeding years, small patches of decolored hairs were noticed also on the anterior and lateral portions of the scalp. In the spring of 1880, infiltration of the apex of the right lung; of late years, violent headaches, never lasting longer than half a day, chiefly manifesting themselves in pressure within the orbits. Otherwise subjective feeling of health. Present condition: Patient is of stout build; nothing abnormal in the internal organs except some dulness over the apex of the lung. Complexion delicate throughout. Eyebrows and lashes dark-brown. Moustache and whiskers blond, in the latter a few small groups of white hair. The skin containing them is considerably lighter than the surrounding parts; there is no accumulation of pigment or even darker coloration of the periphery. The scalp is covered with numerous scales; its color throughout is uncommonly light. The parts covered with decolored hairs are clearly less pigmented than their surroundings, but this contrast is certainly enhanced by the visibility of the follicular portions of the dark hairs. There is no sharp demarcation of the vitiligo spots from the adjoining parts bearing brown hair. The localization of the decolored patches is shown by the illustration; they are chiefly on the left half of the head. The hairs growing on them are nearly quite unpigmented, but otherwise normal and firmly inserted into the scalp. The skin of these patches, aside from the decoloration, is perfectly normal. At the nucha there is a small spot beset with white hairs; on the rest of the body, in part amply supplied with hair, no perceptible absence of pigment anywhere. The patient states that his head never sweats.[1]

[1] I am indebted to the kindness of Dr. Michelson, of Königsberg, for the history and illustration of this case.

It is true, we have to emphasize certain deviations from the general type of acquired leucopathy—the absence of the sharp demarcation and of the increased pigmentation of the regions around the unpigmented spots. But we find the same deviations, too, in those decolorations of the hair occurring simultaneously with vitiligo of the rest of the skin, and we are justified, therefore, in ascribing them to variations in the development of the affection produced by the peculiar localization. I hold it to be altogether unquestionable that these cases owe their origin to the same morbid process as the vitiligo.

The course of vitiligo is progressive, the white spots steadily enlarging, so that they finally may occupy the entire skin.[2] But the pigment atrophy may also stop at any point and remain forever stationary. Näcke[3] states that in a case observed by him—this was an auto-observation, and we may therefore all the more exclude any deception—the white spots at one point became again normally pigmented, while they remained unpigmented on the rest of the body and presented absolutely the characteristic aspect of vitiligo. But this behavior is exceptional; the spots once having lost their pigment, generally remain permanently white. The disease has not the slightest influence on the functions of the skin nor on the general health of the affected person.

I have examined three cases anatomically; in two, the vitiligo was an accidental discovery at the post-mortem, while in the third, a piece of skin was excised during life. I can only confirm Simon's statements, that the skin presents nothing abnormal but absolute absence of pigment in the decolored spots, and more or less intense pigment hypertrophy in the darker portions. Remarkable appeared to me only the very large quantity of pigment in the corium, especially where the brown parts adjoined the white

The etiology of vitiligo is rather obscure, still some facts which have a bearing upon it can be established. There does not seem to be any greater disposition of one or the other sex, but age has a decided influence. In the large majority of cases it begins between the tenth and the thirtieth years; much more rarely later, and quite exceptionally earlier. I know of but two cases in early life—the above-mentioned case of Näcke, in which the disease began in the fifth year, and another commencing in the eighth year. In many instances the onset succeeds some acute disease; thus, in the cases detailed above

[1] This must be regarded as an exception, the absence of any further disturbance of function in the decolored parts having been otherwise regularly observed.

[2] Lévy (Recueil de mém. de méd., de chir. et de pharm. mil., 1865, p. 193) has seen three cases in which the pigment diappeared completely.

[3] Berl. klin. Wochenschr., 1881, p. 523.