Asphalt Varnish. This can be procured from any painter's supply store, and is to be diluted with turpentine to the required consistency. Kitton recommends asphalt dissolved in benzol; to this solution he adds a little gold size.

Gold Size. What is known in commerce as Japan gold size is to be used. This sets very quickly, and may be used uncolored or colored with any of the mineral pigments.

Shellac Varnish. Shellac should be dissolved in alcohol, so as to obtain a thick solution. The addition of twenty drops of castor oil to each ounce of the solution has a tendency to render it less brittle. This is an excellent cement for specimens that are to be examined with oil-immersion lenses, as it is not attacked by the immersion fluid.

Gelatin. If the covers are first painted around with a warm, strong solution of gelatin in water, allowed to dry, and then painted with a saturated solution of potassium bichromate, an insoluble cement is formed which adheres firmly to the glass, and by the absorption of a small amount of glycerin that may be on the slide, is rendered semi-elastic. This is also a good cement for specimens to be examined by homogeneous immersion lenses.

Marine Glue. This is found in commerce already prepared. It is soluble in ether, naphtha, or solution of potash. It is used chiefly for making shallow cells, and cementing glass cells to the slide.

Mounting in Canada Balsam.—This process is divided into three steps: (*a*) dehydrating; (*b*) clearing; (*c*) enclosing in balsam.

(*a*) Dehydrating. As water is not miscible with the reagents used for clearing, or with the Canada balsam, it is to be removed. This is accomplished by soaking in absolute alcohol. The specimen is first washed in ordinary alcohol to remove the surplus of water, and then placed in the absolute alcohol for from three to five minutes.

(*b*) Clearing. For this purpose we must use a reagent that is miscible with both alcohol and balsam. The specimen is to be carefully removed from the alcohol with a spatula, the adhering fluid removed by filter paper, and the section floated off into the clearing medium. If the section is perfectly anhydrous it will float on this, and in the course of a few moments become transparent and sink to the bottom.

For clearing we use chiefly the essential oils. Of the most commonly employed are the oils of cloves, cedar, anise, origanum cretici, bergamot, and the white oil of thyme. Carbolic acid, creosote, xylol, benzol, turpentine, and chloroform are also used. Old samples of wood creosote, xylol, benzol, chloroform, oil of origanum or thyme, are to be used for specimens embedded in celloidin, when we wish to retain the embedding material.

FIG. 2704.—Balsam Bottle.

It is sometimes best to clear large or delicate specimens on the slide. First float the sections on the slide, and absorb the surplus alcohol with filter paper; then drop the clearing reagent on the specimen and place the slide under a bell-jar until the specimen is transparent; absorb the surplus of the clearing reagent, and add the balsam and cover.

(*c*) Enclosing in Balsam. The transparent section is removed from the clearing reagent with a spatula (Fig. 2687), and floated upon a slide, care being taken that it lies perfectly flat and that it is not wrinkled or folded upon itself. The excess of the clearing reagent is sucked up with a pipette (Fig. 2700), or soaked up with filter paper. A drop of balsam is placed upon the specimen, and the cover glass laid on as in glycerin mountings (Fig. 2701). As the balsam hardens in time, there is no need of cementing the cover. In all these manipulations great care must be taken to have the slides, covers, and all instruments perfectly dry—any moisture will cause a precipitation of the balsam, and thus cause an opacity of the specimen.

Canada balsam as found in commerce should never be used. The commercial balsam is heated on a sand bath until all volatile matter is driven off, and it becomes brittle when cold. This hard balsam is then dissolved in xylol, benzol, or oil of cedar, enough of the solvent being used to give the required consistence. These solutions, with the exception of that in oil of cedar, set quickly. The solutions of balsam are to be kept in capped bottles (Fig. 2704), or in tin tubes, such as are used for the oil colors of the artist.

Hard balsam is also used for mounting, especially sections of hard bone and teeth, in which we wish to demonstrate the lacunæ. The process is as follows: A bit of hard balsam is placed in the centre of a slide and warmed gently over the flame of a lamp, care being taken not to let it boil, or bubbles will be formed. When melted, the specimen is plunged into it and covered quickly, and the slide is placed on a cold surface, which sets the balsam immediately and prevents its entering any of the lacunæ, which, being filled with air, show as dark spaces.

Instead of Canada balsam, dammar varnish and other preparations of dammar may be used. Gum dammar dissolved in xylol or oil of cedar is now generally used in place of the above mixtures.

Glycerin Jelly.—Of the numerous published formulæ for this medium, that of Kaiser is the best. He soaks one part, by weight, of French gelatin for two hours in six parts, by weight, of distilled water; then adds seven parts of glycerin and 1 gm. of carbolic acid for every 100 gm. of the mixture; warms on a water bath, with constant stirring, until all the flakes produced by the carbolic acid disappear; filters warm through paper and preserves in a tightly stoppered bottle.

Soak the sections for a short time in this warm mixture, and then transfer to a melted drop of the same on a slide. Cover, and when the jelly has set, remove any excess and ring the cover glass.

For Weigert's hæmatoxylin method, and its modifications, for the central nervous system; Golgi's methods of impregnation with silver chromate; Nissl's method for staining nerve cells; Ehrlich's method of staining nerve fibres with methylene blue, and its modifications; Marchi's method for staining degenerated nerve cells; and Weigert's and other neuroglia stains—see *Brain, Histology of*, Vol. II., pp. 322–331.

For further details of histological methods consult "The Microtomist's Vade-Mecum," Bolles Lee; "Pathological Technique," Mallory and Wright; *Zeitschrift für wissenschaftliche Mikroskopie.* *George Cornell Freeborn.*

HODGKIN'S DISEASE.—(Synonyms: Pseudo-leukæmia, lymphadenoma, anæmia lymphatica, adenia, lymphosarcoma, malignant lymphoma, lymphomatosis.)

DEFINITION.—A disease characterized by a progressive enlargement of the lymph glands and often of the spleen, a gradually developing anæmia, and secondary growths of lymphoid tissue in the liver, spleen, kidney, alimentary tract, bone marrow, and other structures of the body.

The affection differs from leukæmia chiefly in the absence of a marked leucocytosis.

ETIOLOGY.—The disease occurs most frequently in males under forty years of age. The exact etiology of Hodgkin's disease is as obscure as that of leukæmia. The fact that the disease often follows inflammatory processes and runs a rapid febrile course suggests an infectious origin. Bacteriologic examination of the blood and lymph glands has revealed micro-organisms in over fifteen cases. The Staphylococcus pyogenes aureus, the Streptococcus pyogenes, the pneumococcus of Fraenkel,

and unidentified bacilli have been cultivated. Roux and Lannois claim to have reproduced the disease by injecting animals with a coccus cultivated by them from the blood and lymph glands of a case. Delbet claims the same for a bacillus. The multiplicity of organisms found suggests that all are probably accidental.

PATHOLOGY.—The most important morbid changes in Hodgkin's disease are hyperplasia of the lymph glands, enlargement of the spleen, and the presence of lymphoid growths in the liver, bone marrow, and intestinal tract.

Lymph Glands.—As a rule, the lymph glands show the greatest change. The glands involved in order of greatest extent and frequency are the cervical, axillary, inguinal, retroperitoneal, bronchial, mediastinal, and mesenteric. In addition, the popliteal and epitrochlear glands may be enlarged. The lymphatic structures of the mouth and alimentary tract are relatively infrequently involved. Lymphoid nodules in the liver are often observed. Microscopic collections of lymphoid cells may be found in various organs that present no abnormal naked-eye appearance. The glands of the neck are usually largest. They vary in size from a hen's egg to minute nodules; unless crowded together, the glands are freely movable, and not attached to the skin. Glandular enlargement is usually symmetrical, although one side may be more extensively involved. Rarely the process is confined to one side. The natural shape of the enlarged gland is round or oval. Pressure may produce many alterations in form. A thin capsule surrounds each gland, and when not crowded together, loose connective tissue unites them in chains. The enlarged glands may be soft or hard. On section, if no secondary changes, such as hemorrhage, have occurred, the surface presents a soft mass, grayish-white in color, with a faint tinge of red or yellow. In the soft variety the cut surface bulges beyond the capsule, and a turbid fluid, made up largely of lymphoid cells, may easily be expressed. No stroma is apparent. The hard variety possesses a relatively greater reticulum than a normal gland. Little or no fluid exudes from its cut surface. Enlargement of the thoracic glands may compress the bronchi or trachea. Thrombosis of large thoracic veins may occur from pressure. The heart and lungs may be displaced by enlarged glands. Lymphoid growths may occur in the lungs; rarely the aorta, thoracic duct, and œsophagus are compressed by the posterior mediastinal glands. The recurrent laryngeal nerve may be injured. In the abdomen the retroperitoneal glands are most frequently involved; the mesenteric seldom reach a large size. Displacements of the uterus and compression of the ureters have resulted from growth of the pelvic glands.

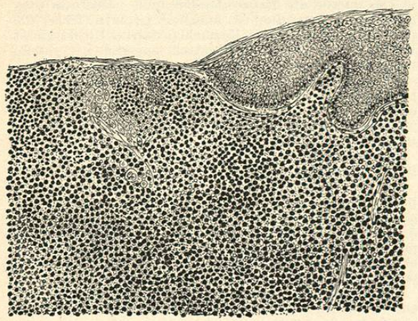

FIG. 2705.—Adenoid Growth in the Skin. (Author's case of Hodgkin's disease.)

Histology of the Lymph Glands.—The microscope shows hyperplasia of all the elements of a lymph gland. In the soft variety the increase in the lymphoid cells is relatively much more marked than that of the connective tissue. Cells presenting the appearance of ordinary lymphocytes are crowded together and held in position by an exceedingly fine network of fibrils. In the hard variety the parenchyma is likewise made up of lymph cells but the connective-tissue increase predominates. Widely varying grades of sclerosis may exist in the different cases and in the various groups of glands in the same case. The gross appearance and histologic change in the lymph glands are practically identical with those in lymphatic leukæmia.

Spleen.—Hyperplasia of the spleen exists in eighty per cent. of all cases. In the splenic variety of the disease the hyperplasia may be enormous, the organ at times filling the greater part of the left half of the abdominal cavity. In the majority of cases of the usual type of the disease, the enlargement is moderate in degree, the spleen rarely exceeding thirty ounces in weight. The organ is firm and its original shape is preserved. Local thickening of the capsule due to perisplenitis may exist. The enlargement may be a true hypertrophy. In about seventy-five per cent. of the cases in which the spleen is enlarged, however, lymphomata are found varying in size and number. The histologic structure of the spleen approaches more closely than normal the picture of a lymph gland. As a rule, the pulp is relatively more increased than the lymph sinuses and reticular tissue. Even in the hard variety of splenic enlargement the increase in the lymphocytes predominates. Sclerosis of the Malpighian bodies is now and then found. Degenerative changes in the lymphoid cells do not occur, as a rule.

Liver.—The organ is often slightly enlarged. Lymphoid growths varying in size from a minute point to a hazelnut invade the liver structure. They develop in the interlobular spaces, and may grow between the liver cells.

Bone Marrow.—A fœtal condition of bone marrow is usually present, similar to that in pernicious anæmia. Adenoid growths are found in the medulla.

Alimentary Tract.—Adenoid growths in the digestive canal seldom attain large size. They may be scattered along its entire length. The tonsils, glands at the base of the tongue, Peyer's patches, and solitary follicles may become hyperplastic. Ulceration of adenoid growths in the stomach may take place. Lymphomata may develop in the kidney, lung, testicle, thymus and thyroid glands. They are sometimes found in the dura; now and then they involve the cranial and peripheral nerves. Lymphomatous growths are practically never found in the brain and spinal cord. Adenoid growths have been found in the heart. In rare cases the skin is the seat of adenoid growths. Retrograde metamorphoses in the new-formed tissue rarely take place in true Hodgkin's disease. When marked changes are present, the condition is usually tuberculosis or mixed infection.

SYMPTOMS.—In the majority of cases Hodgkin's disease begins insidiously and progresses gradually to a fatal termination. In rare instances, however, the onset is severe; and its course rapid. The important symptoms of the disease are progressive enlargement of the lymphatic glands, a gradually developing anæmia, associated with a relative increase in the lymphocytes, enlargement of the spleen, loss in strength and weight, irregular temperature, œdema, and grave cachexia.

Lymph Glands.—As a rule, the earliest symptom noted by the patient is enlargement of the lymph glands superficially located. In most instances the cervical glands are the first involved; rarely the inguinal or the axillary glands are the first to become affected. A few cases have been described in which anæmia, loss of weight and strength, apparently preceded glandular enlargement. At times the deep thoracic or abdominal glands are diseased first, producing early pressure symptoms, such as pain in the chest, cough, dyspnœa, or pain in the abdomen or legs, with œdema. If the cervical group is primarily affected, the enlargement is usually confined to one

side for a time. It may be several months before the other side is involved. The glands of the posterior triangular space and those which lie beneath the jaw are usually enlarged first. In the early stage of the disease the enlarged glands are not adherent to the skin or to each other. As the disease progresses, periadenitis may unite the glands in a firm mass. Such masses in the cervical region may project far beyond the angle of the jaw and produce great deformity of the neck. The larynx may be pushed to one side, and grave dyspnœa has resulted from narrowing of the trachea by pressure. Pressure effects upon the carotid artery, jugular vein, and pneumogastric nerve have been noted. Enlarged glands in the thorax have produced spasmodic cough, dyspnœa, paralysis of the vocal cords, œdema of the arms and lower extremities. Enlargement of the axillary glands has resulted in pain and swelling of the arms from compression of nerves and veins. The inguinal glands may compress the femoral vein; the retroperitoneal glands are sometimes palpable. Bronzing of the skin, possibly from pressure on the sympathetic plexus, has been observed in a few cases. The enlarged glands may compress the ureters, interfere with the function of the lumbar and sacral nerves, and produce œdema by occluding the iliac vein. Uterine fibroids may be simulated when enlarged glands become adherent to the uterus or broad ligament. As a rule, the glands of rapid growth are softer than those that grow slowly. Pain is not present, except when nerve trunks are compressed. Glands of very rapid growth are sometimes tender on pressure. The rapidity of growth varies in different cases, and in the different groups in the same patient. Not infrequently the glands become smaller for a short time. Under the influence of an erysipelas, a marked temporary reduction in size has been noted.

Spleen.—Moderate enlargement of the spleen is present in about eighty per cent. of the cases. No special symptoms referable to this organ are present in the common form of Hodgkin's disease. In the splenic variety, the spleen may attain enormous size. Bruits have been heard; pain from perisplenitis is often present.

Anæmia.—Anæmia is one of the characteristic features of the disease. It may not be pronounced until glandular enlargement is of considerable extent. As the anæmia develops, the patient complains of dizziness, tendency to syncope, headache, dyspnœa on exertion, and cardiac palpitation. Pallor of the mucous membranes appears. The skin assumes a hue peculiar to anæmia. The conjunctivæ become subicteric. Epistaxis may occur. The advent of cachexia is characterized by a tendency to œdema, effusion into serous cavities, marked asthenia, hemorrhages, and fever.

Circulatory System.—The heart is usually somewhat dilated. Hæmic murmurs may be heard. In the later stages the carotids pulsate visibly. The veins are often prominent. The pulse is full and frequent, and may approach the water-hammer character. Retinal hemorrhages may take place.

Blood.—In the early stages of Hodgkin's disease the blood may show no marked alteration.

Red Cells.—As the disease progresses there is usually a gradual reduction in the number of red cells, and the individual cell is moderately poor in hæmoglobin. The loss in red cells and hæmoglobin does not approach that found in a corresponding stage in leukæmia; even at the time of death the red cells may number two million or more per cubic millimetre. In a few cases they have been reduced to less than one million per cubic millimetre. As a rule, no marked change in the size and form of the red cells is present. Occasional megalocytes are found, but more frequently the corpuscles are undersized. Nucleated red cells of the normoblast type are usually scarce, even in the late stage of the disease.

Leucocytes.—The number of leucocytes may be normal or even diminished. In the majority of cases of true Hodgkin's disease, the lymphocytes are relatively increased. The polynuclear cells are correspondingly decreased.

In many cases the number of leucocytes is markedly increased, although, as a rule, no greater than fifty or sixty thousand per cubic millimetre are found. The rapidly developing cases, with febrile disturbances, are more likely to show a leucocytosis than those of chronic course. A few myelocytes may be found, as in all cachectic processes. The eosinophiles are rarely increased. The coagulability of the blood is greatly reduced. A diagnosis of Hodgkin's disease cannot be made on the blood findings alone. A relative lymphocytosis is a valuable sign, but the same condition is often found in true lymphosarcoma, and in tuberculosis of the lymph glands.

Alimentary System.—The tonsils and glands at the base of the tongue are frequently enlarged. Deafness may arise from extension of adenoid growths from the pharynx, occluding the Eustachian tube. Ulceration of lymphoid growths in the stomach may simulate gastric ulcer. Diarrhœa and hemorrhage may occur from the same condition in the intestinal tract. Constipation may result from pressure of enlarged glands; jaundice from occlusion of bile ducts. The liver is often enlarged, due at times to the growth of lymphoid tissue in its structure.

Temperature.—A moderate elevation of temperature from time to time is the rule in Hodgkin's disease.

Respiratory System.—Dyspnœa incident to anæmia or pressure on the respiratory passages by lymphatic growths is a common symptom. Crepitant râles, produced by the pressure of adenoid growths in the lung may be heard. Pleural transudates take place in the cachectic stage. The terminal event is often a pleurisy or a pneumonia.

Nervous System.—Paraplegia may result from pressure on the spinal cord, as in a case reported by Osler. Epileptiform convulsions of short duration may occur. Coma may precede death. Disturbance in function of nerves from pressure is frequent.

Genito-Urinary System.—The urine often contains a trace of albumin. A real nephritis is to be considered a complication.

Skin.—Bronzing, such as occurs in Addison's disease, has been observed. Adenoid growths in the skin presenting small raw surfaces, from which serum exudes, have been observed in a few cases. In one recently studied by the writer, the growths progressed over the surface of the skin, leaving behind a healed surface, slightly indurated (Fig. 2705).

Diagnosis.—Hodgkin's disease is clinically and anatomically closely related to several affections.

Leukæmia.—The essential difference is in the blood findings. A few cases of Hodgkin's disease have terminated in true leukæmia.

Tuberculosis of the Lymph Glands.—Musser and others believe that Hodgkin's disease is probably a lymphatic tuberculosis. Most observers, however, are of the opinion that Hodgkin's disease and tuberculosis of the lymph glands are two distinct affections. All admit the difficulty at times in differentiating the two processes, both clinically and anatomically. The following points are of some value in distinguishing the two processes:

1. Localized glandular enlargement favors tuberculosis.

2. Fever is often absent in Hodgkin's disease. A fever is usually present in tuberculosis.

3. In Hodgkin's disease, deposits of lymphoid tissue may be found outside of the glands.

4. In tuberculous disease, the glands often caseate or suppurate, and become adherent by inflammation to each other and to the skin. In Hodgkin's disease the glands do not caseate or suppurate, and are freely movable beneath the skin.

5. The tuberculin test often results in local reaction in tuberculous adenitis. The positive diagnosis of Hodgkin's disease had better be reserved in all cases until tuberculous lymphadenitis has been excluded by animal inoculation and histologic examination.

Chronic Intermittent (Rückfalls) Fever.—This condition is characterized by a chronic intermittent fever, with

swelling of the lymph glands. It was brought into prominence by Pel, Ebstein, Renvers, and others. It is probably a tuberculous lymphadenitis.

Lymphosarcoma.—This condition, sharply differentiated by Kundrat, is clinically and anatomically more closely related to Hodgkin's disease than to sarcoma of the lymph glands. However, the glandular enlargements possess some of the characteristics of malignant growths. Like Hodgkin's disease, they originate in lymphatic structures, although in perhaps one-half of the cases they do not develop from typical lymph glands, but from glandular elements, such as are found in the mucous membrane of the mouth and alimentary canal. The growths remain more regional than in Hodgkin's disease. They develop along the line of the lymphatics; extremely rarely do metastases occur through the blood. Universal glandular enlargement, as in Hodgkin's disease, does not occur. Histologically, the cells often present atypical development, contain at times many nuclei, become distinctly aggressive, penetrate the capsule, and invade the surrounding tissue. The glandular structure of the growth is often effaced. In many cases the histologic picture is the same as in Hodgkin's disease. Metastases in distant organs rarely occur. Retrograde metamorphoses do not occur as a rule. In rare instances lymphosarcoma develops from Hodgkin's disease.

Splenic Anæmia.—Splenic anæmia presents the clinical and histological picture of Hodgkin's disease, with the exception that the spleen is the lymphatic structure that is chiefly involved. The organ may be enormous in size. Enlargement of the lymph glands is absent, or decidedly in the background. It is, in reality, the splenic form of Hodgkin's disease.

Syphilis.—Glandular enlargement in syphilis is in the group nearest the indurated sore. Rarely does the adenopathy become general. One gland becomes enlarged first, the others of the group soon afterward. They seldom are larger than a hazelnut. In the secondary or tertiary stage of the disease glandular enlargement may be present in the proximity of a local syphilitic lesion.

Prognosis, Course, and Termination.—The onset of the disease varies. Acute cases have been described by Cohnheim, Eberth, and Falkenthal. In one case the duration of the disease was only eleven days; in another four and one-half months. The most rapid course has been noted in children. The majority of cases are fatal within the first two years. Few last longer than five or six years. The most favorable cases are those in which glandular enlargement remains localized. General lymphatic enlargement may occur early, or it may rapidly develop after several years of local involvement. As a rule, soon after glandular hyperplasia becomes general, anæmia and emaciation develop, and the disease progresses steadily to a fatal termination. The immediate cause of death is often some intercurrent affection, such as pneumonia or pleurisy. Cases have been reported in which death occurred from asphyxia and starvation, due to pressure of enlarged glands upon the trachea or œsophagus. In a case recently observed by the writer, general convulsions and transitory unconsciousness were repeated several times during the day preceding death. Recovery has apparently taken place under treatment. The slowly developing cases are more likely to be benefited than the acute. Even in the latter arrest or improvement may occur. The prognosis is best in the splenic form of the disease, because it is amenable to surgical treatment.

Treatment.—Patients affected with Hodgkin's disease should avoid physical and mental fatigue. They should receive nourishing food, easily digested. Lean meats, milk, cream, butter, and eggs are especially valuable foods.

Medicinal Treatment.—Arsenic is recognized as the best drug. It may be given internally in the form of Fowler's solution, or arsenious acid. Certain advantages accrue from its subcutaneous administration. Injection of arsenic directly into the enlarged glands is advocated. When Fowler's solution is given internally, it is well to begin with two drops, three times a day, after meals, and gradually increase the dose by from one to three drops each day. If no symptoms of arsenical intoxication appear, the dose may be increased to fifteen or twenty or thirty drops three times a day. Should symptoms of arsenical poisoning appear, such as pronounced metallic taste, salivation, nausea, severe epigastric pain, vomiting, diarrhœa, tenesmus, irritable heart action, oppressed breathing, œdema, tremor, and muscular stiffness, the dose should be reduced to the point of tolerance. If a diarrhœa of moderate grade is the only symptom of intoxication, it can often be advantageously controlled by giving from three to six drops of the simple tincture of opium, three times a day. If no diarrhœa exists, it is well to administer laxatives and diuretics to help free the system from arsenic, and its products of altered metabolism. Arsenious acid may be given in the form of the so-called Asiatic pill: one part arsenious acid to eighty parts black pepper. Black pepper seems to increase the tolerance of the stomach for arsenic. Marked improvement sometimes follows the internal administration of arsenic. In chronic cases, glandular swellings have rapidly disappeared, and in some instances recovery has followed its use. Even in the rapidly developing cases, arsenic has apparently checked the course of the disease. In many cases of Hodgkin's disease, arsenic may be given to better advantage subcutaneously. The disagreeable gastro-intestinal symptoms are delayed, and much larger doses of the drug are tolerated. Pearson's solution produces the least local irritation. It is best injected in the region of the buttocks, or in localities rich in subcutaneous areolar tissue. It should be diluted with equal parts of distilled water, the mixture sterilized, and the skin and instrument rendered thoroughly aseptic. Pain, which sometimes continues for a short time after the injection, may be controlled by adding one-tenth grain of cocaine hydrochlorate. The injections may be given once daily, and subsequently twice daily. Gradually increasing doses may be given each day, until a larger amount than advised by mouth may ultimately be given and tolerated for a longer time. The effect of the subcutaneous injection of Pearson's solution is often very gratifying. The general condition may improve, the glands may diminish in size, and the patient often gains in weight. Severe pain is rarely complained of at the site of the injection. If care is taken in the preparation of the solution and instruments, inflammation and suppuration do not occur. Good results are claimed for the injection of Pearson's solution directly into the enlarged glands. This sometimes gives rise to a slight elevation of temperature. Such injections have been made directly into the enlarged spleen. The wisdom of this procedure may be justly questioned.

The manner in which arsenic acts in Hodgkin's disease is not known. If the disease is bacterial in origin, its effect may be germicidal; possibly it acts in the same manner as mercury in syphilis. Unfortunately, only a relatively small number of cases are permanently benefited by arsenic, and in a few cases no improvement follows its use. Iron is of very little value in the treatment of the disease. Quinine and phosphorus in small doses have seemed to be of some use. Cod-liver oil is a good tonic. Extracts from various glands and tissues have been used without apparent results.

Local Treatment.—Aside from the intraparenchymatous injection of arsenic, already described, the enlarged glands have been injected with solutions of various drugs. Iodine, potassium iodide, nitrate of silver, carbolic acid, and chromic acid have been used, without satisfactory results. Galvano-puncture has proved of no permanent value. Iodine applied to the skin over the gland is ineffectual. If the disease is primarily located in the glands, and if the disease spreads from them by secondary infection, an early removal of the glands primarily diseased would be rational. The subsequent course in a number of cases in which the disease was local and the glands were early removed justifies the procedure in selected cases. If the disease is widespread

and deep-seated from the beginning, extensive operative treatment is not advisable. Some think it best to remove as many glands as possible, even though the glandular enlargement is general, in the hope that medicinal treatment may better control the disease. The results obtained do not warrant the procedure. All cases, chronic in character, with a tendency to localization of the process, should be treated by removal of the growths, supplemented by the administration of arsenic. Operation is indicated when accessible growths produce serious pressure symptoms. In most cases the glands are easily removed. In some cases, however, adhesions are firm and extensive. The results obtained by splenectomy in the splenic variety of the disease are exceedingly gratifying. A removal of the spleen should be seriously considered in all cases in which the diagnosis is certain, and the progress of the disease is apparently toward a fatal termination. Recovery has followed splenectomy in such cases, even after cachexia was advanced.

Bertram W. Sippy.

HOLARRHENA.—*Conessi* or *Tellicherry Bark.* The bark of *H. antidysenterica* Wall. (fam. *Apocynaceæ*), a woody plant of India. It is one of several plants whose barks have gone under the name of "Kura" or "Kuda" in India. The active constituent is an alkaloid which has been called *Wrightine* ("conessine"), and there is some doubt about its identity with what has been regarded as the same from other sources. It is contained also in the seeds. The bark appears to be a carminative and intestinal astringent, and the alkaloid somewhat antiperiodic. It is very largely used in native practice in India as an antidysenteric, and has been considerably so used in Europe. Reports as to its efficacy are discordant, but its use has declined. An aqueous extract is used in three-grain doses. *Henry H. Rusby.*

HOLOCAIN, para-diethoxy-ethenyl-diphenyl-amidin hydrochloride $[(C_6H_4.O.C_2H_5)_2.NH.C.CH_3:N.HCl]$, is obtained by the union of molecular quantities of phenacetin and paraphenetidin with separation of water. It crystallizes in bitter, white needles which are freely soluble in alcohol and ether and in forty parts of water. It is not affected by a temperature of 212° F. (100° C.). With alkalies it is decomposed and precipitated, the presence of a calcium salt in the water used for solution being sufficient to produce turbidity. It attacks any free alkali in glass; so, to prevent precipitation, the glass container should previously be boiled with acid.

Holocain has a deleterious effect on protoplasm, as in 0.1-per-cent. solution it stops fermentation and putrefaction, in 0.5-per-cent. solution it arrests the development of germs, and in one per cent. it stops amœboid movements and kills most micro-organisms. Hence the solutions are sterile, though if desired they may be boiled without harm. Holocain paralyzes the sensory nerve endings, and is a local anæsthetic of great power. It is claimed by Hotz, Wurdemann, Knapp, Jackson, and others to be quite as anæsthetic in the eye as cocaine, quicker in its action, and its effect more lasting, and as it is more penetrating the iris is more anæsthetized. It does not dry the cornea, increase intraocular tension, or influence the pupil or accommodation. Neither does it constrict the vessels, and, on the contrary, it tends to produce slight hyperæmia. This comparison with cocaine can be well demonstrated by dropping cocaine solution in one eye, and holocain solution in the other eye of the same patient. The amount used for eye work is two to five drops of one-per-cent. solution, and in one-half to two minutes this produces anæsthesia lasting ten to fifteen minutes. Derby and Knapp recommend it for the removal of foreign bodies as it leaves so little effect on the eye. They also find it the most serviceable drug in corneal ulcers of microbic origin, and in purulent ophthalmitis. Holocain cannot be used like cocaine by hypodermic for local anæsthesia, as it is much more toxic, its action in overdose resembling that of strychnine (Heinz).

W. A. Bastedo.

HOLZIN, HOLZINOL. See *Formaldehyde.*

HOMATROPINE.—Atropine and hyoscyamine when decomposed break up into tropic acid and tropin. The latter when combined with mandelic acid forms homatropine; mandelic acid being the product of the action of hydrochloric acid on amygdalin. Homatropine combines with acids to form salts; the hydrobromide, hydrochloride, and salicylate are those most employed. The hydrobromide is official in the British Pharmacopœia. Pure homatropine is almost insoluble in water but is slightly soluble in oil and vaseline. A two-per-cent. solution in oil and gelatin discs are prepared for ophthalmic work. The advantage claimed for the solution in oil is that it is not so readily washed from the eyes by the tears. Homatropine is weaker in its action than atropine and when administered internally acts in much the same manner as does the more common alkaloid. It is said to differ from the latter in this respect, viz., it causes a slowing of the pulse, but this difference is not marked when large doses are administered. The dose of the hydrobromide as given by the British Pharmacopœia is from one-eightieth to one-twentieth of a grain. It has been recommended for use in all conditions in which atropine is indicated, particularly in the night sweats of phthisis. It, however, has not been much employed, as it has not proved so trustworthy as atropine.

Homatropine is almost entirely employed as a mydriatic in ophthalmic work. Its action is much less intense than that of atropine, but it dilates the pupil and paralyzes the ciliary muscle almost as rapidly, and its effects pass off in a much shorter time. The pupil begins to dilate in ten or twenty minutes and paralysis of accommodation is complete in about one hour. In from twelve to twenty-four hours its action is quite recovered from. A one- or two-per-cent. solution is used. *Beaumont Small.*

HOMBURG, GERMANY.—This popular watering-place is situated in the Rhine land, ten miles north of Frankfort-on-the Maine. It is reached from Paris, from which it is 477 miles distant, direct by rail, or viâ Cologne and the Rhine.

The town is built on a spur of the Taunus Mountains at an elevation of 643 feet above sea level. Its natural situation is not picturesque, but art has done much in the way of beautiful pleasure grounds, extensive parks, and promenades. It contains 9,278 inhabitants and is annually visited by 10,600 persons, forty per cent. of whom are said to be foreigners, including a large number of English. Homburg has been one of the favorite resorts of the late Prince of Wales, now King of England.

The mineral springs and sanatoria are in a large Kurpark which extends toward the northeast into the forests of the foothills of the Taunus.

The climate is that of Central Germany, the average yearly temperature being 47.5° F.; and for summer, May, 56.3° F.; June, 66.2° F.; July, 65.6° F.; August, 66.5° F.; September 56.3° F. The yearly rainfall is 26.6 inches. The season extends from May to the end of September.

The waters of Homburg are saline-chalybeate, and are derived from the Taunus schist and quartzite. The principal constituents are the chlorides of sodium, calcium, magnesium, and lithium; the carbonates of iron and calcium; and free carbonic acid. Unlike the waters of Ems, they are cool and have to be artificially heated when used for baths. They come under the general classification of common salt or muriated waters and are similar to those at Wiesbaden, Kissingen, Baden-Baden, Kreuznach, and Nauheim.

There are seven springs, as follows, with their temperatures: Elizabethbrunnen, 51.1° F.; Ludwigbrunnen, 53.4° F.; Louisenbrunnen, 52.1° F.; Landgrafenbrunnen, 51.8° F.; Kaiserbrunnen, 52.9° F.; Stahlbrunnen, 51.8° F.; Soolsprudel, 51.8° F.

The Louisenbrunnen and Stahlbrunnen are distinguished by their excess of carbonate of iron. All these

springs are used for drinking except the Soolsprudel and Landgrafenbrunnen.

The Ludwigbrunnen, Kaiserbrunnen, Louisenbrunnen, and Soolsprudel are used for bathing, the water being warmed by hot steam chambers at the bottom of the baths, with the least possible escape of carbonic acid gas. The waters of the Ludwigbrunnen are used for inhaling. All the springs are the property of the town of Homburg, which has erected the various bath-houses: the Kaiserbrunnen with sixty bathrooms, and two piscinæ for natural carbonic-acid salt baths; mud baths and mineral and fresh-water baths: Kurhausbad with thirty-three bathrooms. In the former 26,147 baths were given in 1899, and in the latter over 7,000. In the Kaiser Wilhelm's bath are inhalations with spray produced by compressed air.

Besides the mud baths mentioned there are pine-needle, electric, medicated, and steam baths; and there are also good facilities for Swedish gymnastics and massage, as well as for the milk and whey treatment.

The chief centre for visitors is the Kurhaus, containing handsome apartments, reading-room, etc., with a terrace partly covered with glass, and corridors, affording a sheltered promenade. At the back of this Kurhaus extend the beautiful pleasure grounds, with a palm-house, orangery, and well-kept flower beds.

The town contains water-works, a sewerage plant with facilities for filtration, and a steam disinfecting apparatus.

Therapeutics.—When these waters are taken internally they gently stimulate the gastric and intestinal mucous membrane, at the same time rendering the contents of the bowels more fluid; they are therefore beneficial in catarrhal affections of the alimentary tract. Taken in small quantities they are constipating, but laxative in larger quantities. They help to increase the general nutrition, according to Weber, by their action in aiding the digestion of albuminous materials.

According to the same authority, they often increase the weight in thin persons, and for such cases are preferable to the alkaline-sulphated waters.

They are also beneficial in catarrhal affections of the respiratory tract; in gout, uric-acid diathesis, obesity, hemorrhoids, diseases of women, heart disease, and malaria. Those springs containing iron are useful in cases of anæmia and chlorosis.

Fifty-five thousand litre bottles of these waters are yearly exported. *Edward O. Otis.*

HONEY.—Mel. "A saccharine secretion deposited in the honeycomb by *Apis mellifica* L. (class, *Insecta;* order, *Hymenoptera*)" (U. S. P.). For the collection and sources of honey, the reader is referred to the article *Wax.* Freshly separated from young or "virgin" combs it is a pale yellow, or greenish-yellow, or light sherry-colored liquid, about as thick as glycerin, of peculiar odor, and of very sweet and slightly sharp taste. All these properties vary with the conditions of its collection, such as season, the prevailing flowers, climate and country, and (but not in commercial honey) the species of insect producing it. The honey of older combs is darker colored and more disagreeable. With age, after removal from the combs, it becomes darker, and granular from the formation of crystals of sugar in it. Specific gravity 1.430 to 1.440. The following tests and reactions are from the Pharmacopœia:

"When recent honey is diluted with two parts of water, the resulting liquid should be almost clear, not stringy, and should have a specific gravity not lower than 1.100 (corresponding to a specific gravity of 1.375 for the original honey).

"Honey has a faintly acid reaction toward litmus paper.

"If one part of honey be dissolved in four parts of water, a clear or nearly clear solution will result, which should not be rendered more than faintly opalescent by a few drops of silver nitrate T.S. (limit of *chlorides*), or of barium chloride T.S. (limit of *sulphates*).

"If one volume of honey be diluted with one volume of water, and a portion of this liquid gradually mixed with five volumes of absolute alcohol, it should not become more than faintly opalescent (as compared with the reserved portion of the solution), and should neither become opaque nor deposit a slimy substance on the inner walls and bottom of the test tube. And when honey is incinerated, in small portions at a time, in a platinum crucible, it should not leave more than 0.2 per cent. of ash (absence of *glucose* and *foreign inorganic substances*).

"On boiling one part of honey with five parts of water, the resulting solution, when cold, should not be rendered blue or green on the addition of iodine T.S. (absence of *starch*)."

Of this, the Pharmacopœia provides a clarified form, under the title "*Mel Despumatum*, or *Clarified Honey*," which is required to respond to the above tests and which we are directed to prepare as follows:

"Mix the honey intimately with *two* (2) *per cent.* of its weight of paper pulp, which has been previously reduced to shreds, thoroughly washed and soaked in water, and then strongly expressed and again shredded. Then apply the heat of a water-bath, and, as long as any scum rises to the surface, carefully remove this. Finally, add enough distilled water to make up the loss incurred by evaporation, strain, and mix the strained liquid with *five* (5) *per cent.* of its weight of glycerin."

Composition.—Honey is a solution of several sugars in water, together with minute quantities of several acids (lactic, acetic, etc.), coloring matter, mucilage, albuminoids, and the odorous principles. Occasional pollen cells are seen in it, and, when old, crystals of sugar. The sugar of honey is principally *levulose*, or uncrystallizable fruit-sugar, but *dextrose* and even sometimes *saccharose*, or cane-sugar, are also present; *mannit* has been observed. In old honey these crystalline sugars (which perhaps increase in it with age at the expense of the levulose) are the cause of its granulating. The result of six analyses by König were: fruit-sugar, 78.74 per cent.; cane-sugar, 2.69 per cent.; nitrogenous substances, 1.29 per cent.; water, 16.13 per cent. (Hager).

Poisonous substances are frequently found in honey, apparently collected by the bees. Their origin has sometimes been traced to *Rhododendron* and other members of the *Ericaceæ*, but no method of detecting them, except by eating, has been found. The poisoning is usually mild, but numerous fatal cases have been recorded.

Uses.—The employment of honey as an article of food and luxury, as well as a medicine, is of great antiquity, and extends over nearly every temperate country on the globe. In the tropics the bees are less provident, and honey is not so regularly collected. But, in spite of this popularity, honey has no medicinal value beyond that of sugar or syrup, and can be considered only a vehicle for other medicines. Partly as a convenience on account of its taste and consistence, and in part from deference to tradition, it has been used in numerous preparations; it is still official in the Honey of Rose (*Mel Rosæ*, U. S. P.), made by mixing 12 parts of a fluid extract of red rose (vehicle, diluted alcohol) with 88 of honey. It is simply a pleasantly astringent vehicle. Confection of rose contains twelve per cent. of honey. *W. P. Bolles.*

HONTHIN is a tasteless and odorless compound of tannin, keratin, and albumin, which is said to pass through the stomach unchanged, and to be separated into its constituents in the intestine. It is an intestinal astringent, is insoluble in water, and may be given alone or with chalk mixture for diarrhœa or intestinal fermentation (Reichelt, Frieser). *W. A. Bastedo.*

HOOF-AND-MOUTH DISEASE.—Hoof-and-mouth disease, also known as foot-and-mouth disease, is spoken of technically as epizootic aphtha, and has also been called eczema epizootica, vesicular aphtha, vesicular epizootic

(The author acknowledges his indebtedness for many of the above facts to "Deutschlands Heilquellen und Bäder," herausgegeben vom Kaiserlichen Gesundheitsamt zu Berlin, Berlin, 1900.)