skin and mucous membranes present, the diagnosis presents little or no difficulty to one who has previously studied a single case of the disease. On the other hand, when the constitutional symptoms are well pronounced in a primary case, and the bronzing of skin is not yet developed, the diagnosis is to be made only, if at all, by the exclusion of other wasting diseases, especially cancer of abdominal organs and progressive pernicious anæmia. Many years ago there came under my care at the Episcopal Hospital of Philadelphia a case of lumbar abscess with several open sinuses leading to carious vertebræ. The general surface of the body was of a dark dingy hue, and the orifice of each sinus was surrounded by a broad, deeply pigmented ring. The patient had been previously at another institution, where secondary disease of the adrenals had been suspected. The autopsy showed these bodies to be perfectly healthy and the kidneys to be involved in extensive amyloid degeneration. A dingy discoloration of the skin is not uncommon in amyloid disease of the kidney, as first pointed out by Grainger Stewart.

The discoloration of skin, although not the most essential characteristic of the disease, is justly regarded as its most important diagnostic feature. It is to be distinguished from melasma gravidarum, pityriasis versicolor, lichen, and pigmentary syphilides, and this is readily done by any one familiar with these affections. The melanoderma of phthisical patients presents more serious difficulty. Although the latter is often confined to the face and does not invade the mucous membrane of the buccal cavity, the difficulty is a real one, and is augmented by the fact that pulmonary tuberculosis is the most frequent complication of Addison's disease. The seat of the melasma suprarenale, or its greater intensity, upon the face and neck, the dorsum of the hands, areola of the nipple and about the umbilicus, in the axilla, groin, and upon the genitals, is characteristic. Other diagnostic features of the pigmentation have been described above under the head of Symptoms. A discoloration of the skin liable to be confounded by the inexperienced with that of Addison's disease is sometimes seen in badly nourished paupers of dirty habits, whose skin is the abode of vermin. This pigmentation shows itself in the form of patches separated by healthy skin; the epidermis is often roughened, and the discoloration more marked upon the trunk than on the face and hands. The skin is also often marked with scratches, the result of the intense itching. Under the microscope, the particles of pigment in this affection are found in all the layers of the epidermis, instead of being limited, as in Addison's disease, to the deeper layers of the rete Malpighii. The pigmentation of chronic malarial poisoning is distinguished from that of Addison's disease not only by its distribution, but by the history of the case and the frequent presence of splenic enlargement; chronic icterus, with which Addison's disease was formerly confounded, is distinguished by the presence of pigment in the ocular conjunctiva and in the urine.

Other discolorations of the skin simulating closely the pigmentation of Addison's disease are mentioned by systematic writers, but are so rare as to be in themselves pathological curiosities. Among them may be mentioned a diffuse pigmentation associated with chronic scurvy (Bramwell), and a few other cases of melasma occurring without obvious cause. According to the author just cited, there are certain forms of pigmentation of the skin associated with chronic peritonitis, or malignant disease of the abdomen or pelvis, which it is impossible to distinguish from Addison's disease. This fact, though discomfiting to the clinician, is of great interest to the pathologist, as tending to prove that the most characteristic symptom of the affection, the melasma suprarenale, is to be attributed rather to the implication of the abdominal sympathetic than to that of the adrenals.

Prognosis.—The prognosis is in the highest degree unfavorable, although recoveries of cases presenting every sign and symptom of the affection have been reported by the most competent observers. Among these may be mentioned Sir William Gull and Dr. Finney. In making predictions as to the duration of life, the remittent character of the disease should be borne in mind. A case seen during a period of exacerbation may lead to the prognosis of a speedily fatal result, but the worst symptoms may disappear and be followed by a prolonged period of remission. The average duration of the life of hospital patients who, as a rule, do not apply for treatment until forced to acknowledge the fact of their illness, has been estimated at two years. Sudden death without preceding exacerbation is sometimes observed, the fatal result being apparently due to syncope.

Treatment.—At the present time, there may be said to be a specific treatment of Addison's disease—that with adrenal extract. This fact, however, in no way diminishes the importance of general therapeutic measures, of which the most important are the following: The cessation of work is the first thing to be insisted upon in the way of treatment, and during the exacerbations strict confinement to bed. An immediate mitigation of the symptoms has often followed the admission to hospital of a patient who, up to that time, had been endeavoring to resist the gradually increasing asthenia. A moderate amount of stimulants is generally well borne, but cod-liver oil, which might seem appropriate on account of the tuberculous nature of most cases of the disease, is, as a rule, not tolerated. Remedies to allay irritability of the stomach are frequently indicated, such as ice, lime water, carbonic acid water with brandy, bismuth, creosote, hydrocyanic acid, and small doses of opium. Massage and faradization are well worthy of a trial in order to derive the blood from the abdominal vessels. Iron and arsenic should be employed tentatively and will be generally found useful, and the same is true of nux vomica and its derivatives. Cathartics are to be avoided, as profound depression has often followed their employment in this disease. When constipation is troublesome it should be relieved by enemata and suppositories. The diet should be simple but nourishing, consisting of soups, milk, eggs, meat jellies, koumyss, and the like.

Treatment with Adrenal Extract.—The success that has attended the use of adrenal extract is such as to make it imperative in all cases of Addison's disease. This is not a mere *obiter dictum*, but is the result of a careful study of many of the reports upon the subject. A few examples will suffice to show the kind of evidence on which the administration of the adrenal extract is based.

Osler (*International Medical Magazine*, February, 1896) reports a case in which there was marked improvement under the use of the extract, attended with considerable gain in weight and restoration of general vigor. The pigmentation, however, which was of advanced grade, had not diminished except on the palate. A case is reported by Suckling (*British Medical Journal*, May 28, 1898) in which the symptoms and signs were well pronounced except pigmentation of mucous membranes, of which there is no mention. Tablets of suprarenal extract (āā gr. v.) were given to the extent of from twenty to thirty-five daily. In the course of a year recovery was complete with disappearance of melanodermic and leucodermic patches. Kinnicutt has tabulated 48 cases (*American Journal of the Medical Sciences*, July, 1897) treated with adrenal preparations. "Six patients are reported as cured or practically well, 22 improved, 18 unimproved, and in 2 instances an aggravation of the symptoms is stated to have occurred during treatment." In the second class of cases, those in which improvement took place, the improvement was but temporary; but this was as much as could be expected, since in many the disease of the adrenals was associated with grave tuberculous lesions in other parts of the body.

On the theory that Addison's disease is chiefly due to suppressed function of the adrenals, the use of adrenal extract would find its most successful employment in those cases in which the lesion consists of simple atrophy or fibroid degeneration. *Frederick P. Henry.*

ADENITIS. See *Lymphatic Glands, Diseases of.*

EXPLANATION OF
PLATE VI.

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FIG. 1.—Shows the Discoloration of the Tongue in a Case of Addison's Disease. *a*, Dark ink-like stains near the free border of the tongue; *b*, fungiform papillæ on the dorsum of the tongue, discolored by deposit of pigment; the papillæ circumvallatæ remaining uncolored.

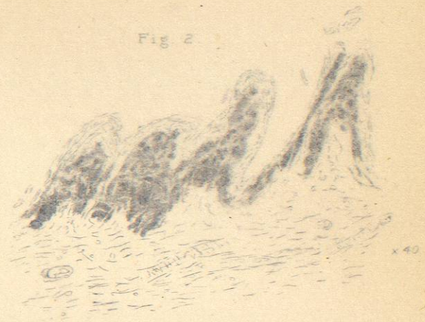
FIG. 2.—Section of Pigmented Patch on the Tongue, Viewed with a One-Inch Objective. The lower, plumper cells clothing the papillæ are seen loaded with pigment; the subepithelial connective tissue remaining quite uncolored.

FIG. 3.—Section of Bronzed Skin. *a*, Rough scarf skin free from pigment; *b*, plumper cells of the rete mucosum, the deepest layer loaded with pigment; *c*, subepithelial connective tissue free from pigment.

FIG. 4.—Section of Discolored Patch of Skin, Site of a Recent Blister. *a*, Brown pigment deposited in the deeper layers of the epidermis; *b*, scattered masses of pigment situated in the cutis vera.

Fig. 1.

Fig. 2.



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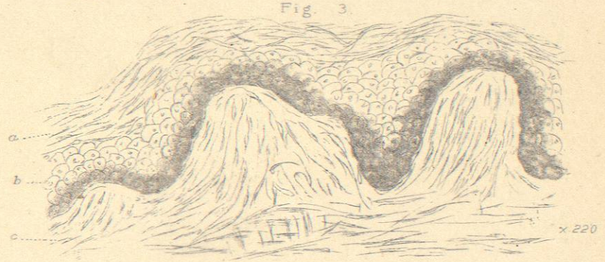
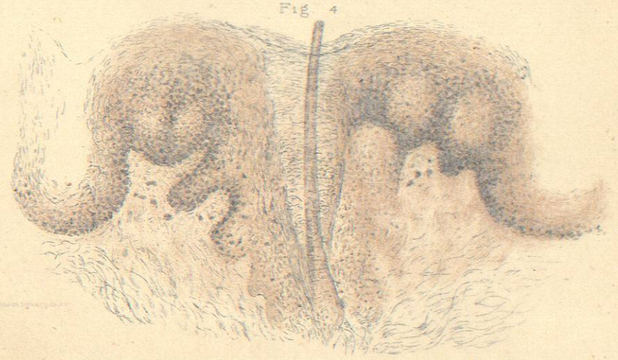


Fig. 4.



PIGMENTATION OF THE SKIN AND OF THE MUCOUS MEMBRANE OF THE TONGUE OBSERVED IN ADDISON'S DISEASE.—*(Copied from the Treatise of Edward H. Greenhow, M.D., F.R.S.)*

G. H. Ford sc.

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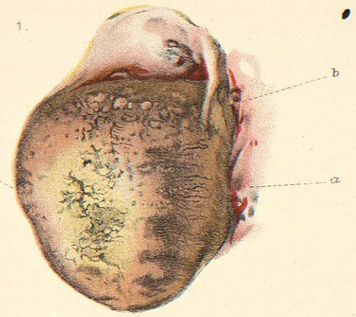

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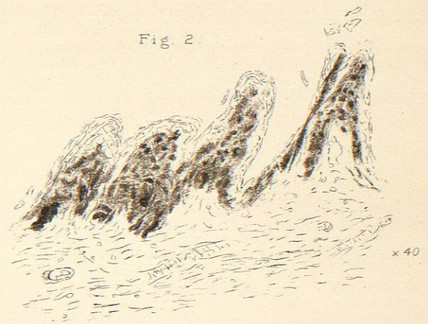

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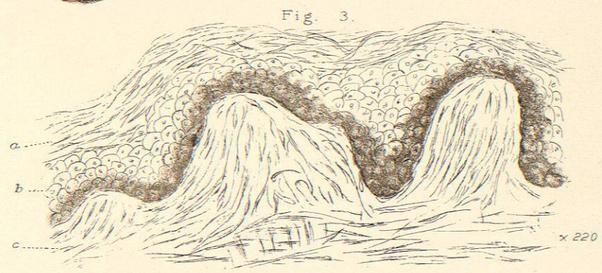
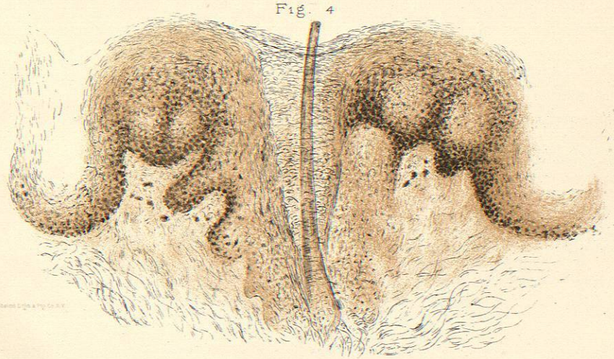


Fig. 4



PIGMENTATION OF THE SKIN AND OF THE MUCOUS MEMBRANE OF THE TONGUE OBSERVED IN ADDISON'S DISEASE.—*(Copied from the Treatise of Edward H. Greenhow, M.D., F.R.S.)*

G. H. Ford sc.

ADENO-CARCINOMA. See *Carcinoma.*

ADENO-CYSTOMA. See *Cystoma.*

ADENOID VEGETATIONS. See *Tonsils, Pharyngeal.*

ADENOMA.—Adenoma is the term applied to a new growth originating in glandular epithelium and corresponding in histological structure with the general type of gland tissue.

Every new formation of glandular tissue, every glandular hyperplasia, cannot be regarded as an adenoma, and sometimes it is impossible to say whether an apparent growth is a simple hyperplasia or a tumor. A gland which is increased in size in consequence of excessive nutrition and function cannot be called an adenoma, but must be considered a hyperplasia.

In the same way must be considered those formations in mucous membranes which frequently develop in consequence of chronic inflammation and take the form of tumors. These are local new formations which project above the surface in the form of polypi or papillary masses. The new growth commences in the connective tissue, and the epithelium also takes part in that, by the increase of the surface, the covering epithelium also must increase. If there are glands present their ducts are usually obstructed, and cysts are formed with papillary projections within them. This must be considered simply as a growth due to chronic irritation, and as entirely distinct from the true glandular polyp of the mucous membranes in which a formation of new glands actually occurs. Clinically, these can usually be distinguished, for the simple polyp disappears when its cause, chronic irritation, disappears.

Etiology.—The causation of adenomata is obscure, though probably no more so than that of new growths in general.

In some forms congenital misplacement of tissue elements appears to play an important part. Thus in the kidney, adenomata sometimes are found which correspond in structure to the adrenal. These, as pointed out by Grawitz, develop from aberrant remnants of the adrenal embedded in the kidney substance. This is also true of adenomata corresponding to the structure of the mamma occasionally seen in the axilla, and of the rather unusual substernal tumors in which a tissue similar to that of the thyroid body is found. Here it is probable that the theory of embryonic remains of Cohnheim gives the true explanation: the tumor in each of these instances develops from embryonic fragments which become separated from the gland in its development. Although in certain locations, as the stomach and rectum, the adenomata appear to bear out Virchow's irritation theory, in other locations they offer it no support at all.

The parasitic theory receives absolutely no support from the adenomata, for it is impossible to conceive of a vegetable or an animal parasite causing the reproduction of definite gland tubules.

Varieties and Structure.—The appearance of adenomata varies greatly with their location. Naturally, any particular cell or arrangement of cells cannot be described as peculiar to this tumor, any more than any type of cell can be regarded as characteristic of all physiological glandular structures. The adenomata differ from one another in structure as much as the structure of the liver differs from that of the lachrymal gland.

In the stomach, intestine, and uterus, in a general way, the epithelial cells are arranged as tubular acini with a central lumen, the cells generally occurring in one layer, though there may be more. The acini are separated from one another by connective tissue in which the blood-vessels and lymphatics are borne. Why the cells in their growth should grow as tubules instead of breaking through the basement membrane and forming atypical groups of epithelial cells, as is seen in the form known as adeno-carcinoma, is difficult of explanation. It is probable that the inherent tendency thus to develop is not early influenced by their altered environment. That they do not break through and grow as carcinoma is frequently seen in some large and rapidly growing adenomata. The cells lining the tubules may be columnar or cuboidal, according to the gland from which the tumor develops.

In addition to the tubular form there is an uncommon variety, the racemose adenomata, in which the appearance is that of a complicated gland structure with closely aggregated acini of circular outline containing columnar, cuboidal, or polyhedral cells.

Then, again, in the liver, kidney, and adrenal occur adenomata resembling more or less closely the normal structure of those organs.

As in any other epithelial tumor, the relation between the epithelial cells and the connective tissue varies. When the development of the connective tissue is excessive, far beyond that of the normal gland, it must receive some recognition in naming the tumor, for it is as truly new formed as is the epithelial portion: in such cases it is called an adeno-fibroma. When this connective tissue is especially abundant in cells and represents an embryonic tissue, the term adeno-sarcoma is used. In the ovary occurs an adenoma in which the acini line cyst cavities. This is termed an adeno-cystoma.

Adenomata, as far as known, do not contribute to the body metabolism. That there is a partial preservation of function is occasionally seen. In the adenoma of the liver sometimes a biliary pigmentation occurs; in the adenoma of the breast there may be a secretion of milk-like fluid; in the adenoma of the intestine the tubules may contain mucus; in the adenoma of the thyroid colloid material may collect. But these substances remain in the tubules in which they are formed, and take no part in the general metabolism.

Secondary Changes.—All forms of degeneration are common in adenomata. Hyaline transformation may give the tumor an appearance justifying the term "cylindroma." This, however, is rare. Myxomatous and calcareous degenerations occasionally occur. Cystic change may result from gradual dilatation of the glandular acini. Hemorrhages are common, and on free surfaces ulceration is frequent.

The most important change, however, is a carcinomatous transformation. This is especially common in the stomach, intestine, and uterus. The proliferation of the epithelial cells becomes excessive; the acini become more abundant and irregular; the cells depart from their tubular arrangement and grow as solid epithelial masses outside the acini, forming an adeno-carcinoma, or, as Ziegler named it, *adenoma destruens*. The growth may eventually become purely carcinomatous, but it usually retains more or less its adenomatous type.

General Character.—The rapidity of growth of an adenoma differs in various parts of the body in which it has its seat, and the same holds true for its malignancy. There are few which can be considered as strictly benign tumors. The pure adenoma seen in the liver may form metastases in the spleen and less frequently elsewhere. Fatal metastases from adenomata of the thyroid have been reported. In the sweat, sebaceous, and lachrymal glands the tumor usually grows slowly, remains local, and may be considered benign. In some locations, although adenomata never produce metastases, they may endanger life by their size, as in the ovary; or may obstruct important canals, as in the intestine; or may cause great disfigurement, as displacement of the eye in adenoma of the lachrymal gland. The general health may also be influenced by interference with the normal function of the organ in which they are located, or in consequence of ulceration and hemorrhage. There are few tumors more malignant than the adenomata of the intestinal tract. They extend rapidly, infiltrating all coats of the intestine, and frequently produce metastases in the liver. Their malignancy does not always depend on carcinomatous transformation, for some of the most destructive tumors of this canal are pure adenomata.

As regards the terms Malignant Adenoma and Adeno carcinoma, it seems best to use the former in designating those growths in which, although there is extensive infil-