tissues it may closely simulate a benign encapsulated tumor.

Various types of cancer occur. The *papilliferous adenocystoma* may take on a low degree of malignancy and

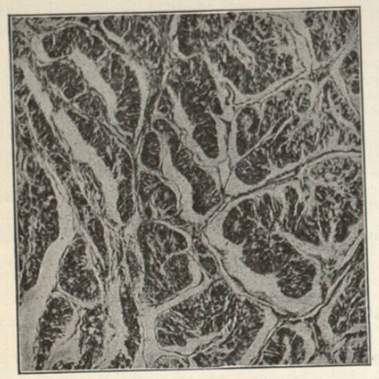

Fig. 2338.—Cylindrical-celled Carcinoma of the Thyroid. Acini filled with high cylindrical epithelium; no colloid present. (× 86 diam.)

would then be classed as a cancer. Cases of this nature have been described by Barker and Wölfler.

A rare but interesting form is the *cylindrical-celled carcinoma*. The high cylindrical-celled adenomas probably are always malignant, although in places their his-

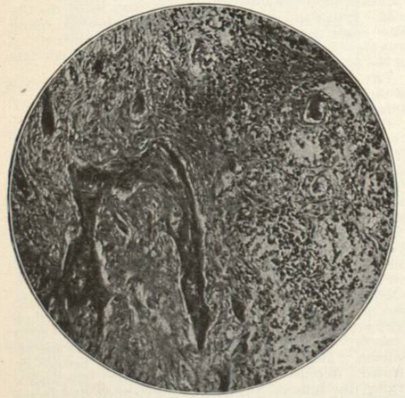

Fig. 2339.—Primary Squamous-celled Carcinoma of the Thyroid; margin of new growth. The tumor which lies to the left of the median line consists of nests of squamous cells separated by large areas of dense fibrous stroma. Beyond the tumor the normal glandular tissue of the thyroid has largely disappeared. There is marked infiltration with lymphoid cells. One shrunken vesicle filled with colloid is distinctly seen. (× 86 diam.)

tological structure may not suggest it. Fig. 2338 is from a cylindrical-celled adenoma that invaded the trachea.

The *squamous-celled* is also a rare but well-recognized form of primary thyroid carcinoma. It has been described by Forester, Lücke, Kaufmann, and Wölfler. Fig. 2339 is from a case that was examined by Dr. J. Homer Wright, of the Massachusetts General Hospital. It is held that this peculiar tumor originates from the remains of the branchial clefts which are enclosed within the thyroid.

Housell has collected twelve cases of benign thyroid tumors that formed metastases. I have found two other cases in the literature. The original tumor as well as the secondary growths in all the cases had the structure of simple adenomas. Metastases in the bones have been a constant occurrence, and they usually form pulsating tumors. The first case was studied by Cohnheim. The thyroid tumor was of moderate size, and there were metastases in the bones, lungs, and bronchial lymph nodes. A nodule of the original tumor projected into the lumen of a small vein. Riedel, and Oderfeld and Steinhaus (*Cent. f. allg. Path. u. path. Anat.*, 1901, vol. xii., p. 209) have described cases in which the thyroid gland was normal. The latter hold that normal thyroid tissue may grow into blood-vessels, and the epithelial cells swept along in the current form metastases in the bones. Chris-

Fig. 2340.—Carcinoma of the Thyroid which has Invaded the Trachea and Formed a Button-like Nodule which Projects into the Lumen. (Warren Museum, No. 4,892.) (Natural size.)

tiani (*Jour. de phys. et path. Anat.*, 1901, vol. iii., p. 22) has demonstrated the great vitality and viability of thyroid tissue.

Symptomatology and Diagnosis.—Clinically it is difficult to distinguish between sarcoma and carcinoma. The latter usually are of smaller size and develop more slowly.

The malignant tumors develop rapidly. Pain is an early and important symptom. It is usually severe and radiates to the head or shoulders. Tenderness on pressure is often present. Fever is the rule. Enlargement of the lower cervical lymph nodes is strong evidence of the malignant nature of the thyroid tumor, provided strumitis can be ruled out. Immobility of the tumor does not occur until the capsule of the thyroid has been penetrated and the tissues of the neck are infiltrated. Hence it is a late sign. Kaufmann considers thrombosis of the veins of the neck one of the most reliable signs of malignant tumors.

Penetration of the trachea is common. An elevated nodule, sometimes of considerable size, is found projecting into the lumen. It is usually situated about 2 cm. below the cricoid. Fig. 2340 is from a specimen in the Warren Museum of the Harvard Medical School. The patient entered the Massachusetts Hospital suffering from extreme dyspnœa, hoarseness, and some dysphagia. Dr. Knight examined the larynx and found paralysis of one posterior crico-arytenoid muscle, and made out an obstruction of the trachea. The dyspnœa continued until death occurred two days later. The autopsy was performed by Dr. Fitz. A tumor mass the size of a small lemon connected with the thyroid was found. The growth extended through the anterior wall of the trachea projecting into the lumen to such an extent as to reduce the calibre fully two-thirds. The œsophagus was so compressed as barely to admit the little finger.

A peculiar chronic inflammation of the thyroid which closely simulates an infiltrating tumor has been described and studied by Riedel, Tailhefer, and Berry. A number of cases have been reported within the past five years.

Treatment.—Early and radical operation offers the only hope of cure.

Tuberculosis.—Although rare, tuberculosis of the thyroid is more common than is generally stated. Chiari found the thyroid was involved at autopsy in seven out of one hundred cases of tuberculosis. Roger and Garnier (*Arch. gén. de méd.*, 1900, vol. iii., p. 385) assert that while tubercles rarely develop, a sclerosis of the gland is a constant feature of chronic tuberculosis of the lungs or elsewhere.

Syphilis.—Swelling of the thyroid is common in the early stages of syphilis. Engel-Reimers found the gland enlarged in fifty per cent. of the cases. Gumma is extremely rare. The few instances that have been recorded were nearly all in children, and usually associated with severe visceral manifestations of the disease. For details in regard to syphilis of the thyroid the monographs of Fürst and Küttner may be consulted.

Echinococcus Disease.—Berry has collected twenty-two cases. A single cyst has usually been found. The tumor when large may be very irregular in shape. The symptoms are those of an ordinary goitre. Dyspnœa is usually present. There is a tendency to spontaneous suppuration. Diagnosis can be made only after microscopical examination of the cyst contents. The aspiration of a clear, limpid, colorless fluid is suggestive (Berry). The demonstration of hooklets or scolices confirms the diagnosis. The known association of urticaria with hydatid led Lannelongue to make the correct diagnosis. Perforation into the trachea has caused suffocation in a number of instances. *Joseph Hersey Pratt.*

Bibliography.

Adami: Goitre. Sajous' Annual and Analytical Cyclopædia of Practical Medicine, 1899, iii., p. 328.
Barton: A Memoir Concerning the Disease of Goitre as it Prevails in Different Parts of North America, Philadelphia, 1800.
Baurowicz: Ueber Schilddrüsengeschwülste im Innern des Kehlkopfes und der Luftröhre. Arch. f. Laryngol. u. Rhinol., 1898, viii., p. 362.
Berry: Lectures on Goitre; its Pathology, Diagnosis, and Surgical Treatment. Brit. Med. Jour., 1891, i., pp. 1269, 1326, 1372.—Diseases of the Thyroid Gland and their Surgical Treatment, London, 1901.
Bircher: Der endemische Kropf, Basel, 1883.
Bradley: On Hæmorrhagic Cysts of the Thyroid Gland. Jour. of Experimental Medicine, 1896, i., p. 401.
Bruns: Weitere Erfahrungen über die Kropfbehandlung mit Schilddrüsenfütterung. Beiträge zur klinischen Chirurgie, 1895, xiii., p. 303.
De Cyon und Oswald: Ueber die physiologischen Wirkungen einiger aus der Schilddrüse gewonnener Producte. Pflüger's Archiv, 1901, lxxxviii., p. 199.
Dock: Goitre in Michigan. Transactions of the Association of Amer. Physicians, 1895, x., p. 101.
Edmunds: The Pathology and Diseases of the Thyroid Gland. Lancet, 1901, i., pp. 1317, 1381, 1449.
Ewald: Die Erkrankungen der Schilddrüse, Myxodem und Cretinismus. Nothnagel's specielle Pathologie und Therapie, Vienna, 1896, xxii., p. 1.
Freund: Ueber die Beziehungen der Schilddrüse und der Brustdrüse zu den schwangeren und erkrankten weiblichen Genitalien. Deutsche Zeitschrift für Chirurgie, 1891, xxxi., p. 446.
Gley: The Pathogeny of Exophthalmic Goitre. Brit. Med. Jour., 1901, ii., p. 771.
Gutknecht: Histologie der Struma. Virch. Arch., 1885, xcix., p. 314.
Halstead: Carcinoma of the Thyroid Gland. Medicine, 1901, vii., 107.
Hirsch: Handbook of Geographical and Historical Pathology, second edition, translated by Creighton, London, 1885.
Hitzig: Beiträge zur Histologie und Histogenie des Struma. Arch. f. klin. Chirur., 1894, xlvii., p. 464.
Housell: Ueber gutartige metastrende Strumen. Beitr. z. klin. Chir., 1899, xxiv., p. 112.
Kinnicutt: Internal Secretions considered in their Physiological, Pathological, and Clinical Aspects. Trans. Cong. Amer. Phys. and Surg., 1897, iv., p. 144.
Kocher, T.: Bericht über ein zweites Tausend Kropfexcisionen. Archiv für klin. Chir., 1901, lxiv., p. 454.
Lartigau: Primary Sarcoma of the Thyroid Gland. Amer. Jour. Med. Sci., 1901, cxxii., p. 156.
Morf: Sarcoma of the Thyroid Gland. Jour. Am. Med. Assn., 1899, xxxii., p. 911.
Müller: Beiträge zur Histologie der normalen und erkrankten Schilddrüse. Ziegler's Beiträge, 1896, xxx., p. 127.
Munson: The Occurrence of Goitre Among the Indians of the United States. New York Medical Journal, 1895, lxii., p. 513.
Murray: Diseases of the Thyroid Gland. Twentieth Century Practice of Medicine, 1895, iv., p. 809.—The Treatment of Simple Goitre in Young Adults. Edinb. Med. Jour., 1900, viii., p. 113.
Osler: Fatal Hæmorrhage into a Large Bronchocele. Johns Hopkins Hosp. Bull., 1889, i., p. 23.—On Sporadic Cretinism in America. Am. Jour. of the Med. Sciences, 1893, cvi., p. 503.
Poncet et Rivière: Le cancer du corps thyroïde. Congrès français de chirugie, 1899, xiii., p. 327.
Reinbach: Ueber die Erfolge der Thymusfütterung bei Kropf. Mittheilungen aus den Grenzgebieten der Med. u. Chir., 1896, i., p. 242.
Roger et Garnier: Des lesions de la glande thyroïde dans la tuberculose. Arch. gén. de méd., 1900, iii., 385.
Stengel: Acute Enlargement of the Thyroid Gland, with Report of Cases. Univ. Med. Mag., 1900, xiii., p. 276.
Sultan: Beitrag zur Kenntniss der Schilddrüsen-Function. Archiv für klinische Chirurgie, 1901, lxiii., p. 620.
Virchow: Die krankhaften Geschwülste, Berlin, 1863, iii., p. 1.
Watson: Report of Two Cases of Accessory Thyroid Gland at the Base of the Tongue. New York Med. Jour., 1899, lxx., p. 579.
Welsh: Concerning the Parathyroid Glands. A Critical, Anatomical and Experimental Study. Jour. of Anat. and Physiol., 1898, xxxii., p. 292, 380.
Wölfler: Ueber die Entwickelung und den Bau des Kropfes. Arch. f. klin. Chir., 1883, xxix., p. 1.
Zielinska: Beiträge zur Kenntniss der normalen und strumösen Schilddrüse des Menschen und des Hundes. Virchow's Archiv, 1894, cxxxvi., p. 170.

GOITRE AND CRETINISM.—Definition.—Cretinism is a peculiar type of mental and physical degeneracy, either congenital or developing in childhood, due to absence or disturbance of the function of the thyroid gland. An individual afflicted with cretinism is called a cretin.

Etymology.—The etymology of the word cretin is shrouded in obscurity. It seems that the word originated as a colloquialism in the Canton of Wallis in Switzerland. Esquirol (quoted by Demme, "Ueber den endemischen Kretinismus," Berne, 1840) derives the term from an old word *cretine*, an inundation (Anschwemmung), and connects it with the marshy character of many cretin districts. There is, however, no proof of such a derivation. According to Fodéré, the word comes from *chrétien*, a Christian, the term, "bon chrétien," having formerly been applied to the cretin, on account of his contented disposition. Another interpretation, according to which the word is also derived from chrétien, is based upon the fact that cretins were popularly believed to be elected Christians, and were considered holy, inasmuch as they were supposed to fulfil the lofty function of expiating in their unhappy lot the sins of their fellowmen. According to Gross ("Ueber die Ursachen des endemischen Kropfes und des Kretinismus." Inaugural Dissertation, Tübingen, 1837), the word comes from *Christiani* (spelled *Chrestiani* by Tertullian), because the Romans looked upon the converts to Christianity as fools and imbeciles. Celsus also spoke of the Christians as a society of slaves and idiots. Some have traced the term cretin to a word *cretina*, meaning stupid or silly. According to Ackermann, cretin comes from a Romance word, *cretira*, a creature. Others have derived it from *creta*, chalk, on account of the chalky complexion of the cretins. This derivation finds some support in the German colloquial word for cretin; viz., *Kreidling*, from *Kreide*, chalk.

Nearly every locality has its special name for cretins. In Austria they are known as Trotteln or Gacken; in Germany, as Kretins or Kreidlings; in German Wallis, as Gauche, Tampe, or Nollen; in French Wallis, as Crétins, or as Marrons, on account of the dark color possessed by some; in Salzburg, as Fexen, Trepped, or Trutsched; in Würtemberg, as Dackel, Dippel, Tralle, or Simpel; in the Pyrenees, as Cajots or Capots; in Piedmont, as Pazzi;

in Italy, as Gavas, Totolas, or Cristiani; in South America, as Bovos or Tontos. In Latin writings the word Christiani is generally employed.

Synonyms of Cretinism.—The synonyms of cretinism are infantile myxœdema, cretinoid idiocy; in French, idiotie avec cachexie pachydermique, pachydermie crétinoide.

Historical.—According to the Sardinian Commission's Report, the first mention of a cretin occurs in the fifteenth century. Demme (*loc. cit.*) says that the first reliable mention is in the writings of Peter van Foreest, a Dutch physician who lived from 1522 to 1597 (P. Foresti: "Observat. et curat. opera omnia," Francof.). A contemporaneous reference is found in the writings of Felix Plater (1536–1614) (F. Plateri: "Observat. in hominis affectibus plerisque," Basle, 1614). A description of the cretins of Wallis also occurs in the writings of Giosia Scentero (about 1574) (quoted by Gross, *loc. cit.*). One of the most graphic descriptions dates back to the eighteenth century, and is that of Horace Benedict de Saussure, the famous Alpine traveller, and the first to scale Mont Blanc ("Voyage dans les Alps," four volumes, 1779–96). The first real scientific work on the subject is that of Ackermann ("Ueber die Kretinen, eine besondere Menschen-Abart in den Alpen," Gotha, 1790). In the nineteenth century cretinism formed the theme of many writers, and the literature is now almost unlimited. Particular mention should be made of the reports of the Sardinian and French Commissions, and of the article on cretinism by Baillarger and Krishaber in the "Dictionnaire des Sciences médicales." Among the most important articles of recent date are those of Ewald, Osler, Kocher, Klebs, and Murray. An interesting picture of the cretin communities in France is to be found in Balzac's magnificent novel, "The Country Doctor."

Distribution.—Cretinism may occur in any part of the world, but there are certain limited districts in which it is an endemic disease affecting a large percentage of the population (endemic cretinism). Isolated cases of the disease (sporadic cretinism) have been observed in many widely separated places that are far removed from foci of endemicity. It is, indeed, probable that if the characteristics of the disease were universally known, some cases would be found to exist in nearly every large community.

Several observers have noted conditions in the lower animals suggestive of cretinism: thus, Müller (*Würzburg med. Zeitschr.*, 1860) speaks of cretinoid changes, particularly of the bones, in calves; and Eberth ("Fötale Rachitis und ihre Beziehung zu dem Kretinismus," 1878), of the condition in calves and puppies.

There is one very interesting feature connected with the endemicity of cretinism, namely this: cretinism is endemic in the same localities in which goitre prevails as an endemic affection. This, as we shall see, is a fact of tremendous importance in the study of the pathogenesis of the disease.

Endemic Distribution.—Cretinism is endemic in certain parts of Switzerland; in the Valais, Tarantaise, Maurienne, and in the upper valleys of the Rhone. In Germany, the foci are Würtemberg (2 cretins per 1,000 population. Schmid, *Correspondenzbl. d. ärtzl. Landesver.*, 1886), the Black Forest, and Alsace; in Austria, Salzburg (1 to 139, according to Wallmann, *Wiener med. Jahrbücher*, 1863, vol. i., p. 120), Galicia, and the Kärnthner (1 to 110) and Styrian Alps (1 to 116); in France, the Pyrenees, the Vosges, and the French Alps; in England, according to Murray ("Diseases of the Thyroid Gland," Part I., 1900), the upper valleys of the Pennine Range, the north of England, the neighborhood of Allston, Stanhope, and Kendal. In these places goitre is also endemic. Formerly (Morris, *Medical Times*, 1847, vol. xvii., p. 257), cretinism was strongly prevalent in Chiselborough, in Somersetshire; but it has died out. There are also said to be foci in Scotland and in Spain. In some portions of the Caucasus (the valley of the Zschomarski and Swanetia) (Witke, *Münchener medicinische Wochenschrift*, 1896, p. 292) cretinism prevails endemically. According to Kandaratski (Congress der russ. Aerzte, 1899), goitre and cretinism are widespread throughout Western Russia, which has many marshy districts. In Asia the disease is found in certain parts of the Himalayas, in Thibet, in Turkestan, and in Tartary. As to the occurrence of the affection in Africa, very little is known. According to Blumenbach (quoted by Gross, *loc. cit.*), the disease is found in Madagascar. In South America we find it prevalent in parts of Brazil and along the slopes of the Cordilleras. No foci of endemic cretinism exist in North America at the present time (Osler, *American Journal of the Medical Sciences*, 1893). Goitre formerly prevailed in this country, and is yet endemic in Eastern Ontario, where even the lower animals suffer from it. Demme, in his American travels, found many cases of goitre, especially in Pennsylvania, about Pittsburg, in the valleys of the Allegheny, Monongahela, and Ohio rivers, and in New York; but he saw no cretinism.

Endemic cretinism is confined to certain altitudes, being most common between the elevations of 1,300 and 2,000 feet; it is hardly ever found above the level of 3,000 feet. Its homes are not the tops of the mountains, but the dark, sheltered valleys and clefts, through which course the mountain streams.

The occurrence of goitre in dogs, hogs, cats, cattle, and antelopes has been demonstrated; but as to the existence of cretinism, little is known, with the exception of the brief reference made above.

Etiology and Pathogenesis.—As stated in the definition, the cause of cretinism is absence or disturbance of the function of the thyroid gland (athyroidism, dysthyroidism, hypothyroidism). This applies both to the endemic and to the sporadic form of the disease. The proofs of the thyroidal theory, as we may call it, are as follows:

1. The most constant lesion in cretinism is that involving the thyroid gland. In the case of the endemic form, there is generally goitre; in the sporadic, the gland is either atrophic or absent.

2. *The occurrence of operative cretinism*, that is, the development of the cretinoid state after the removal of the thyroid gland. Küster (quoted in the Report of the Committee on Myxœdema, Transactions of the Clinical Society, 1888, No. 21, Supplement) extirpated the thyroid gland in a fourteen-year-old boy. Thereafter, the lad's growth was arrested, so that he always retained the characteristics of a boy of that age. Kappeler (*ibid.*) performed total thyroidectomy in a boy twelve and a half years old, who afterward did not grow, and developed some of the symptoms of myxœdema. Intelligence, however, was preserved. Kocher (*ibid.*) removed the entire thyroid from a child aged six, with the result that the physical symptoms of cretinism developed, although the mental symptoms remained in abeyance. Costengo (*Riv. Ven. di Sc. med.*, vol. xx., No. 2) reports a case of total thyroidectomy in a boy. Nine years after the operation the patient was a complete cretin. In a case reported by Sulzer (*Deutsche Zeitschrift für Chir.*, 1893) a goitrous thyroid was removed from a boy twelve and a half years old. Within five years typical cretinism had developed. On the appearance of a new thyroid, the boy improved, and within four years had regained all that he had lost. It was found that a piece of the gland had been left behind, and that it did not begin to grow until eight years after the operation. Palleske (*Deutsche medicinische Wochenschrift*, 1895) removed the thyroid from a girl of thirteen, who three years afterward was a typical cretin. Other cases are reported by Grundler (*Beitr. zur klin. Chir.*, 1883, No. 1), Julliard, Lancereaux, and Dolega (cited by Hofmeister, *Beiträge zur klin. Chir.*, 1894). Schmid (*Berliner klin. Wochensch.*, 1886, p. 509) removed the thyroid gland *in toto* from a boy fourteen years old, who afterward developed typical cretinism. He had absolutely no memory, and did not grow after the operation. Brian and Sargnon (*Gaz. hebdom. de Méd. et de Chir.*, 1898) report the case of a man thirty years old, who was in a moderate cretinoid state, and had a goitre. This was removed by operation; within one year later complete cretinism had developed.

3. *Animal Experiments.*—The removal of the thyroid gland in young, growing animals, if the animals survive any length of time, is generally productive of an arrest of growth, and a state comparable to cretinism in man (Hofmeister, *loc. cit.*). The majority of animals die if the whole gland is removed, whether it be done in one or in two operations. In some experiments made by W. S. Carter and myself, this was the invariable result. Eiselsberg, however ("Ueber Tetanus im Anschlusse an Kropfoperationen," 1890), found that if only four-fifths of the gland are removed, the animals survive, and subsequently develop a myxœdematous state. It must be admitted that not all experimenters have been able to produce the same results. Munk, for example (Sitzungsberichte der königl. preuss. Akademie der Wissensch., 1888, No. 40) was never able to produce myxœdema or cretinism in apes by thyroidectomy. The animals all died with tetanic symptoms. The most suggestive experiments are those made more recently by Eiselsberg (*Langenbeck's Archiv*, 1895, vol. xlix.). He removed the thyroid from two lambs when they were about a week old. At the end of six months they weighed 10 and 14 kgm., respectively, while the control animals weighed 35 kgm. The disturbances were general, and involved the brain functions as well as the skeleton. Similar results were obtained in four goats and in one pig. One goat, however, developed in a normal manner, probably owing to the possession of an accessory thyroid gland.

4. *Therapeutic Results.*—The use of thyroid-gland extract in the treatment of cretinism has brought about remarkable results. It is true that these have been more brilliant in the case of sporadic, than in that of endemic cretinism; but it has not been systematically tried in the latter, and there are other factors of influence in the development of the disease. The successes obtained are, however, a strong confirmation of the view that cretinism is consequent upon disturbance or absence of the thyroid function.

The relation between the thyroidal changes and the development of cretinism is not definitely understood. The subject involves a consideration of the physiologic function of the thyroid gland, and that is not in place here. Suffice it to say that in the opinion of most authorities the thyroid gland produces a substance that acts as an antidote or antitoxin to certain toxic products of daily metabolism. Where the neutralization occurs is a matter of doubt, some holding that it takes place in the thyroid gland, and others that it takes place in the blood. If the toxins are not antagonized, they remain in the body and exercise a deleterious influence, primarily upon the nervous system, but also on the skeleton and other connective tissues. If the individual is young, the result will be an arrest of both physical and psychical development.

Normally the antitoxic action of the thyroid gland begins to be exercised early in life—according to Kinnicut (*Medical Record*, 1893), between the sixth and the eighth months of fœtal life. Failure of development (aplasia), imperfect development (hypoplasia), and morbid conditions in later life (such as atrophy, fibroid change, calcareous infiltration, acute inflammation, and goitre in all its forms), are the pathologic conditions that rob the body of the benefits conferred by a functionating thyroid gland.

Relation to Myxœdema.—The studies of English physicians, particularly Ord, Horsley, and Murray, have conclusively demonstrated that there is an intimate relationship between cretinism and myxœdema. Etiologically, the two affections are identical, in that their basis is a morbid condition of the thyroid gland; symptomatically, they also have considerable in common. The differences which they present are due to the fact that cretinism begins in childhood, at a time when the growing system is most impressionable to deprivation of the thyroidal influence; while myxœdema is the same disease developing after the body has reached its growth. Thyroid treatment produces beneficial results in both.

If it be accepted then as proved, that cretinism is due to absence or disease of the thyroid body, the next question to arise is, "What influences bring about the morbid condition in the gland?" The cause of its absence, poor development, or goitrous state, in sporadic cretinism, we do not definitely know. A number of reasons have been assigned: consanguinity of the parents, conception during alcoholic intoxication, fright during pregnancy, tuberculosis, and a neurotic taint; but the frequency of these conditions compared with the rarity of cretinism indicates that they possess little real importance. A study of embryologic pathology may throw light upon the subject. In rare cases, as in the one reported by Shields (*New York Medical Journal*, 1898, vol. ii., p. 476), the disease has followed upon an acute thyroiditis, undoubtedly of infective origin.

In the case of endemic cretinism, our knowledge is less meagre, although still far from complete. The fact that endemic cretinism and endemic goitre are in a large measure coextensive in distribution suggests a relationship between the two. At present, this relationship is interpreted as being that of a common causation: goitre and cretinism, it is believed, are due to the same cause. This view dates back to the early part of the nineteenth century, and was advocated by Fodéré ("Traité du goitre et du crétinisme, precédé d'un discours sur l'influence de l'air humide sur l'entendement humain," Paris, an. viii., 1800), Gross (*loc. cit.*), Baillarger and Krishaber ("Dictionnaire des Sciences médicales, 1re série," vol. xxiii.), and Virchow. The common cause, nearly all observers agree, is to be found in the drinking-water. Goitre and cretinism always grow less frequent in affected localities when the water supply is changed. Thus, Bircher states that 59 per cent. of the school children of Rapperswyl, in the Swiss Canton of Aarau, had goitre in 1885. The town then made a change in the water supply, obtaining it from beyond the Aar, from a goitre-free district; and the percentage fell rapidly to 44 per cent. in 1886, 25 per cent. in 1889, and about 11 per cent. in 1895. In contiguous communities, living under identical conditions with the exception of the water supply, goitre and cretinism may prevail in one and be absent in the other. Thus, the Bozel district in the Tarantaise had, in 1848, 1,742 inhabitants, of which 900 had goitre and 109 were cretins, and a number semicretins. The St. Bon district, which is only a short distance away, using a different water supply, had no goitre and no cretinism. Upon the advice of the Sardinian Commission, Bozel changed to the St. Bon water, with the result that in 1864 there were but 39 goitres and only 58 cretins.

An active discussion has been waged upon the question as to the constituent of the water bringing about goitre and cretinism. It is known that only water from the soil, not rain or snow water, produces these disorders. At first, certain minerals—for example, gypsum—derived from the particular geologic formation in which the goitre streams have their source, were believed to be the active agents; but the occurrence of endemic goitre in localities the waters of which have an entirely different mineralization, makes this view untenable. The favorable influence exercised by iodine upon goitre led to the theory that the waters of goitrous districts were deficient in this substance. Against this not unreasonable supposition is the fact that goitre may and does exist in valleys the streams of which are rich in iodine—as the valleys of the Po, Aosta, and Isère—and may be absent where the water is free from iodine.

From this dilemma an escape was found in the assumption that the efficient agent in goitrogenic waters was a *contagium vivum*. This hypothesis is now generally adopted, Ewald in particular having strongly defended it; but it is not new, and was long ago expressed by Alexander von Humboldt, Troxler, Virchow, and Hirsch—to be sure, in pre-bacteriologic language. Demme and Gross had assumed the existence of a miasm which arose in the vapors of the marshes. Baillarger and Krishaber (*loc. cit.*) had also come to the conclusion that the goitrogenic substance was organic, although they did not go

so far as to make of it a living substance. The fact that the boiling of the water renders it innocuous is one of the strongest arguments in favor of the modern theory. What the substance is, still remains a mystery. It may be bacterial, although no definite organism has been isolated. Tavel (quoted by Kocher, *Deutsche Zeitschrift f. klin. Chir.*, 1892, vol. xxxiv., p. 556), in a beautiful, clear stream in a goitrous district, found thirty-three varieties of plant life, although he was not able to prove definitely that any one of them was the sought-for cause of goitre.

Whatever the cause may be, it is not long-lived in the body. Goitre increases only as long as the infected water is drunk, and it may even disappear if the individual afterward consumes a pure water. Immunity to goitre may exist in goitrous localities. According to Kocher, persons who pass the tenth year in such a locality without the development of goitre, will usually remain immune. Whatever the nature of the morbific agent, it seems to expend itself upon the thyroid gland; and in the end it is the disturbance in the function of that organ that brings about cretinism.

There are, however, certain predisposing causes:

1. *Locality.* Endemic goitre occurs especially in sheltered, damp, and imperfectly aired valleys.

2. *Geologic Formation.* Goitre and cretinism are most common in sections characterized by marine sedimentary rocks, particularly those of the Paleozoic Era (Devonian, Silurian, Carboniferous, and Dyas), the Triassic, and the Tertiary. McClelland, in his Himalayan studies, found goitre most common in places in which the soils were rich in lime and magnesia, there being one goitre in every thirty-three, and one cretin in every thirty-two persons.

3. *Social Condition.* Endemic cretinism prevails among people eking out a meagre existence under unfavorable conditions. The influence of such conditions has been proved indirectly by the lessening of goitre and cretinism as such communities become more affluent and more civilized, the water supply remaining unchanged. Wallmann (*Wiener med. Jahrb.*, 1863, vol. i., p. 120) also considered despotic government a factor in the production of cretinism. There was an opinion, found not uncommonly in older writings, that cretins were the relics of an ancient, inferior race of human beings—an hypothesis that has, of course, no proof whatever.

4. *Consanguinity.* Inbreeding and consanguineous marriages are an important factor in the perpetuation of cretinism.

5. *Heredity.* When the parents are goitrous, even if the thyroid disease is slight, the children are very apt to develop cretinism; and this is particularly true, as indicated in the preceding paragraph, if the parents are related.

The Sardinian Commission found that of 3,613 fathers of cretins, 962 had goitre, and 51 were cretins; and of 3,652 mothers, 1,281 were afflicted with goitre. But that heredity is not of controlling moment is proved by the fact that, given good surroundings, the descendants of goitrous parents may develop normally, although they do not always do so. Goitre does not, however, of necessity bring about endemic cretinism; for in Ontario goitre is, according to Osler, quite prevalent, but cretinism is unknown. Goitre also formerly prevailed in Pennsylvania and New York (Demme, Gross), but cretinism was rare or unknown. Regarding Canada, however, while endemic cretinism does not occur, sporadic cretinism is by no means uncommon; and Macphedran (*Canada Journal of Medicine and Surgery*, 1898, vol. iv., p. 275) was able to collect no less than seventeen cases.

General Features.

Nothing is more characteristic than the physiognomy of a typical cretin. There is, moreover, a remarkable uniformity in the appearance of all persons afflicted with this disease, so that the characteristic individuality of normal human beings is largely obliterated. To such an extent is this the case that older writers, as already mentioned, considered cretins to be the remains of a degenerate aboriginal race.

The typical cretin is short of stature—a stunted, dwarfish being, with a large head resting almost upon the shoulders or sinking forward upon the chest. As a rule, the hair is short, coarse, and abundant, though sometimes long and silken, and grows well down over the low forehead. The skin is pale, thick, dry, rough, at times scaly, and has a tendency to form thick folds or waddles. The face is stupid, expressionless, and repulsive. The eyes gaze vacantly, seldom fixing objects. The nose is short and thick, with a deep-lying root and flaring nostrils. The mouth is large; the lips are thick and fleshy, and constantly open, permitting the swollen tongue to protrude and the saliva to drool. The teeth are few in number, large, wide apart, and badly formed. The ears are fleshy, pale, often deformed, and usually stand out. Sometimes they are small and grown flat to the head. A short, thick neck, at times deformed by the presence of a goitre, joins the head to the thorax. The latter is disproportionately short, flattened irregularly at the level of the lower end of the sternum, and often scoliotic and kyphotic; it is usually smaller in circumference than is normal. The breasts in female cretins are either not developed at all, or are very large and pendulous. The abdomen is protuberant and inclined to hang downward; often a hernia, either umbilical or inguinal, is present. Lordosis is common. In both sexes the genitalia are usually small and infantile, with absence of hair in the pubic region, but in rare cases the external organs of generation are excessively developed. The extremities are short, fleshy, and grooved by deep furrows; the feet and hands are large; the nails roughened. Often there is a tendency to bow-leg or knock-knee. Many cretins cannot walk; some cannot even stand unless supported.

Intellectually, the cretin, as a rule, presents a degree of degeneracy that is on a par with that of his body. His wants are confined to the most rudimentary desires, such as hunger and thirst; and to these, even, he gives expression in ways that are intelligible only to those that are constantly about him. Speech he usually has not, and is able only to make monotonous, inarticulate noises, and does not employ gestures. If he speaks at all, his voice is shrill and unpleasant. He remains in all respects a helpless child, and often wears, even at two-score years or more, the garb of childhood.

In the foregoing I have given a brief sketch of the cretin in his worst estate—the type that Maffei calls plant-men (Pflanzenmenschen), on account of their purely vegetative existence. The picture is not overdrawn, and characterizes wellnigh the majority of cretins; but there are many in whom the disease does not reach such a profound degree, and in every locality in which the disease is endemic there are gradations, from the fully developed to the mild type—so mild, indeed, that only a few features of the disease remain. These slight cases are termed cretinoid.

Age.—Cretinism may be congenital; that is, it may be present at birth. In such cases the child rarely lives any length of time; indeed, it is often still-born. More frequently the disease develops some time after birth: in the endemic type, between the fifth and the eighth months; in the sporadic, after the second year, or later. The condition usually reaches its height at the age of fifteen years, and remains stationary after the twentieth year. According to Ord (Medico-Chirurgical Transactions, 1878), cretinism never develops in a child that is healthy up to its sixth or seventh year. Operative cretinism naturally begins after the operation, if that be done within the period of growth. The duration of life is generally short, especially in the sporadic form, in which the fourth decade is rarely attained. In endemic cretinism, subjects sometimes reach the exceptional age of seventy, or even one hundred years. Tuberculosis seems to be rare in cretins.

Sex.—Endemic cretinism is more common in the male sex. In sporadic cretinism there seems to be a decided preponderance of females. I have collected from the literature 93 cases of the sporadic type. The sex was mentioned in 86; of these, 48 occurred in females, 38 in males. Osler, in the American cases, only a few of which are included in my list, found the difference in favor of the female sex even greater; 35 females to 23 males.

Features of the Disease in Detail.

A. Somatic Features.—1. *General Skeleton.*—The cretin is almost never of the normal stature of persons of his age; in the majority of cases indeed, his height does not exceed that of a child of three or four years. Maffei (quoted by Kocher, *loc. cit.*) found 22 out of 25 cretins to be less than 4.5 feet (140 cm.) in height; several were even less than 3 feet tall (95 cm.). Macphedran (*Canadian Journal of Medicine and Surgery*, 1898, vol. iv., p. 275) found the height in 9 cretins to vary from 26 to 55 inches. I have tabulated the heights of 28 cretins, ranging from four to fifty-three years of age, and found the average to be 96.6 cm. (38⅜ in.).

There is a disproportion among the different parts of the body. At times the arms are very long; the hands, large; the fingers, short; the nails, broad, flat, short, and brittle. The lower limbs are crooked, and there is often a backward extension of the knees. The clavicles are thin, delicate, and slightly curved. The hair is coarse, dry, and abundant; often reddish in the sporadic form, and chestnut-color in the endemic. There is usually no pubic or axillary hair, but sometimes a considerable hirsute growth is noted between the scapulæ. Fatty tumors are found above the clavicles, and occasionally between the shoulder-blades, but only in the sporadic, not in the endemic, type. Umbilical and inguinal hernias are common features. As already mentioned, the genitalia are small; but in some instances (Friedreich, "Ueber die äusseren Geschlechtsorgane der Kretinen in Iphofen," 1828) the male sexual organ reaches an enormous length, the testicles being in proportion, and usually very hard. Puberty, if it occurs at all, is late in appearance, sometimes, as in Wagner's observation (Medic.-chir. Centralblatt, 1893, 245), at the fortieth year. The cretin's skin is dry, harsh, and brownish or pale ashen in color. The veins of the chest are prominent, and there is often, as Bramwell ("Atlas of Clinical Medicine," vol. i., p. 16) has noted, a venous mottling of the legs. Eruptions are common in the sporadic form. The body temperature of cretins is nearly always subnormal.

The Head.—The head is unduly large, with a flat top and a prominent occiput. (Bulldog-like is the comparison made by some writers.) The circumference is, however, not so large as might be expected from the general appearance of the head, the average in twenty cases being 51 cm. (20⅛ in.); at times there is actual microcephaly. The fontanel and sutures remain open very long, although sometimes they close early. The shape of the head varies. It is usually brachycephalic in endemic cretinism and dolichocephalic in the sporadic type. The head is often so heavy that it cannot be held up by the weak neck muscles. The forehead is low, the supraorbital ridges are prominent, the eyebrows thin, the eyelashes short and few in number. The eyelids are swollen. The eyes are usually open, but sometimes half closed from ptosis. Many cretins have pronounced squint. Lachrymation is common, from occlusion of the lachrymal duct, and there is often well-marked epicanthus. The nose is retracted, short, and homely, with large, flaring nostrils. The upper jaw is usually unduly prominent, while the lower recedes. The lips are thick and fleshy (macrocheilia), and at times there is a pinkish flush upon the cheeks. The naso-labial folds are indistinct. The mouth is always open, and the breath offensive. There is constant drooling of saliva. The tongue is large, swollen, and in advanced cretinism protrudes from the mouth (macroglossia). The teeth appear late, and the milk teeth generally persist throughout life, second dentition being rare. The teeth are subject to early decay, and are always badly formed and of large size. The palatal arch is generally high and narrow. The neck is short. The thyroid gland as a rule cannot be felt in sporadic cretinism, and was absent at autopsy in nine out of ten cases collected by Bramwell (*loc. cit.*).

I have analyzed 88 cases of sporadic cretinism recorded in the literature with reference to the condition of the thyroid gland. There was no thyroid demonstrable in 44; there was no goitre, or the gland was normal in 9; goitre existed in 7; and no mention was made of the gland in 27. Osler, in his cases, a few of which are embodied in my table, found goitre present in 7, the gland normal in 12, and small in 2; it was not felt in 16, and not mentioned in 20. In one case of cretinism on which I had an opportunity to make the autopsy, the thyroid gland was absent. In endemic cretinism the thyroid is not only present, but is, as a rule, the seat of goitrous change. Wagner (*loc. cit.*) gives the frequency of goitre as high as ninety per cent.; others generally find a lower percentage. Among 20 cretins, Bircher found 15 with goitre, the thyroid not being palpable in one, and being normal in 4. Regarding the statement that the gland is normal, it must always be remembered that it is difficult to determine merely by palpation the condition of a thyroid gland. Cretinism is always worse in non-goitrous persons than in those having goitre.

Fleshy lipomatous masses are found above the clavicles and between the scapulæ, but only in sporadic cretinism. During wasting diseases and before death, these tumors generally atrophy.

Circulatory System and Blood.—The heart sounds are weak; the pulse is slow and feeble. The blood has not been carefully studied in endemic cretinism; and with regard to the sporadic form, the reports are also meagre. Koplik (New York *Medical Journal*, 1898, vol. ii., p. 84), in a female cretin one month of age, found the hæmoglobin ranging from 85 to 53 per cent.; the red blood corpuscles numbered 4,200,000, and the white cells, 10,000. In another case, an infant of nine weeks, presenting a typical cretinoid appearance, the hæmoglobin was 105 per cent., the red corpuscles numbered 3,000,000, and the white cells 13,500. After a short treatment with thyroid gland, the hæmoglobin sank to 55 per cent. In a case reported by Mendel (*Berliner klin. Wochenschrift*, 1896), the red cells were 4,700,000, the white cells 30,000, the differential count showing: polymorphonuclear cells, 58 per cent.; lymphocytes, 33 per cent.; eosinophiles, 5 per cent.; transitional forms, 4 per cent. Osler (*American Journal of the Medical Sciences*, 1893), in one case, found anæmia, leucocytosis, and poikilocytosis; and in another, absence of leucocytosis. Phillips (Transactions of the Clinical Society, 1885) reports finding in one case slight anæmia and no increase in the number of leucocytes. Garré (cited in *Virchow-Hirsch's Jahresbericht*, 1890, 341), in a female cretin of twelve years, found 3,900,000 red corpuscles, 5,730 white, and 63 per cent. hæmoglobin. In a female cretin twenty-six years old, Routh (Proceedings of the Medical Society of London, 1884, vol. vii., p. 309) found the red cells 86 per cent. of the normal; the hæmoglobin, 77 per cent.; and the relation of the white to the red cells as 1 to 250, showing a decided leucocytosis. From these blood studies, it is apparent that cretinism—at least, the sporadic form—is accompanied by anæmia, manifesting itself in a decided reduction of the red corpuscles and a diminution in the hæmoglobin; sometimes the red corpuscles present alterations in form. The leucocytes seem to be increased in the majority of cases, without any noteworthy alteration in the proportion of the different elements; in some instances, however, there is no leucocytosis. A thorough study of the blood—both of its cellular and of its liquid elements—is a distinct desideratum.

Digestive Tract.—The drooling of saliva and the thick, protuberant tongue have been mentioned. The appetite of the cretin is usually voracious, and he bolts his food. Constipation is generally present. In extreme types of the disease the bowels are moved involuntarily. In the terminal stages diarrhœa sets in, and may be the cause of death.

Genito-urinary Tract.—The sexual sense is usually absent. Puberty is rarely attained; and if so, not before the age of twenty-five, and sometimes as late as forty. Menstruation, if it occurs at all, is scanty and irregular. Cretins are generally sterile. The size of the external genitalia varies; as a rule, they are infantile; exceptionally, as already mentioned, very large. The urine

FIG. 2341.—Bartine Mills, a Cretin, about Thirty-three Years Old, formerly in the Philadelphia Hospital. The man beside him was his voluntary caretaker for many years.

is normal, but small in amount. In one case Ord (*Lancet*, 1893, vol. ii., p. 1113) estimated the quantity of urea, and found it to be 0.4 per cent. Urinary incontinence is the rule in typical cretins.

B. MOTOR PHENOMENA.—On account of the short legs and large bodies, the gait of cretins is of a peculiar, grotesque, waddling character. Many can progress only by pushing a chair; some cannot even stand. The use of the hands for delicate movements is limited in varying degrees. Often the cretin cannot even feed himself. Regarding the reflexes, the statements in the literature differ considerably. Some have found the tendon reflexes normal; others, the knee jerks increased, and the abdominal, cremasteric, and other superficial reflexes, unaltered. Mayer (*Revue médicale de la Suisse romande*, 1883, 523) found a diminution in the faradic excitability of the muscles.

C. SENSORY PHENOMENA.—All the special senses are blunted, particularly that of hearing, complete deafness being a common feature. Some have attributed the low intelligence in part to this deafness. As to its cause, Wagner (*loc. cit.*) suggests that it is due to a myxœdematous swelling of the mucous membrane of the middle ear.

Hitchmann (*Wiener klin. Wochenschrift*, 1898, 655) has made a study of the eye conditions in 58 cretins. Lesions of that organ were, on the whole, rare. He found epicanthus in 12 and myxœdema of the lids in 56. Chronic catarrhal conjunctivitis was common, and was either an accidental condition, or due to disturbance of the tear duct. Eczema of the lids was frequent. Strabismus was found in but 1 case, senile cataract in 2, and posterior capsular cataract—due to prolapse of the retina—in 1. The retina was normal in 42. There was conus, with a downward axis, in 5 cases, which is a high percentage, as ordinarily this is found but 27 times in 1,000 cases. In one case there was beginning gray degeneration; and in 2, increased pigmentation of the choroid and retina. Nystagmus is sometimes present.

Touch, pain, and temperature sense, like the more highly specialized functions, are also greatly dulled.

D. PSYCHIC PHENOMENA.—I have already stated that cretinism presents all gradations from the most profound amentia and idiocy to mere feeble-mindedness, or even to a fair state of mentality. The majority of cretins are dull, apathetic, silent, unteachable, and incapable of work, and have to be cared for like infants. A few, particularly in endemic cretinism, are able to do light tasks, run errands, etc. Cretins, as a rule, are good-natured but jealous, and are not emotional; at times, however, they have violent outbursts of animal fury, or pass into states of deep depression. In rare instances, they present delusions or are maniacal; and Kraepelin refers to one case in which paresis existed. Convulsions have also been observed. In exceptional instances some one faculty will be extraordinarily developed, as, *e.g.*, the musical memory.

PATHOLOGICAL ANATOMY.—The general characters of the skin, hair, and nails have been described. A peculiar feature to which I might again allude is the gelatinous infiltration of the skin (cachexia pachydermica), which is particularly marked in sporadic cretinism. According to Beach, it is due to an excess of mucin in the subcutaneous tissue. In nearly all autopsies an absence of subcutaneous fat has been noticeable. Fatty tumors are found above the clavicles in sporadic cretinism.

With regard to the skeleton, I have already spoken of the shortening of the bones and the peculiar external features of the skull. The cause of the skeletal characteristics has been a subject of much dispute, but it is now proved that the fundamental defect is a delayed ossification of the cartilages. There is a retardation in the formation and growth of the centres of ossification, in the transformation of the epiphyses into bone, and in the disappearance of the epiphyseal discs. Eventually, if the individual lives long enough, ossification may be accomplished; but it is common to find, as did Dolega ("Beiträge zur pathol. Anatomie u. allgem. Pathologie," 1890, vol. ix., p. 488), in a cretin twenty-eight years of age, that the sutures remain open and that the epiphyses persist in their cartilaginous state. These facts also explain why cretins may continue to grow until the third or fourth decade of life.

Periosteal osteogenesis shows no constant characters; it may be normal, or it may be excessive. Sometimes there is a projection of the periosteum between the epiphysis and diaphysis, such as was observed in Dolega's case, but this is not the rule. Little is known of the condition of the bone marrow. In the only case in which it is mentioned—that of Langhans (*Virchow's Archiv*, 1892, 128)—the marrow was fatty. The case was that of a cretin fourteen months old.

In two fœtuses presenting cretinoid characteristics, Virchow ("Gesammelte Abhandlungen," 1856, 969; also in Verhand. d. phys.-med. Gesellschaft, Würzburg, 1856, 199) found synostosis of the spheno-occipital sutures—of the so-called os tribasilare—and concluded that this was an important feature in cretinism; one probably responsible for the arrest of growth in the other parts of the skeleton. Normally the sutures of the os tribasilare do not disappear until the twelfth or thirteenth year. There is, however, a general belief among authorities at the present day that the disease found in the fœtuses described by Virchow was not a form of cretinism, but a condition somewhat analogous, yet different in its essence, known as

chondrodystrophia fœtalis, about which more will be said later. In true cretins there is no premature ossification of the sphenobasilar sutures.

The foramina for the cranial nerves and blood-vessels are often small, including the foramen magnum; sometimes, however, they—especially the latter—may be of normal size. Wormian bones are frequently present along the sutures.

In shape the skull, as has been stated, may be either dolichocephalic or brachycephalic. Shortening of its base is one of the most constant features of the cretinic skull. The root of the nose is depressed and prognathism is marked. Allen (New York *Medical Journal*, February 2d, 1895), in a supposedly cretinic skull, found projection of the occiput, and such a union of the parietals with that bone that a conspicuous depression was formed between them, giving rise to a shape of the head called "cat head."

Histologically the osseous changes are but little known. They can be satisfactorily studied only in juvenile cretins, and autopsies upon them are rare. Langhans (*loc. cit.*) found that in his case the cartilage cells were small and spindle-shaped; in places they were abnormally disposed, being longitudinal to the axis of the rows of cells. Sometimes, also, the rows were interrupted. The marrow spaces showed irregularities, being often very large and widely separated in the youngest portions of the bones, and exhibiting shortening of the bony trabeculæ.

The Brain.—An interesting pathological change is enlargement of the pituitary body, which, however, is not constant. It was noted by Boyce and Beadles (*Journal of Pathology and Bacteriology*, 1893) and by Packard and Hand (*American Journal of the Medical Sciences*, September, 1901). Langhans (*loc. cit.*) found the brain and cord normal, but in the peripheral nerves he observed dilatation of the lymph spaces of the endoneurium and perineurium. The dilated spaces, besides having fine fibrillæ, contained unilocular and multilocular vesicular cells, which seemed to have originated from the endoneurium. There were also peculiar cylindrical or spindle-shaped, solid structures, probably the result of degeneration of the connective tissue.

Thyroid Gland.—The condition of the thyroid gland, to which allusion has been made upon page 393, is of great interest. In sporadic cretinism it is usually absent; when present it is small and atrophic. In such cases the acini are smaller than normally, are devoid of colloid, and often are surrounded by thick bands of fibrous tissue. The blood-vessels, as in the case of Packard and Hand (*loc. cit.*), may show advanced calcareous infiltration of their walls. In endemic cretinism the gland is usually goitrous; sometimes, however, the thyroid is not demonstrable in the neck, but at autopsy a retrosternal goitre or one behind the sterno-cleido-mastoid muscle may be found.

The enlargement of the tongue is usually due to a lymphangiomatous condition of the organ. The viscera, in general, show no characteristic changes. Beach found an increase in the fibrous tissue; and in a case examined by myself the liver was the seat of an enormous number of cavernous angiomata and the hepatic cells were deeply pigmented.

DIFFERENTIAL DIAGNOSIS.—But little need be said regarding the differential diagnosis of cretinism. The endemic form usually presents no difficulties; and the sporadic in its fully developed state is also easily recognized. Occasionally it is necessary to distinguish between cretinism and *dwarfism* (nanosomia). In border-line cases the distinction may be impossible; but ordinarily we find that the dwarf does not present the typical skeletal changes nor the myxœdematous condition of the skin. There are likewise no real deformities: the large tongue is absent; and the psychic defects, so prominent in cretins, are not a feature of dwarfism. It may be difficult to distinguish between cretinism and that form of idiocy known as *Mongolian idiocy*. There are, however, mental differences that are of help in the diagnosis. The cretin is dull and apathetic; the Mongolian idiot, though stupid, has a smiling countenance, and is more or less vivacious and observant. The œdematous condition of the skin and the fatty tumors are also absent.

Under the term *infantilism*, several writers have described a condition of under-development, the individual retaining the characteristics of childhood at a period when these should have disappeared. The secondary sexual characters in particular fail to develop. Infantilism may be, and usually is, general, but according to Hertoghe ("Die Rolle der Schilddrüse bei Stillstand und Hemmung des Wachstums und der Entwicklung," from the French by Spiegelberg, Munich, 1900), it may affect single features, as the voice, the hair, the genitalia, etc. Brissaud considers infantilism an attenuated form of cretinism.

A few words must be bestowed upon the subject of so-called *fœtal rickets*, which by some is considered a form of fœtal cretinism. Few diseases are honored with so many high-sounding names as this. Besides being called fœtal rickets, it is known as cretinoid dysplasia, pseudorhachitism, chrondritis fœtalis, micromelia chondromalacica, achondroplasia, and chondrodystrophia fœtalis. Without going into the details of the affection, which are out of place in the present article, the following statements may be made:

1. The disease is not a form of rickets.

2. It has very little in common with cretinism, differing from the latter in certain essential points:

(*a*) In its period of development: it begins during fœtal life, and the child is generally still-born or dies early. Cretinism rarely begins before from the fifth to the eighth month.

(*b*) The thyroid gland is usually normal.

(*c*) It may occur anywhere, and is not more frequent in the foci of endemic cretinism than in other places.

(*d*) Although the osseous changes present no fundamental difference, there is in chondrodystrophia a sclerosis of the diaphysis which is absent in cretinism.

3. The essential feature of chondrodystrophia fœtalis is a disturbance in the development of the primordial cartilage, characterized by irregular growth of the cartilage cells with defective formation of the cellular rows. Regarding the cellular proliferation itself, it may be deficient, the cells being spindle-shaped in their hyaline matrix, or it may be excessive, or the cells may form groups lying in a soft, glassy matrix. These three types of abnormalities correspond with three types of the disease: chondrodystrophia hypoplastica, chondrodystrophia hyperplastica, and chondrodystrophia malacica.

4. Periosteal osteogenesis is not, as a rule, disturbed. Occasionally it is in excess of the normal.

5. An almost constant feature is the penetration of a periosteal process between the epiphysis and the diaphysis.

6. There is a sclerosis of the marrow, especially of the ends of the bones.

7. Ossification of the sutures of the os tribasilare is common, but not constant.

8. The dystrophy leads to a stunting of the growth, particularly of the lower limbs; hence the middle of the body is not at the umbilicus, but much higher—near the ensiform cartilage.

It is not impossible, however, that chondrodystrophia, although anatomically differing from cretinism, may like the latter be due to hypothyroidism.

TREATMENT.—The treatment of endemic cretinism is primarily a matter of broad public hygiene and sanitation. As the drinking-water is chiefly at fault, the first effort should be directed to its improvement. Whenever possible, water should be secured from a goitre-free district, the advantages accruing from such a change being truly remarkable. To one famous instance of the kind—that of Bozel—I have referred on page 391. When an entirely new water supply is unobtainable, an attempt should be made—of course, this is then not a matter for municipal performance, but of household initiative—to provide cistern water, which, it has been shown, is not goitrogenic, and, hence, not cretinogenic. Sedimentation of the water seems also to rob it, to a large extent, of its

noxious properties; but boiling is the surest way to render it innocuous. In addition to giving attention to the water supply, amelioration of the general social conditions of the afflicted community must be sought, by preventing intermarriage, diversifying the industries, shortening the hours of work, improving the food supply, widening the streets, and modernizing the sewage system.

In sporadic cretinism remarkable results have been achieved by the so-called substitution treatment, *i.e.*, the substitution for the deficiency in the activity of the thyroid gland of either the gland itself, obtained from animals, or preparations made from it. It is unnecessary to dwell upon the development of this treatment, although it forms an interesting chapter in the history of medicine. The father of it, as at present practised, is G. R. Murray, of Newcastle-on-Tyne; although the value of the gland in the treatment of conditions dependent upon absence or disease of the thyroid body had previously been recognized both by Bircher and by Horsley. They, however, had recommended the implantation of the gland—a method not devoid of danger. At the present day numerous preparations of the thyroid are on the market. Some represent the gland in a dried state—the so-called desiccated thyroid; others are glycerin or ethereal extracts in liquid or solid form. As a rule, the gland from the sheep or the calf is employed, but that of the hog also seems to be efficacious. Attempts have been made to isolate the active principle and to use it instead of the extract or the gland itself. Different investigators, however, have isolated different substances, each claiming that his is the active principle; thus, there are Baumann's thyrolodin, Notkin's thyreoprotein, Fränkel's thyroantitoxin, and Hutchinson's colloid. The active principle seems to contain iodine.

The dose of thyroid is more or less arbitrary and varies with the preparation. It is well to begin with small doses (for example, a minim of the liquid or a grain (0.06 gram) of the solid extract nightly), increasing the dose with care. The younger the cretin, the more brilliant are the results; but there is no period, except, perhaps, extreme old age, at which it is not wise and proper to make a trial of the remedy.

Under the treatment a wonderful change comes over the entire system of the individual. There is a growth in height and a diminution in the general bulk of the body; a disappearance of the œdema of the skin, of the swelling of the tongue, and of the fatty tumors; a rise in body temperature; an improvement in the condition of the bowels; and a very striking increase in the intelligence. There is in the beginning, as pointed out by Thomson (*British Medical Journal*, 1893, vol. ii., p. 677), a slight tendency to muscular debility, connected with the tremendous change in bodily metabolism; but this soon disappears.

If the thyroid medication is too active, symptoms of intoxication—so-called hyperthyroidism—may develop. These are tachycardia, pains in the limbs and elsewhere, slight fever, and diarrhœa.

Under thyroid treatment the diet should receive some attention. The use of meat should be restricted, and the food should be largely vegetarian in character.

A number of cretins that were under thyroid treatment have succumbed with astonishing rapidity to infectious diseases, such as diphtheria, typhoid fever, etc. Whether the thyroid medication had in any way lessened the patients' resistance to these is a fair question, but one which cannot as yet be definitely answered. The benefits obtained from the treatment so far outweigh any possible disadvantages that the latter need scarcely be given a thought.

In order that the beneficial effects of the thyroid treatment may not be lost, it is necessary to continue the administration of the drug throughout the patient's life. The lowest efficient dose should be determined, and then kept up uninterruptedly.

Specific medication with thyroid gland, which has been of such signal benefit in sporadic cretinism, has, so far, not met with striking success in the endemic form. The reasons for this are manifold. In the first place, the method has not been tried upon any large scale; secondly, the causes underlying the endemic cretinism continue; and thirdly, the majority of cretins were at a comparatively advanced age when the treatment was begun. It would seem advisable to administer the substance in a more or less routine way, as is done with quinine, for instance, in malarious districts, and thereby to aid the hygienic factors which have been mentioned. In any case the earliest manifestations of the cretinoid condition should be a spur to the use of thyroid preparations. Unfortunately, the state of civilization in cretin and goitre communities is, as a rule, so low that the people are slow to accept benefits, even if they do not actively resist them. To them applies the saying of Goethe: "Die Menschen wollen zu ihrem Glücke gezwungen sein."

I have referred to border-line cases that seem to bridge the chasm between idiocy and cretinism, and between dwarfism and cretinism. In them, as well as in infantilism, it is proper to make a test of thyroid treatment. A beneficial effect is proof that in the given case some of the elements of cretinism were present.

David Riesman.

GOITRE, EXOPHTHALMIC. See the APPENDIX.

GOITRE. (SURGICAL.)—In the treatment of goitre, surgical measures may become necessary, because internal medication has failed to stop the growth of the tumor or to relieve dyspnœa or other severe symptoms; or an operation may be resorted to, merely to free the patient from a disfiguring tumor.

External applications have little effect upon a goitre. The reports of success from the application of iodine in some form or other, or from the use of electricity, have been too few and too scattered to count for much.

Injection.—Many surgeons have reported excellent results from the treatment of goitre by injection, but on the other hand not a few deaths have been reported, so that one should be careful in advocating the use of injections. Since the perfection of the operative treatment, and the greatly diminished mortality of the operations performed for goitre in the last few years, the field for injection has been much limited. There will still be instances, no doubt, in which patients will absolutely refuse an operation, or in which on some other account a surgeon will be justified in injecting a goitre with iodine or iodoform; but such injection should be made with a clear understanding of its danger, and, it is hardly necessary to add, under strict aseptic precautions. Even then there is danger from hemorrhage and embolism.

Besides the tincture of iodine which has been most generally employed for injection, carbolic acid, alcohol, arsenic, and ergotin have been tried, but they are less effective than iodine, and do not decrease the danger of this method of treatment. Iodoform is the only substitute which has found many friends. It should be mixed with ether and olive oil in the proportions of 1 part of iodoform to 7 parts each of ether and oil. When the mixture turns brown it contains free iodine, and should be discarded.

To lessen the risk of hemorrhage, the hollow needle should be separately introduced. When it is seen that no blood escapes from it, the syringe should be attached, and ten or fifteen drops of the chosen mixture slowly injected. The resulting pain is sometimes very great, but lasts only for a few moments. The effect upon the gland is more or less marked according to circumstances. There may be an initial swelling, followed in a few days by more or less shrinking. Usually ten or twenty treatments will be required. These may occur at intervals of three days or more according to the amount of reaction. Parenchymatous goitre is best suited to treatment by injection, and this is the type of the disease which is most benefited by internal remedies. If the treatment is successful, there will in a few days be a distinct shrinking of the gland apparent to the eye and finger, and also capable of demonstration by measurements of the neck.

Operation.—Many operations have been advocated for the relief of goitre. Three of them have proved their worth and may be spoken of as classical. They are partial resection, enucleation, and ligation of the thyroid arteries.

Removal of the whole gland was formerly practised, but has been pretty nearly given up on account of the fact that acute or chronic "cachexia thyreopriva" follows in twenty-five per cent. of the cases. The acute form of this trouble is marked by tetanic symptoms which may terminate in speedy death. In the more chronic form surgical myxœdema develops, and this too may increase in severity till the patient succumbs. Hence total thyroidectomy, except for malignant disease, may be considered an unjustifiable operation. Partial resection is rarely followed by symptoms of tetanus, and when they do occur they are light and usually transitory.

Before any operation is performed upon a goitre, the patient should be prepared with all possible care. The difficulty of carrying out perfect asepsis so near to the mouth, the proximity of the tumor to important vessels and nerves, and above all the risk of sudden and severe hemorrhage, make the operations upon the gland much more serious than they appear at first sight to be. True, the mortality is small when a single surgeon operates upon a long series of patients, Kocher, for example, having reported a mortality of much less than one per cent.; but under ordinary circumstances a mortality of five per cent. may be expected.

Choice of an Anæsthetic.—Some surgeons advocate the use of ether, some of chloroform, and some prefer to use cocaine or some other local anæsthetic. The last plan possesses one advantage, namely, that the patient by speaking can demonstrate that the recurrent laryngeal nerve is not injured. A local anæsthetic should be chosen in cases of goitre accompanied by severe dyspnœa.

Incision.—A transverse incision is now generally preferred, as it well exposes the tumor, and leaves a scar in the direction of the wrinkles of the neck, and therefore not a conspicuous one. In case of a very large or deep-seated swelling, Kocher employs an angular incision, extending transversely on the level of the thyroid cartilage, from the sterno-mastoid muscle to the median line, and then bending downward to the sternum if necessary. This incision avoids the complete division of the sterno-laryngeal muscles.

Partial Resection.—When the skin incision has been made, and all superficial veins have been divided between ligatures, the muscles which lie in the way must be divided or drawn to one side, and the superficial fascia which overlies the true capsule of the gland must be divided and retracted. Beginning then with the upper and lower poles of the gland the surgeon carefully separates it from the surrounding tissues, placing ligatures around arteries and veins, and gradually dislocating the gland—as fast as it is freed—toward the median line. It is very important that every vessel should be clearly seen before it is clamped or ligated. If this rule is followed, the recurrent laryngeal nerve, which is closely associated with the inferior thyroid artery, will not be injured. Sudden hemorrhage should be controlled by compression, not by hasty clamping. The gland is often intimately attached to the trachea, and it is therefore better to leave a small portion of it behind, rather than to risk injury to the nerve by too violent attempts at removal. Hemorrhage from the substance of the gland, either where the isthmus is divided or elsewhere, may be controlled by cauterization or by ligature. The divided muscles are to be sutured. If the wound is deep, it should be drained for a couple of days.

The amount of gland tissue to be left depends a good deal on the shape of the goitre. If only one side of the gland is affected, the other is naturally left. If both sides require removal, enough gland tissue should be left to equal in bulk at least one-fifth of a normal gland. This tissue should be left at the poles of the gland, preferably about the inferior thyroid arteries, so as to reduce the risk of injuring the recurrent laryngeals.

Enucleation.—If a goitre is due to the development of distinct nodules within the thyroid gland, these may be enucleated. The ease with which this procedure may be carried out depends largely on how free these nodules are. Sometimes they may be shelled out from the surrounding gland tissue, almost as readily as non-inflamed tuberculous glands from their fibrous coverings. At other times the enucleation, on account of close attachment of the nodules, becomes virtually a partial resection. In such cases bleeding may be very troublesome, while on account of the depth of the holes which remain infection is more likely to follow in any case of enucleation than in a partial resection. Moreover, recurrence of the goitre is said to be more frequent after enucleation than after partial resection. Previous treatment by injection makes enucleation very difficult. There is little danger of injury to the nerves or jugular veins during enucleation. The skin incision is the same as that for partial resection.

Ligation of the Thyroid Arteries.—By the ligation of the thyroid arteries a certain amount of atrophy of a goitre may be accomplished. The superior artery is easily found through an incision along the median border of the sterno-mastoid muscle. The inferior may also be reached through this incision; but an easier method is to make a transverse incision situated far enough backward to allow the sterno-mastoid muscle to be drawn forward out of the way. The thyroid axis can be reached in this manner, and the inferior thyroid separated and tied near its origin.

Exothyropexy.—Jaboulay and a few other surgeons have succeeded in bringing about atrophy of a goitre by dissecting the enlarged gland sufficiently free to allow it to be brought into the wound, there to remain until healing by granulation shall have taken place—*i.e.*, for from three to eight weeks. Of the first sixty-five patients so operated upon four died, so that the operation is not without danger, and on account of its other obvious disadvantages it has not been generally taken up.

The two operations, therefore, which are most valuable are enucleation and partial resection; the former for isolated cysts and solid tumors, and the latter for diffuse and adherent goitres and all rapidly growing ones, since it best provides against recurrence.

Edward Milton Foote.

GOLD.—So far as determined, the action of gold upon the animal system resembles that of mercury more nearly than that of any other of the well-known heavy metals. Locally, soluble gold salts are powerfully irritant, and, constitutionally, gold compounds affect nutrition. In therapeutic doses they tend, like mercurials, to improve nutritive tone, but in poisonous quantities to derange it, with the development of stomatitis and gastro-enteritis, and, in continued dosage, of emaciation and progressive general enfeeblement. Gold has the common reputation of being a nerve tonic, especially in cases of nervous derangement in the genital apparatus, particularly the ovaries. Therapeutically, it has been used in ovarian inflammation and irritation, in amenorrhœa, in loss of virility, and in various conditions of impaired nerve power, and also as a substitute for, or adjuvant of, mercury in the treatment of constitutional syphilis.

In none of these applications can gold be considered a medicine of first-rate, nor possibly even of second-rate power. The sole compound of gold official in the United States Pharmacopœia is that entitled *Auri et Sodii Chloridum*, Gold and Sodium Chloride. This is "a mixture of equal parts, by weight, of dry gold chloride and sodium chloride" (U. S. P.). The compound is easily obtained by mixing in proper proportion solutions of the two salts and evaporating to dryness. It crystallizes in elongated prisms, but is commonly found as "an orange-yellow powder, odorless, having a saline and metallic taste, and slightly deliquescent in damp air" (U. S. P.). The compound is freely soluble in water, and the solution has a slightly acid reaction. This preparation is locally irritant even to causticity, and constitutionally exerts the virtues