eral salts the leaves contain contribute somewhat to its diuretic effects. Diuresis may be obtained with digitalin, however, a fact which shows that the drug is itself active in this connection. Its mode of action becomes plain, in view of its main general property, that of a potent stimulant of the adrenal center.* As this stimulates metabolism in all tissues, we have again an unusual production of tissue-wastes and the same central excitation (reflex) of the renal functions that saline solution affords,* though caused in a different way. Of material aid to the process is the increased vascular tension which the drug causes by activating indirectly metabolism in the muscular coat of all arteries.* A rise of blood-pressure is a recognized cause of diuresis. Digitalis is especially efficient in cardiac dropsy—a result readily accounted for by the above-described physiological action.

Squill acts much as does digitalis, including its action on the cardiac muscle, the arteries and general metabolism induced by a stimulating action on the adrenal center through the test-organ.* In large doses it stimulates the kidneys violently, causing sometimes hæmaturia. It is used in *dropsy, pleural* and *pericardial effusions* and the *cardiac dropsy,* but any form of nephritis is a contraindication to its use.

Calomel.—We have seen that this salt is an active diuretic also by enhancing general metabolism, thus causing rapidly an excess of waste-products in the blood.* When its use is prolonged it is also capable of causing grave renal disorders, including hæmorrhagic nephritis. It is very efficient in *cardiac dropsy,* however, and in *anuria* of asthenic origin in which the blood-pressure is low.

* *Author's conclusion.*

CHAPTER XXIII.

THE INTERNAL SECRETIONS IN THEIR RELATIONS TO PATHOGENESIS AND THERAPEUTICS.

THE ADRENAL SYSTEM AS IMMUNIZING MECHANISM, AND CANCER.

In the first edition (which appeared in January, 1903) of the present work,[1] the following lines appear: "Certain growths, particularly the more malignant forms, sarcoma and carcinoma, seem closely connected with adrenal insufficiency and its normal consequences. We have seen that *trypsin,* fibrinogen [a nucleoproteid compound] and the oxidizing substance were simultaneously necessary to insure the destruction of cells *in vitro,* and furthermore, that this process required, in addition, the presence of alkaline salts. That the destruction of worn-out or degenerated cells is a function of these very elements in the blood, is evident. Insufficiency of the adrenals, therefore, by reducing the relative proportion of these four constituents in the blood-stream, must correspondingly inhibit this physiological process in all parts of the organism." Thus, any region "may become the seat of this malignant growth, or rather of a local accumulation of the aberrant or worn-out cells which enter into its formation. The great vascularity of these growths suggests *an effort* of Nature to cause their elimination, but mitotic proliferation is alone induced, the blood being deficient in the four constituents which should insure destruction of the morbid cellular elements."

I pointed out also in this connection, in the same volume,[2] and under the caption "The Internal Secretions in their Relation to Immunity," that these "four constituents" were "the active immunizing agents of the organism," and that they owed their immunizing properties "to trypsin."

Over two years after I had done so, the close relationship between immunity and cancer was emphasized by several investi-

[1] *Cf.* vol. i, p. 785, 1st Ed., 1903.
[2] *Cf.* vol. i, pp. 609 to 666 incl., 1st Ed., 1903.

gators: in this country by Gaylord, Clowes, and Baeslack;[3] in Germany by Ehrlich,[4] Schöne,[5] Sticker,[6] and others. The researches of the Imperial Cancer Research Fund investigators for 1906, 1907, and 1911[7] have shown, moreover, that a high degree of resistance to the transplantation of cancer in mice could be obtained. But curiously enough, this did not prevent the spontaneous development of cancer in these animals. Might not *exuberant* resisting power entail a correspondingly active tendency toward morbid cell proliferation, and *normal* immunizing power exert a positive protective influence against spontaneous development of malignant neoplasms? The possibility that a loss of balance in this respect, both deficient and excessive immunizing activity standing as etiological factors, is suggested in the following pages, in which thyroiodase acting as opsonin, trypsin acting as complement, adrenoxidase acting as amboceptor and nucleo-proteid play, with the leucocytes, the leading rôles.

The need of a *working proposition* in this direction, the most promising one as to pathogenesis, is enhanced by the fact that the Cancer Research Fund investigations have also shown that cancer was not due to a common causal parasite.

CANCER.

Definition.—Cancer is primarily due to hypoactivity of the body's auto-protective mechanism, the adrenal system, the result, in turn, in most cases, of premature senility. It is a vicarious over-growth of tissue-cells which the agents of this system, leucocytic and humoral, should have destroyed in its incipiency, *i.e.*, when but a nidus of proliferating cells formed as a result of local irritation by traumatisms, inflammatory foci, parasites, moles, warts, etc. The defensive agents, phagocytes and auto-antitoxin, being those which, under normal conditions, carry on general nutrition, they are able only, owing to their insufficiency, to nourish the tumor and promote its development.*

This definition differs radically from those previously adduced by others, but the need of new lines of thought in this connection is

* *Author's conclusion.*

[3] Gaylord, Clowes, and Baeslack: Med. News, Jan. 14, 1905; see also Clowes: Bull. Johns Hopkins Hosp., Apr., 1905.
[4] Ehrlich: Zeit. f. ärztl. Fortbildung, Bd. iii, S. 205, 1906.
[5] Schöne: Münch. med. Woch., Bd. liii, S. 2517, 1906.
[6] Sticker: *Ibid.*, Bd. liii, S. 1904, 1906.
[7] Bashford: Fourth Rep. of the Imperial Cancer Research Fund, 1911.
[8] Bashford: *Ibid.*

emphasized by the labors of the Imperial Cancer Research Fund investigators, whose director, Dr. E. F. Bashford, wrote:[9] "In our investigations we have obtained evidence against all the explanations yet advanced as to the cause and nature of cancer," and, moreover, that "at present any attempts to directly ascertain the cause and nature of cancer are surrounded by so many sources of fallacy that," in his opinion, "they remain today as unprofitable as they have been in the past."

Symptoms.—The symptoms of cancer differ according to their location. The typical phenomena of the disease are in reality only witnessed when some external organ, the skin, the mammary gland, etc., is affected; while all the internal cancers soon provoke, in addition, morbid effects due to any interference with physiological functions which their presence entails. Common to all cases, however, is the terminal phase of the disease, *i.e.*, the cancerous cachexia, which consists of more or less rapid emaciation, anæmia and muscular weakness, the precursors of final exhaustion.

A brief survey of the leading symptoms can alone be given in this connection, and the reader is referred to special works for greater detail. In fact, the symptomatology would have been omitted were it not that the reader would have to consult works on dermatology, surgery, practice and special works on cancer to obtain even the present brief résumé of the various organs referred to. The division into "external" and "internal" cancers renders it impossible to illustrate the specific symptoms of the disease, those of cutaneous cancers, and, therefore, to differentiate them from those due to interference with functions.

External Cancers.—*Skin.*—The starting point of *carcinoma* of the skin or mucous membrane may be an excrescence of long standing, such as a pigmented mole, an ordinary mole, a senile wart, or cutaneous disorders, a fissure or abraded area of the lip, a psoriatic or scaly sebaceous patch, an adenoma, a nodule, a scar, etc. Without apparent cause, but occasionally after irritation or injury, any of these apparently benign cellular aggregates begin to grow. They ulcerate at the base, mainly at the expense of the cutaneous structures, until finally the typical epitheliomatous ulcer is formed, *i.e.*, irregular in shape, with raised everted edges. The bottom of the ulcer is very uneven and covered with a fœtid sanious secretion, and bleeds readily when touched. It may assume various shapes; hence the "cauliflower" and other appearances. In most cases pain only comes on late, the discomfort being due to the ulceration.

[9] E. F. Bashford: Brit. Med. Jour., Dec. 9, 1905.

When it appears it is of a lancinating character and may become very severe. The duration of cutaneous carcinoma varies greatly—from less than four years to decades. A favorite site is the lower lip; other regions frequently affected are the face, breast, genitalia, rectum, etc.

Cutaneous sarcoma is usually secondary, but it may develop primarily from a pigmented nævus or other cutaneous excrescence, especially when irritated. Sarcomata develop and multiply, break down and provoke metastases more rapidly than carcinomata, and death may occur within a few months, though in most cases life is prolonged a few years. The form that develops from nævi may retain its color, and merely grow and ulcerate, or it may become bluish or black, sessile, oval or spherical and hard; after growing for a while it ceases to do so, but others develop in other regions. All finally break down, forming melanotic ulcers which secrete a black substance and some pus. Death usually occurs from intestinal metastasis. Sarcoma may also appear as a diffused path or patches, beginning from minute brownish or purplish nodes, which become infiltrated and project, the skin being glossy and irregular. Various other rarer forms have been described, all embodying more or less prominently the characters just described.

Mammary Gland.—Two forms of cancer occur in this organ, the scirrhous, hard or fibrous cancer; and the encephaloid, or soft, cancer. In *scirrhous* cancer, the organ may preserve its form though becoming large and hard, the growth being deep-seated, or it may collapse or atrophy, the nipple being retracted, the so-called "withering" form. Again, a part of the breast alone may be affected, fibrous bands radiating through it and causing distortion of the organ. Conversely, it may be superficial at first, in patches or *plaques,* the skin appearing as though tanned, hard, rough and red. This may extend to the adjoining cutaneous tissues of the chest, the so-called "en cuirasse" cancer. The malignant growth may appear in the form of small, hard nodules of irregular size which may remain as they are if left alone, or ulcerate, and which promptly recur if removed. Ulceration may also occur when the growth is diffused, the ulcer resembling a crater with hard, everted edges, which bleeds easily and gives off a thin, offensive discharge.

The axillary glands are involved early, and as they enlarge may cause œdema of the arm or neuralgia by pressing upon the vessels and nerves. The entire lymphatic system is exposed to contamination; hence the visceral metastases often witnessed. After the tumor has reached a certain size, stinging, burning or neuralgic pains are complained of. As the ulcerative process advances, the toxæmia and cachexia do likewise, until the patient dies exhausted. *Encephaloid* cancer is not as frequently observed as the scirrhous form. It grows insidiously in the depth of the organ and finally reaches the skin. By gentle palpation, the tumor may be detected early in most instances; it may be fixed or movable, or nodular. At first, the skin is free, or traversed by prominent bluish veins, some of which may become varicose; red areas then appear—the precursors of adhesions with the cancerous mass. This soon becomes a fluctuating mass which ulcerates, becomes fungous, bleeds readily when touched, and gives off a foul odor. Cachexia appears earlier than in scirrhous cancer, and the burning, shooting pains and involvement of the lymphatics likewise. The softness of the growth predisposes it to hæmorrhages which are sometimes severe. Death occurs, as in scirrhous, from exhaustion.

INTERNAL CANCERS.—*Tongue.*—The anterior portion of this organ is the usual seat of cancer, which begins, as a rule, in a small fissure, ulcer or nodule on the side or edge, often where a sharp tooth, the stem of a pipe, a badly-fitting tooth-plate, etc., has for a time caused irritation. Psoriasis, scars, leucoma, cicatrices due to injury or syphilis, may likewise become the starting-point of a lingual epithelioma. When any one of these lesions becomes malignant, it soon assumes the aspect of a more or less deep and irregular ulcer with prominent edges, while the neighboring tissues, including often the floor of the mouth and gums, become infiltrated. Both the ulceration and infiltration may then extend posteriorly and involve the pillars of the fauces, the soft palate, the tonsils, etc. There is profuse salivation and the breath becomes extremely fœtid. The neighboring lymphatic glands become involved sooner or later, the prompt involvement denoting an unfavorable case. Gradually, deglutition and speech become difficult and starvation soon causes marked emaciation and weakness—a condition

greatly aggravated when the ulceration invades arteries and causes hæmorrhages. After a year or two of intense suffering, death occurs from exhaustion.

Larynx.—Hoarseness, dyspnœa and cough and pain are early signs of cancer of the larynx. The pain is usually quite severe and lancinating, generally radiates toward the ear, and is sometimes especially marked during deglutition. Ulceration has usually begun when such is the case. Laryngoscopic examination often shows, at first, enlargement of one cord, then congestion of a restricted area which finally ulcerates. This becomes fungous and necrotic, and secretes a fœtid, sanious liquid which gives the breath and the sputa a foul odor. Ulceration of a large artery may cause profuse hæmorrhage, sufficient in some instances to compromise the patient's life; asphyxia by the entrance of food particles in the diseased larynx, and pneumonia from aspiration of detritus from the malignant mass, are additional dangers of cancer in this region. The general health is soon undermined owing to deficient nutrition, and the patient lapses into the cachectic state, dying of general marasmus.

Œsophagus.—Dysphagia, pain, and finally regurgitation of food and fluids are the characteristic symptoms of cancer in this region. As the morbid process advances the neighboring organs, the larynx, bronchi, pericardium, mediastinum, lymphatic glands, etc., may be involved either by ulceration or pressure, causing suffocation, bronchitis, inhalation pneumonia or other complications. Ulceration of the aorta or one of its branches may also occur and cause fatal hæmorrhage. As a rule, however, starvation, owing to the œsophageal obstruction, and exhaustion are the causes of death.

Stomach.—Pain in the epigastrium is present in practically all cases; but it is often preceded by a period of dyspepsia, sometimes attended with vomiting. In others the gastric disorders may be slight or absent, the main signs being those of pernicious anæmia, with intense pallor. Progressive emaciation is a constant feature of the disease, and is accompanied by more or less asthenia. When the cancer is situated near the cardia, spasm of the œsophagus and dysphagia may occur. Fever is present in about one-half of the cases, and may reach 104° F. (40° C.); in some cases the febrile process is continuous.

Glycosuria and indicanuria are commonly observed, peptonuria, sometimes. Death results occasionally from diabetic coma. Œdema of the ankles appears in the majority of cases and, in some instances, general anasarca supervenes. Hæmatemesis is observed in about one-fourth of the cases, the material vomited being always brown or black, the "coffee-ground" vomit. The tumor, when it has attained a certain size, can often be discerned both by inspection and palpation; the mass rises and descends during respiration—a sign especially marked in cancer of the pylorus.

Pancreas.—The earlier symptoms are gastro-intestinal, *i.e.*, indigestion and dull paroxysmal pain in the epigastrium, nausea, vomiting or diarrhœa, flatulence, the stools being greasy and clay-colored. Marked jaundice, due to obstruction of the bile-duct when the head of the pancreas is involved, ascites and diabetes are sometimes observed. In some cases a tumor may be felt in the pancreatic region, which differs from that of cancer of the gall-bladder, in that it is fixed. A distinct pulsation may be felt in the organ when the emaciation is sufficiently marked, owing to the fact that the growth lies directly upon the descending aorta. Prominent features of cancer of the pancreas are a rapid loss of strength and emaciation, soon followed by cachexia.

Liver.—Progressive enlargement of the organ, discernible on palpation, when sufficiently advanced, with pain and tenderness are the most common symptoms, especially if the growth is not far from the surface. Gastric disorders are frequently complained of. In about one-half of the cases, jaundice and ascites occur, accompanied in some instances by purpura, though the latter may appear in all cases, causing death frequently within three months.

Gall-bladder.—Cancer of this organ is almost always due to irritation by gall-stones. A firm, hard, irregular mass can often be detected at the site of the organ, which moves with the liver during deep respiration. There is more or less local tenderness on pressure, and severe paroxysmal—though sometimes continuous—pain. When the bile-ducts are involved, marked and persistent jaundice appears. The stools may be

bloody and dropsy may occur, the latter being a feature of the cachetic stage.

Intestine.—The symptoms vary according to the position of the growth. Irregular attacks of acute colicky pains from two to five hours after a meal, according to the location of the tumor, nausea, vomiting, chronic constipation, with diarrhœa and meteorism, are almost always present, jaundice being superadded if the ducts of the gall-bladder are involved. When the intestinal obstruction is marked, the stools may assume a characteristic shape, *i.e.*, very small masses or lumps. The tumor may sometimes be detected by palpation through the abdominal walls, especially when the patient's muscles are relaxed by great weakness and when he has become greatly emaciated.

Peritoneum.—An uncomfortable sensation, with perhaps pain, in the abdomen followed by ascites, emaciation, and weakness are about all the symptoms observed at first. Differential diagnosis alone affords some clue to the nature of the disease: the age of the patient excludes tuberculosis of the peritoneum, which occurs in young subjects; the absence of fremitus distinguishes it from echinococcic cysts, another disorder which it greatly resembles. The neighboring organs, including the uterus, ovaries and rectum, should be examined in view of the fact that cancer of the peritoneum is often secondary. The inguinal glands are often enlarged. The tumor is discerned with difficulty owing to the ascites, but it can usually be felt after paracentesis. The vessels of the malignant mass sometimes rupture, causing severe hæmorrhage and aggravating the cachexia.

Uterus.—If the growth begins while the woman is still menstruating, intermenstrual spotting and a serous discharge are likely to appear. The presence of such signs after menopause is also significant. The slight discharges gradually become more frequent and abundant, and finally emit an unpleasant odor, the fœtor becoming very marked when necrotic tissue is present. Pain does not occur until the morbid process is well advanced, and is due to involvement of the neighboring tissues and their nerves; at first it is apt to radiate into the iliac region and hip, but involvement of the bladder, rectum and peritoneum gives rise to the characteristic pains that attend

inflammation of these organs. Examination of the uterus should be practiced as soon as possible, to confirm the suspicions awakened by the general phenomena. Intense anæmia, general weakness, and the symptoms of the cachectic period finally appear, though death is often due to uræmia.

Rectum.—Uneasiness in the sacral region and along the inner side of the thighs, which after prolonged exertion may become actual pain radiating towards the rectum, are usually the earliest symptoms complained of. Morning diarrhœa, the discharge being watery, differing as to odor from the usual liquids voided, and often tinged with blood, is then observed, though this be interrupted by periods of constipation. When the stools are formed, they may be ribbon-like when the growth is low down. Local pain, which occurs late and is severe, especially during defecation, if the growth is near the anus, eventually becomes continuous. Hæmorrhages may then appear and become more frequent when ulceration occurs, thus aggravating what general debility may be present. The lymphatic glands of the region, pelvic and lumbar, are often enlarged and the liver also in some instances. The body gradually wastes and finally lapses into the characteristic cachetic state.

Pathogenesis and Pathology.—Advanced age is the predominating predisposing cause of cancer, but since the disease does not occur in all aged individuals, an additional predisposing factor is necessary. This factor may be said to include all morbid influences, inherited or acquired, which tend further to debilitate the organism. Although cancer is witnessed among the poor and ill-fed, and its development may follow exhausting toil, great anxiety, prolonged illness and other debilitating conditions, it occurs at least as frequently among subjects who have not been exposed to similar untoward influences, *i.e.*, the well-to-do and well-fed, and even the over-fed. In all these, however, inherited vulnerability to disease, which means inadequate activity of the auto-protective mechanism—the adrenal system—may none the less be present, and when advanced age is reached, the organism is unusually vulnerable to disease among the rich and poor alike.* In the over-fed, the wear and tear imposed upon the digestive apparatus, the excessive stimulation of the

* *Author's conclusion.*

organs which supply the digestive ferments, and the overloading of the lymph and blood with more or less perfectly catabolized waste-products, gradually undermine all physiological functions, thus affording the accessory factor which with senility predisposes any part of the body, any organ, to the development of cancer.*

Bashford,[10] alluding to results reached in the Imperial Cancer Research Fund laboratories, states that "the association of cancer with old age is the only factor known to be constantly associated and intimately bound up with the processes responsible for the development of cancer in man and animals." He also calls attention to the fact that "cancer has the further remarkable common feature that in animals it has the same higher incidence in old age, and therefore the same relation to the duration of life as in man." Freund,[11] after a comprehensive study of the etiology of cancer, concludes that senilism is the primary etiological factor, but moreover, that it could be premature and even localized as well as generalized. This accounts for the occurrence of cancer at times in younger subjects—a fact which the British Research Commission has also elucidated recently, its labors having shown, according to Sir William Church,[12] that cancer in the young occurs for the most part "in tissues and organs which lose their functional activity in early life, and normally undergo degeneration and more or less absorption."

The presence of an additional predisposing cause is shown by the relationship of cancer with tuberculosis—first pointed out by Krauss, in 1832. Thus, Roger Williams[13] states that "no hereditary condition is more favorable to the development of cancer than that which predisposes to and accompanies tubercle." Moak[14] reported five cases in which carcinoma and tuberculosis were present in the same organ. H. R. Jones[15] found that in England and Wales, a high percentage of phthisical persons had a cancerous family history, and the age period at which the mortality of tuberculosis reached its zenith, 35 to 45 years, coincided with the period at which the cancer death-rate began to increase. In Ireland[16] a collective investigation by the registrar-general showed that in many cases cancer occurs in the same family; grandparents, parents and other relatives, and that the family likewise shows a predisposition to tuberculosis. Closely related to this feature of the problem is the observation of Roger Williams,[17] that in multicellular animals and plants, tumors rarely occur when these organisms live in a state of Nature, and that they are met with almost exclusively among domesticated varieties, especially those that have been kept long in confinement.

In a careful analytical study of the twelfth United States census, Guthrie McConnell[18] found, moreover, that those employed in hard outdoor work showed a higher cancer mortality than those of sedentary habits, while Freund[19] witnessed a number of examples in which a

* *Author's conclusion.*
[10] Bashford: *Ibid.*
[11] Freund: Zeit. f. Krebsforschung, Bd. iii, S. 1, 1905.
[12] Sir William Church: Lancet, July 8, 1905.
[13] Roger Williams: "Diseases of the Breast, etc.," London, 1894.
[14] Moak: Jour. of Med. Research, June, 1902.
[15] H. R. Jones: Lancet, Nov. 12, 1904.
[16] Jour. Amer. Med. Assoc., Apr. 18, 1903.
[17] Roger Williams: Brit. Med. Jour., July 30, 1904.
[18] Guthrie McConnell: Jour. Amer. Med. Assoc., Apr. 28, 1906.
[19] Freund: *Loc. cit.*

chronic, though mild, gastric disorder became a rapidly fatal cancer after excessive worry or overwork. Finally, Jonathan Hutchinson[20] refers to twelve cases of cancer which had developed in subjects who had been long under the influence of arsenic, and ascribes the tendency of chimney-sweeps to the large proportion of arsenic in certain coals. We have seen that arsenic is the physiological antagonist of thyroid extract, and that it depresses the functional activity of the adrenal system and, therefore, that of all vital processes. Robert Bell[21] writes: "That the thyroid has an important relationship to the incidence of cancer is borne out by the fact that in cancer subjects it is invariably found to be more or less atrophied, hence it is necessary to supplement the modified dietetic measures recommended by the administration of either thyroid gland substance or its active principles. By these means we have reason to hope the gland may recover its lost power and thus be enabled to resume its physiological activity, which is quite within the range of possibility."

The predisposing influence of over-eating is emphasized by the importance attached to the gouty diathesis, long ago, by French clinicians, Bazin, Bouchard[22] and others, and more recently by Felix and Robert Bell[23] and Vigouroux.[24] Rabagliati,[25] Roger Williams[26] and Chittenden,[27] likewise incriminate excess of nutritive material in general. That the predisposition to cancer is a *result* of the excessive ingestion of food is shown by the fact that the age incidence of cancer succeeds that of gout. Indeed, as stated by Bazin, "the gouty *end up* especially with cancer, particularly by cancer of the rectum and bladder." It is an expression, in these cases, of the chronic phase of gout, which phase, as stated by Levison,[28] is attended by debility of the patient, and may also "appear in feeble subjects as the only manifestation of gout."

Still, if we are dealing with *general* adynamia, why is the cancerous growth localized?

A cancer develops from a preëxisting aggregate of adventitious cells,* whether the latter constitute a mole, a nævus, a wart, a fibroma, etc., or patches of eczema, psoriasis, paraffin acne, cicatricial tissue, etc., or an ulcer, fistula or other lesion of the skin or mucous membranes, or whether it occur as a result of localized and chronic inflammation in the deeper or internal organs. As long as the nutrition of any one of these local cell-aggregates is adequately controlled by its arterial blood, it retains its benign character;* when, however, a debilitated condition of the organism, such as that brought about by senility or any of the other predisposing conditions just reviewed prevails, it develops a malignant growth. The morbid process

* *Author's conclusion.*
[20] Jonathan Hutchinson: Deut. med. Woch., Bd. xxx, S. 1378, 1904.
[21] Robert Bell: Med. Record, Feb. 16, 1907.
[22] Bouchard: "Mal. par ralent. de la nutrition," second edition, 1885.
[23] Robert Bell: Med. Record, Aug. 15, 1903.
[24] Vigouroux: Revue de thérap., Sept. 1, 1906.
[25] Rabagliati: "Air, Food and Exercise," London, 1887.
[26] Roger Williams: Edinburgh Med. Jour., Nov., 1897.
[27] Chittenden: Amer. Medicine, Nov. 11, 1905.
[28] Levison: Sajous's "Analyt. Cyclo. of Pract. Med.," Art. "Gout," edition 1899.