effect of sulphonal. It, however, more frequently gives rise to toxic symptoms. These are the same as are caused by sulphonal: lassitude, giddiness, ataxic symptoms, nausea, irritation of the kidneys, diminished secretion of urine, with discoloration due to *hæmatoporphyrinuria*. Cases of prolonged peripheral neuritis have also been reported to have followed its administration. No deaths have been reported from single doses, but many fatalities have followed its prolonged use. A cumulative effect has been noted, which is observed when chronic constipation is marked. A peculiar camphoraceous odor of the urine is an early sign of its toxic action.

The dose is from ten to twenty grains, in hot milk, at bedtime. It has recently been shown that when given in water charged with carbonic acid gas, its action is much more marked, and that ten grains will produce its full effect. Seltzer water is selected for that purpose.

Beaumont Small.

TRIONAL, POISONING BY. See *Synthetic Products, Toxicology of.*

TRIOXYBENZOPHENONE. See *Salicyl-resorcin-ketone.*

TRIOXYMETHYLENE. See *Paraform.*

TRIPHENETOL GUANIDINE HYDROCHLORIDE is a local anæsthetic used in eye treatment in 0.1-per-cent. solution. Anæsthesia is prompt and the pupil is not dilated.

W. A. Bastedo.

TRIPHENIN, $C_6H_4.C_2H_5O.NH.CH_3CH_2CO$, obtained by heating paraphenetidin with propionic acid, differs from phenacetin only in the substitution of the propionyl radical for the acetic. It occurs as an odorless, white, crystalline powder of feebly bitter taste, and is soluble in two thousand parts of water. It is antipyretic and analgesic, its action being practically that of phenacetin. Dose 0.3–0.7 gm. (gr. v.–x.).

W. A. Bastedo.

TRITICUM. See *Dog-grass.*

TROPACOCAINE HYDROCHLORIDE, $C_8H_{14}.NO.C_7H_5O.HCl$, is benzoyl-pseudotropeine, a principle at first isolated from a Java coca leaf, but now prepared synthetically from atropine or hyoscyamine. It forms colorless crystals which are readily soluble in water and have strongly alkaloidal properties. Resembling cocaine in its physiological effects, tropacocaine is said by Vamossy to be much less toxic and more rapid in its local action, and to cause none of the ischæmia, hyperæmia, and irritation of cocaine. It is employed in solution of one-half to ten per cent. in the same manner as cocaine, but its use is confined to that of an anæsthetic.

In spinal anæsthesia, K. Schwarz, who employed it in one hundred cases, reports better results than with cocaine; but two of the cases had vomiting and eleven headache, and there was more or less pallor, cyanosis, slow pulse or fever. Neugebauer, McLean of Detroit, Willy Meyer, and Fowler prefer it in spinal analgesia, while Bier thinks cocaine superior. For use in the eye Vamossy recommends ℞ Tropacocaine 0.3 gm. (gr. v.), sodium chloride 0.06 gm. (gr. i.), and distilled water 10 c.c. (ʒ iiss.), a solution which is non-irritating and strongly anæsthetic, and has little, if any, mydriatic action. Veasey considers the drug especially valuable in keratitis, as it does not deplete the corneal bloodvessels. Its action seems to be very rapid; Silex was able to perform a painless tenotomy one minute after the application of a three-per-cent. solution. Hugenschmidt injected 0.04 gm. (gr. ⅗) in his own lower jaw region, and in three minutes he became dizzy, felt precordial anxiety, and exhibited a marked lowering of blood pressure. Ten minutes after the injection the effect had passed away. In dental surgery Pinet and others recommend it highly, either as a hypodermic injection or in ten-per-cent. solution locally applied.

W. A. Bastedo.

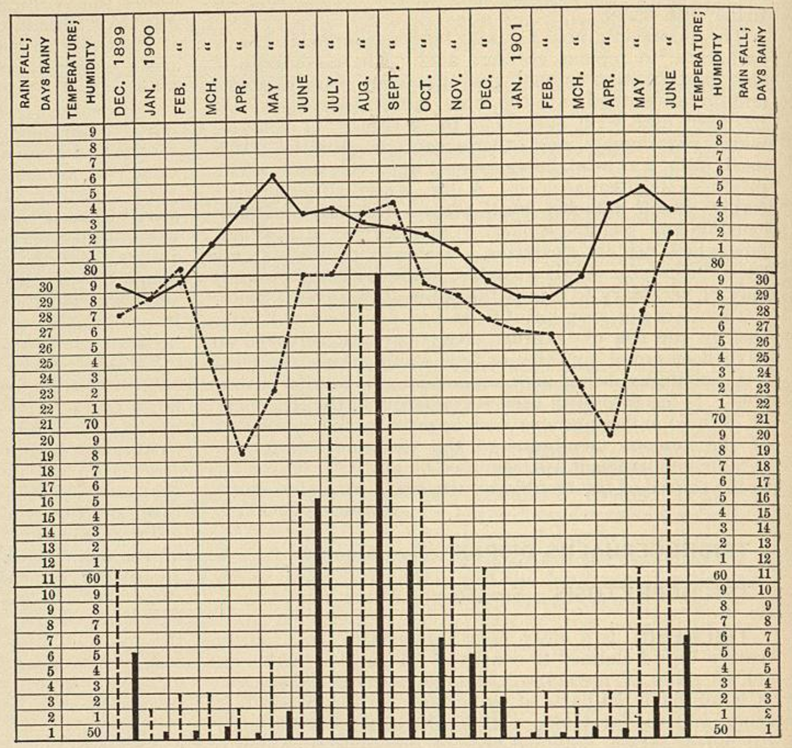

FIG. 4803.—Description of Chart. Each horizontal line represents one degree of temperature and humidity; one rainy day and one inch of rainfall; each perpendicular line, one month; continuous heavy curve, average mean monthly temperature; light broken curve, average mean monthly humidity; heavy black lines in right side of monthly columns, rainfall in inches per month; heavy broken lines near centre of monthly columns, number of rainy days per month; inside column of figures marks degrees of temperature and humidity; and outside figures, number of inches of rainfall and rainy days per month.

TROPICAL DISEASES: GENERAL INTRODUCTION. —Those who desire to acquire a satisfactory knowledge of "tropical diseases," as they are encountered in some special part of the world, must first acquaint themselves to some extent with the surface configuration of the country which is under consideration, with its climatic characteristics, its fauna and flora, and with its people, and then they must study the pathologic aspects of the diseases themselves.

Climate.—To present more clearly the essential features of climate, chart Fig. 4803 has been constructed from data collected in Manila, P. I. Although it is based upon the climatic phenomena observed at only one place in the Philippines, it will serve for most tropical localities, except those situated far inland, where the rainfall may be greatly diminished and where intense hot winds prevail instead of the more pleasant sea breezes.

An analysis of the curves for temperature and humidity shows that these curves cross the 80° (and 80 per cent.) line in February, June, October, and December, thus per-

mitting a more or less arbitrary division of the tropical year into seasons. It will be observed that during December, January, and February, the temperature and humidity are below 80° and 80 per cent.; that during December and a part of January there are a relatively large number of rainy days, but relatively little rainfall; that, as the season progresses, the number of rainy days and the number of inches of rainfall gradually diminish until February, when almost no rain falls. These months are the coldest of the year, and constitute what may be termed the winter season. During the winter the early morning, the late afternoon, and the nights are cool, often cold, on account of the cool monsoons from the north. On the other hand, the middle portion of the day is warm, with blue skies dotted with numerous white clouds. In other words, the days at this season, which is by far the most pleasant of the year, resemble those of our early autumns.

About the first of March the temperature gradually rises above 80° F., each day being just a little hotter than the preceding. In April and May the highest temperature is noted. As the temperature rises humidity sinks to its lowest point in April and May, when the increased rainfall produces a gradual rise to 80 per cent., about the first of June. This is the hot, dry season which continues from the rise of temperature above 80° in March to the rise of humidity above 80 per cent. in June. During this season the temperature is regularly high; humidity low; monsoons frequently absent and often hot, and the skies more or less dotted with white clouds. This is the most unpleasant season of the year. To recapitulate, the hot, dry season continues from early March to June; the temperature is regular and high; humidity low; rainfall almost nil; monsoons often absent and often hot.

In June the number of rainy days and the number of inches of rainfall show a decided increase; in some regions the rainy season may be ushered in by a typhoon. This season continues from the rise of humidity above 80 per cent. in June, to the fall of temperature below 80° F. in November. During the early months, the temperature is a few degrees lower and more irregular than in the hot, dry season. Often during a typhoon relatively low temperatures (62° to 70° F.) are noted. In the last months of the rainy season the temperature gradually sinks below 80° F., when the season merges into winter. The humidity is high; during a typhoon the atmosphere is saturated. These typhoons occur from June to October. They are circular wind and rain storms, the centre of which slowly moves along a fairly well-defined path from southwest to northeast. The nearer the centre is approached, the severer the storm becomes. Destructive winds are frequent during these storms, and the rainfall is often extraordinary; as much as sixteen inches of water having fallen in one day. In the absence of typhoons light showers occur daily. Often every day is rainy. To recapitulate, the rainy season continues from June to November; the temperature is high and irregular; the humidity is high and the rainfall is great; typhoons may occur during this period. The change from one season to another is very gradual.

Throughout the year, monsoons materially diminish the discomforts of a tropical climate. They are winds, the direction of which depends on the location of the centres of high and low pressures. During the summer months the prevailing direction of the wind is toward the north —*i.e.*, toward the northern low-pressure centres. Coming from the equator, these monsoons are warm, often hot. On account of the northern high-pressure centres, winter monsoons have a southerly direction (*i.e.*, they blow from the north) and are cool. Monsoons naturally influence the climate.

In addition to the regular monsoons there are, along the coast, local land and sea breezes which serve to moderate a tropical temperature. These breezes are produced by the difference between the land and the waters as regards the radiation of heat. As heat radiates more rapidly from land, there are, in the late afternoon and during the evening, light winds from the water, whereas in the early morning light breezes blow from inland. These breezes may slightly change the direction of monsoons.

The range in temperature between the hottest and coldest seasons is only eight or nine degrees. This change, with that in humidity and in the monsoons, produces an effect which is felt by the individual in a more decided manner than is shown by the thermometer. The chief features, then, of a tropical climate are a hot, dry season, a rainy season, and a winter season, with a constantly high temperature in each. The latter is the most important feature and more accurately defines the word "tropical" in the expression "tropical diseases" than does the mere geographical signification of the term. In this sense a portion of the year in temperate climates is tropical, and the duration of this tropical period gradually increases as the distance from the equator diminishes, until the Tropic of Cancer and Tropic of Capricorn are reached. Within these parallels the entire year is tropical.

The term "tropical diseases," if used in its strictly geographical sense, includes only a few unimportant diseases; while in the broader sense (which has been given to it in the preceding paragraph) it may properly be said to include the following classes of diseases: First, a small group of unimportant diseases occurring only in the tropics. (Type: yaws.) Second, a larger group of diseases which occur in the tropics and subtropics, and occasionally during the hot months in temperate climates. (Type: yellow fever; dengue.) Third, a group of diseases which occur in all climates, but more persistently in the tropics and subtropics. (Type: malaria.) Fourth, a group of diseases which arise in tropical and subtropical regions—in which they are endemic—and at varying intervals of time spread to different parts of the world. (Type: bubonic plague and cholera.)

In addition to the above-mentioned classes, many diseases common to temperate climates are present in the tropics, but to include them in "tropical diseases" would necessitate a discussion of the entire realm of medicine. Diseases which are produced by factors that constitute an integral part of certain meteorological conditions are very few and, as a rule, unimportant. Except in rare instances, they may be prevented. Here may be mentioned frost-bite, sun-stroke, heat-exhaustion, etc.

Indirectly, climate plays an important rôle in all the diseases that are caused by specific agents, the viability, reproduction, pathogenicity and dissemination of which may be greatly influenced by cold, heat, drought, rain, etc.

The Surface Features of the Country.—The topography of tropical countries is essentially the same as that of countries belonging to higher latitudes. In some districts, by reason of their high elevation, several distinct climates may occur within a remarkably limited area. Woodland, often with heavy undergrowth, is abundant. This feature materially aids the long and severe rainy season to supply numerous small streams which often overflow the lowlands. The soil, which in general is very fertile, plays little or no part in the problem of tropical diseases.

The Character and Condition of the People.—Ignorance and poverty are the prevailing conditions in most of the tropical races. At the same time they are, as a rule, very prolific.

History gives us very little information in regard to the rise and progress of these nations. Most of them were found in a barbarous or semibarbarous state; consequently they fell an easy prey to any or all who had time or inclination to mix in their affairs. Generally speaking, their education has been little advanced. In many of the larger cities schools, colleges, etc., and in some country districts a few schools may be seen, but the type of these seats of learning has not been all that might be desired, and at best only a limited number could be benefited. Religions of various kinds have, too often, gained dangerous power; have handicapped their schools and virtually blocked their education and advancement. Their reading has been limited, travelling has been confined to local districts, and most new-comers have adopted local customs. For these reasons their customs, ideas, etc., have remained unchanged from one generation to another. Of modern ideas, they have no knowledge, especially regarding medical matters; their dogmatic religious beliefs are opposed to advancement, and the disregard shown toward their religions, traditions, etc., by civilized man foster, too often, a spirit antagonistic to modern learning.

Poverty and multitudes go hand-in-hand with ignorance to produce the most horrible conditions. The houses of the ordinary natives are poorly planned and constructed; light and sewerage are bad, and their streets are faulty and filthy. These defects become the more manifest in the presence of multitudes, when there is a rapid accumulation of filth, the decomposition of which is most repulsive and to foreigners often sickening. Their houses are crowded, often two hundred and fifty human beings finding lodgment in a single house not larger than an- eight or ten-room residence. Their food is poor in quality and insufficient in quantity. Their water supply is usually obtained from small streams, surface wells, and pools. Their sewerage is deposited on the surface of the ground about their houses and yards. In habits they are lazy and little influenced by civil law save when coerced. Thus they fall an easy prey to all contagious, infectious, and parasitic diseases, unprepared as they are to combat infection, to seek the world's knowledge or to profit by the experience of other nations. Naturally, under these conditions epidemic diseases are always present, and it is often difficult to determine the extent of these epidemics.

In the tropics, the physical condition of the people is fairly good. In spite of the fevers, anæmias, etc., many aged people are present to demonstrate the facts that the tropics, *per se*, are not inconsistent with long life, and that the normal conditions of man in a warm climate are almost the same as they are in a cold one. The normal temperature, pulse and respiratory rates, digestion and other functions are about the same as in the higher latitudes. Again, the death rate in the larger cities is not materially larger than it is in other climates, except during an extensive epidemic.

Natives in all climates adopt those customs which are best suited to the local conditions. In the tropics, the houses consist mainly of a roof, floor and walls of such a character as will best keep out the intense light, the severe winds, and the copious rains, and will admit, during ordinary weather, as much air as possible. Their clothing is light. They work during early morning and late afternoon, leaving the middle of the day for lounging and napping. Their lack of mental activity is due more to their origin and ignorance than to a direct influence of climate.

In the tropics the heat-regulating apparatus is not so severely tried as in a temperate or cold climate. But when individuals from other climates enter the tropics the activity of their regulating apparatus must be of another kind. In place of the rapidly changing temperatures, the apparatus must adapt itself to a constantly high temperature. This change in activity is not a serious one, but when associated with changes in food, drink, exercise, etc., it may cause more or less disturbance in the general physiological activity, which may last a longer or shorter time, and may to a greater or less degree reduce the natural resistance of individuals to infection. But when this period is passed, no marked inconvenience from the heat should be felt, as the heat-regulating apparatus is sufficient to compensate the external temperature. When the meteorological observations are considered, it is found that only on rare occasions is the weather as hot in the tropics as it is during the summer months in a temperate climate. If harm does follow it is due more to the constancy than to the degree of heat.

Those who go to the tropics must be exposed to the same infections as are the natives—no more, possibly less, on account of their better hygienic surroundings. Consequently a certain percentage of new-comers will be ill for a certain length of time during their stay in a tropical climate; but if the opportunities for infection are the same as they are in other climates, there is no reason why new-comers should be ill oftener in the tropics than in their former homes. In support of this statement we may be permitted to cite the large number of old natives and foreigners who maintain good health in the tropics, the recent extensive movements of troops in the tropics without injurious consequences, and the specific causes of diseases. Usually, if an individual, shortly after entering the tropics, succumbs, some well-known cause for his death may be looked for.

Statistics of military operations possess practically no value in an inquiry of this nature, for troops campaigning in any country are most liable to diseases.

Fauna.—The fauna of the tropics, on account of an abundance of food, shelter and continuous warm weather, is more diversified than in other climates. The importance of this kingdom in medicine has only recently become prominent by the discovery of the rôle acted by mosquitoes in filariasis, malaria, and yellow fever; by flies, ants, etc., in some of the infectious diseases; and by rats, hogs, etc., in certain infectious and parasitic diseases. These discoveries have demonstrated our limited knowledge of the life-history, customs, anatomy, pathology, and ultimate fate of the several members of this kingdom; and they suggest the necessity for a more systematic study than has heretofore been made. The present importance of this subject, in anticipation of future discoveries relating to the propagation and transmission of disease, should give a new impetus to zoology and entomology. As a matter of course, scientific work along this line is important, but when we add to this the practical knowledge which is to be gained in regard to the dissemination and prophylaxis of diseases affecting man, the importance of this whole subject is greatly enhanced. To medical men, especially those working in pathology, the importance of a thorough training in zoology and entomology is manifest; in fact, there has been opened a new field which in time must yield the solution of many of our perplexing problems.

Recent work on yellow fever demonstrates how this disease depends on the life-history of the Stegomyia fasciata. This species of mosquito is tropical, but can thrive in temperate climates during warm months, to be killed by the first frosts. Yellow fever, therefore, is a tropical disease which often prevails in temperate climates during summer months, to disappear after the first few frosts. Dengue fever probably depends on similar modes of transmission. Future developments in this field cannot now be prophesied.

Flora.—In a general way, what has been said of the fauna applies also to the flora. Besides poisons of plants affecting our races, enzymes may play an important and at present an almost unknown rôle in medicine. Recent work demonstrates the importance of enzymes in plant pathology. May not some of these produce disease in the human being? Some have believed that beri-beri is caused by an enzyme. Whether this be a fact or not, it is plain that there is still abundant room for speculation in regard to numerous diseases of which, as yet, we do not know the causes.

Pathological Considerations.—As pathology and bacteriology have in recent years greatly extended the realm of medicine and have explained many of the formerly obscure points in the etiology, course, treatment, and prophylaxis of diseases, one must turn to these branches for more complete information in regard to "tropical diseases." As our knowledge advances, the rôle of specific organisms as etiological factors becomes greater and greater. The number of diseases now believed to be entirely due to the presence of a specific organism is large and increasing. In this way the group of infectious and

contagious diseases has become the most important in medicine.

After the discovery of specific pathogenic organisms, it was found that these organisms usually exist as saprophytes outside of the body, or pass a portion of their life-cycle in some lower animal. These facts expose pathogenic organisms to the struggle for existence and make them, to a great extent, dependent on conditions existing in the several localities or climates.

For saprophytes, a certain amount of warmth, light, moisture, food, and transportation is necessary for their preservation, propagation, and dissemination. Experimentation has shown that many conditions influence the life, reproductive powers, preservation of virulence, etc., of micro-organisms. Consequently conditions present in the tropics may prove unfavorable to organisms which are able to weather temperate or cold climates, and vice versa; it is also possible for an organism to thrive in any climate; and, finally an organism may be so slightly influenced by climatic conditions that for a time it may thrive in almost any locality, only to die out after a longer or shorter period.

Pathogenic organisms, which pass a portion of their life-cycle as parasites in some host of a lower order than man, must depend on the presence of the host, the natural habitat and migrations of which must determine the geographical distribution of the disease produced by the respective parasite. Consequently if the host is tropical or subtropical, or if it has the power to migrate during warm months into temperate climates, the distribution of the disease is in the one case tropical and subtropical, or, in the other, may be present in temperate climates during the summer time. In all cases the fate of the host determines in great measure the fate of the parasite. Pathogenic organisms, which pass a portion of their life-cycle as saprophytes and a portion as parasites, are naturally subjected to all the injurious conditions and fate of the host above noted. On these conditions depend the differences which are observed in certain diseases according as they are encountered in the tropics or in other climates.

Diseases common to temperate and tropical climates may differ in severity, course, etc., even as they do in any given locality; but, as a rule, the clinical course and termination are essentially the same in the two climates. The field of medicine in the tropics has not been so thoroughly worked as it has been in many places; hence there are doubtless many unrecognized diseases which serve to complicate the picture of some common affections. This possible and unavoidable error in diagnosis should encourage the medical man, in the presence of a disease which simulates malaria or typhoid fever, etc., but in which the clinical diagnosis is not confirmed by laboratory methods, boldly to announce the diagnosis as undetermined. In this way the attention of pathologists could more easily be directed to undetermined diseases.

Certain organisms thrive luxuriantly outside of the body and produce toxins, which may, independently of the presence of these organisms, cause disease. This condition is called intoxication. Ergotism and pellagra belong to this class. Owing to the favorable conditions in the tropics for the growth of these parasites, their toxins may play a more important rôle than is at present recognized.

In no climate are the conditions so favorable to parasitic diseases as in the tropics. The dress of the natives and their peculiar customs favor parasitic skin diseases, and, as a matter of fact, these are very common. Intestinal parasites are rife and filariasis is quite a common disease.

Of the diseases which affect both man and animals, cysticercus, glanders, and anthrax, etc., are most important. They naturally vary in frequency in the several districts. In Manila about four per cent. of the hogs killed are infected with cysticercus; only a few with trichinæ. Yet the cases of these diseases in man are comparatively rare. In about two hundred autopsies only one instance of tænia was found; clinically, only a few cases were noted. Glanders is prevalent in some districts, but the disease in man is rarely noted. Anthrax is also rare.

Diseases among animals are rife; epidemics of cattle plague, etc., are frequent.

General Remarks.—While ordinarily the climate is equable, during the rainy and cold seasons sudden changes often occur which have a more pronounced effect on natives than on foreigners. During these times the natives wear their heaviest clothes, yet seem to be cold and uncomfortable. This condition is often intensified by the severe rainfall and high winds accompanying typhoons, at which times all note the marked increase in the amount of urine secreted, this increase being caused by the inactivity of the skin. The fact that an increase in the number of small cells has been observed in sections of kidneys removed at autopsy from cadavers of various ages has furnished ground for the belief that these organs were in a more or less irritated state, and that this irritation was probably due to a diminution in the excretion of urine, dependent upon the general increase in activity of the skin.

During ordinary weather the natives wear very few clothes, are barefooted, and thus are exposed to infection of various kinds. Living, as they do, crowded together in small rooms, usually on the floor, infection rapidly spreads. It is astonishing to see a native well dressed and apparently clean living in the filthiest surroundings. These people seem to like it. Often their food is kept, cooked, and eaten amidst filth. Their domestic animals, cows, hogs, goats, chickens, etc., have free access to the house, and often convert the premises about the home into a pen. In larger residences, in many places, the stable occupies a portion of the house. Night-soil is usually kept in pails in the house, to be carried off by tenders to garden patches. The water supply of the natives is often derived from pools and small streams which are unprotected and which flow through fields on which night-soil has been used, and into which all the filth about the houses drains. Their small streams serve as washtubs for clothing, etc., as bathtubs for the entire town, as wallowing holes for domestic animals, and finally as a source of drinking and cooking water.

When these conditions are realized, and especially when we reflect that cholera, plague, typhoid, etc., are always present in many countries, the wonder is that any of these unfortunate beings survive. Fortunately, Providence has mercifully arranged, through the agency of severe rain storms, for the washing out of many of these filthy places, and through that of a hot sun for the roasting of a goodly portion of the organisms which survive the floods. Notwithstanding these natural prophylactic measures, a variety of circumstances—as, for example, the protection offered by the flora and fauna of the region, and the ignorance and poverty of the people—preserve all the conditions required for the propagation and dissemination of diseases. To this normal condition of disease-promoting factors there must occasionally be added the occurrence of a famine, due to a general failure in crops or to an epidemic among domestic animals, etc. Consequently, preventive medicine must battle, not only with these natural difficulties, but also with unlimited poverty, with ignorance, and with multitudes influenced by dogmatic religious beliefs.

Owing to their origin, education, etc., the nations occupying tropical countries have, with rare exceptions, been incapable of self-government. This fact, coupled with the possible gain of riches, has attracted the attention of civilized nations to the tropics and has led, in many instances, to the active commercial exploitation of these countries. Naturally, the resulting increased intercourse between tropical and temperate climates has awakened a new interest in all conditions prevailing in the tropics, has furnished a means for the introduction of tropical diseases into temperate climates, especially during the summer months, and has given to "tropical diseases" a new interest and a practical bearing. This impetus has, within the past few years, resulted in a rapid development of our knowledge regarding the etiology, course, and prophylaxis of "tropical diseases." Each advance indicates more clearly that the greater number of these diseases are infectious and consequently may be prevented, and that each step in preventive medicine renders the tropics more habitable for races accustomed to temperate climates. Our increased knowledge of tropical diseases enables us to identify, in temperate climates, diseases—such as ankylostomiasis, filariasis, etc.—which, without the knowledge so acquired, would escape recognition. Thus at home, in a temperate climate, we are exposed to many so-called "tropical diseases."

As a result of modern interest in the tropics, of modern research in regard to the dissemination and prophylaxis of "tropical diseases," the monumental work of the late Major Walter Reed, United States Army, must be cited.

Lastly, as our knowledge of "tropical diseases" increases, the importance of their geographical and meteorological relations diminishes, and the conclusion is reached that they are equally as important to the medical men of temperate climates as to those of the tropics.

W. J. Calvert.

TRYPSIN. See *Pancreas.*

TRYPTOPHAN (PROTEINOCHROMOGEN).—In their classic work on "Die Verdauung nach Versuchen" (1831) Tiedemann and Gmelin noted the peculiar red coloration which pancreatic juice and the intestinal contents of animals gave with chlorine water. Claude Bernard failed to observe the reaction with *fresh* pancreatic juice. The researches of Kühne and his followers have indicated that the color reaction is due to a product of the cleavage of proteids, especially through the agency of pancreatic digestion. Kühne found that the characteristic reaction could be obtained equally well with bromine water, which is now more generally used in testing for the substance. If a mixture containing the rose-colored product of the reaction be shaken with amyl alcohol the colored product is taken up by the latter solvent and shows in this a characteristic spectroscopic absorption near the D line. The name *tryptophan* (from θρύπτομαι and φαίνω) was introduced by Neumeister as indicating the origin of the body in the decomposition of proteids. Stadelmann applied the less familiar term *proteinochromogen*, reserving the word *proteinochrome* for the colored compound of which the halogen (Br) forms a part. Trytophan is now known as a typical and constant product of the tryptic digestion of proteids. It may also arise when the albuminous substances are split up by baryta water, dilute acids, or the action of bacteria. When proteids are digested with purified pepsin or papain (?) it is not obtained. Glaessner has shown, however, that it is formed by the enzyme pseudopepsin, which is associated with true pepsin in the gastric membrane. Tryptophan may arise in the autolysis (self-digestion) of tissues, even in the absence of bacteria. The vegetable enzymes bromelin (from the pineapple) and nepenthin (from Nepenthes), as well as those from many other plants, also form products which are said to give the violet color with chlorine or bromine water.

In the earlier attempts to isolate and identify tryptophan, the chromogen was precipitated from its solutions in the form of the halogen compounds which are obtained with bromine or chlorine. The results were not constant, and the products of different investigators varied in their composition, owing to the difficulty of separating them completely from other decomposition products of the proteids, such as peptones. Accordingly various analyses have been reported which showed the compound to contain carbon, hydrogen, nitrogen, and bromine (or chlorine). Pyrrol and indol derivatives were obtained as decomposition products. Nencki regarded tryptophan as the mother substance of some of the pigments (melanins, etc.) which have their origin in the animal body. The latter yield similar products of cleavage.

Tryptophan was first isolated as such by Hopkins and Cole. In composition it corresponds with the formula $C_{11}H_{12}N_2O_2$; and it has been identified as skatol-amido-acetic acid, which Nencki believed would be found as the precursor of those indol derivatives that arise during the putrefaction of proteids. The pure, colorless crystals show great proneness to undergo brown pigmentation on heating with acids, or even with water alone. Tryptophan thus isolated gives the well-known Adamkiewicz proteid reaction (with glacial acetic acid and concentrated sulphuric acid), which has been shown to depend upon the presence of glyoxylic acid in the acetic acid used. Solutions of the isolated tryptophan also give the "pine-slip" reaction direct, offering strong evidence of the presence of the pyrrol ring (or the indol nucleus). The investigations of Ellinger have made it probable that tryptophan is a precursor of indol in the putrefaction of proteids, and that it thus bears a direct relation to the indican of the urine.

For the methods of isolating tryptophan, the reader is referred to the papers of Hopkins and Cole. To test for tryptophan in solutions containing products of proteid decomposition, the following method is usually employed: The solution is acidified with acetic acid, and gradually treated with two or three volumes of saturated bromine water until a reddish-violet precipitate is formed. Large amounts of proteid may first be separated by precipitation with alcohol. The tryptophan is then searched for among the alcohol-soluble products, after removal of the alcohol by evaporation.

Lafayette B. Mendel.

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TUBERCULIN. See *Tuberculosis.*

TUBERCULOSIS.—An infectious disease caused by the bacillus tuberculosis.

HISTORICAL.—It is possible to divide the literature of tuberculosis into six periods. 1st. The description of the tubercle as a specific structure. 2d. The early clinical and anatomical study of phthisis and other lesions of the disease. 3d. The discovery of the infectiousness of the disease and the proof by this of the etiological unity of the lesions. 4th. The discovery of the bacillus and the proof that it was the cause of the disease. 5th. The discovery of tuberculin. 6th. The study of modes of infection and the part played by animals in the extension of infection.

1st. Although the word tubercle had long been used to designate a small nodule, it was not until 1793 that it was described by Bailey as a specific structure. He described under this name a special formation which he found in the lungs in cases of phthisis. The tubercles are small round bodies, never exceeding the head of a pin in size, and which are formed in the cellular tissue of the lung. Large tubercles can be formed by the union of small. The centres of the large tubercles are converted into pus, and this transformation of tubercles into abscesses is the cause of phthisis.

2d. Bayle in 1811 made an anatomical study of phthisis based on one hundred and nine autopsies. He defines as phthisis all lesions of the lungs which produce disorganization and destruction of the lung tissue. He characterizes phthisis clinically as an *ensemble* of symptoms consisting in cough, dyspnœa, marasmus, hectic fever, and sometimes purulent expectoration. Anatomically he distinguishes six varieties of phthisis, but gives special importance to the first two, tuberculous phthisis and granular phthisis.

In tuberculous phthisis the lung contains tubercles formed of an opaque homogeneous substance having a whitish-yellow or grayish color. These tubercles are at first firm, but they afterward soften in their centre, and are finally destroyed by suppuration. The tuberculous affection is a chronic disease of a special character, but probably of a scrofulous nature, and should not be regarded as the result of inflammation. The second variety, granular phthisis, often accompanies the first. In this the lungs are filled with miliary transparent granules of cartilaginous hardness, from the size of a millet seed up to that of a grain of wheat. These granules are not exclusively localized in the lung, but may be met with in the peritoneum, intestine, and heart. This is the first description of miliary tuberculosis.

In 1826 Laënnec proclaimed from his study of pathological anatomy the unity of the different forms of phthisis, and he found the characteristics of the disease in the evolution of the tubercle. "The progress of pathological anatomy has demonstrated that pulmonary phthisis is due to the development in the lungs of a peculiar formation which has received the name of tubercle. The tuberculous material develops in the lungs and in other organs in two principal forms, as isolated bodies and as infiltrations. Each of these forms presents a number of varieties due chiefly to their different degrees of development. The isolated tubercles present four varieties which may be distinguished as miliary tubercles, crude tubercles, granulations, and encysted tubercles. The tuberculous infiltration presents three varieties which can be designated as crude tuberculous infiltration, gray tuberculous infiltration, and yellow tuberculous infiltration. Whatever may be the form into which the tuberculous material finally develops, it presents in its origin the appearance of a gray or semitranslucent mass which gradually becomes yellow, opaque, and very dense. It finally softens, becomes almost as fluid as pus, and is expelled by the bronchi, leaving in its place cavities commonly known as ulcers of the lung, and which we designate as tuberculous excavations." Laënnec also recognized the specific character of these lesions. "One cannot regard the tubercles as the result of inflammation of some one of the constituents of the lung without destroying the results of observation and making a strange abuse of reasoning. If inflammation has any influence on the appearance or the development of the tubercles, it is only to prepare the soil and make it favorable to their growth; in the same way as the soil when cultivated after a long repose will germinate a multitude of seeds which have lain in it for a number of years."

The views of Laënnec prevailed generally until the more careful anatomical investigations of Virchow. In his work on the lymph glands Virchow says: "More careful observation shows that the scrofulous affections of the lymph glands are secondary, and not due to any preceding blood crasis or any general change in the character of the blood, but secondary in relation to the local changes of those parts from which the glands obtain their lymph. The gland swelling is due to certain substances produced in consequence of pathological processes, which are carried over in the lymph to the next lymph nodes and produce in them similar irritation. This can take an inflammatory character or a progressive development without evidences of inflammation. The condition is called scrofula when slight irritation produces extensive glandular swellings. In certain individuals the swelling continues, and this is the reason why it appeals to some as an independent process. The condition is connected with a weakness of the individual or of certain parts of the body. This constitution can be acquired, as is shown by the frequency of such conditions in prisons, where the nutrition of the inmates is not sufficient. The signs of this weakness are a diminished capacity of resistance of the tissue toward disturbances and slighter powers of recuperation." After describing the caseation of the products of inflammation in the lymph glands he says: "A similar condition can take place in the inflammatory products of a mucous membrane when these remain for a considerable time at the place of their formation. They also become thickened and caseous. This takes place in no other part so often as in the lung, where the alveoli and small bronchi become filled with such caseous masses, and that condition arises which, since Laënnec, has been given the name of tuberculous infiltration, and which I consider as caseous infiltration or caseous hepatization. This may involve entire lobes of the lung, or it may be limited to single sections of the lung and then corresponds to what is ordinarily described as crude tubercle. Sometimes it is limited to small groups of lung alveoli; then it is miliary caseous hepatization. There is nothing that justifies us in considering these masses as tubercles. Along with this, tuberculosis can take place, but the tubercles are seated in the walls and not in the lumen of the air passages."

Virchow described the tubercle on the other hand as an organized structure, a neoplasm. It has a cellular structure, but is not vascular. It arises from the proliferation of pre-existing structures and is never an exudation. The larger tubercles are formed from the union of a number of small tubercles. These sharp, precise views of Virchow represent a great advance.

They were purely anatomical, and based on his studies of the histogenesis of pathological processes. His knowledge of microscopic structures enabled him to separate a new formation of tissue from an exudation. It was perfectly logical from such a study to make the distinctions which Virchow made. Laënnec's idea of the unity of the process was based on similarity of the gross appearances, and he was probably also influenced by his clinical knowledge of the disease, finding the same general clinical course in the various types of the lesions. There is no histogenetic unity of the tuberculous lesions, the only unity is the etiological one which was given by the work of Villemin and Koch.

3d. The infectiousness of the disease. Koch in his work on tuberculosis gives Klencke (1843) the credit for the discovery of its experimental transmission, but says he did not continue his experiments, and they were forgotten. Klencke's experiments on tuberculosis were undertaken in accordance with his idea that contagion was carried by pathological cells which have the power of generalizing an affection. He says he has been able to transmit cancer and melanosis, by intravenous injection of the cells, from man to the dog and cat. The tuberculous cells are capable of being transplanted in the same way. Tuberculous cells prepared by one of his assistants were introduced into the jugular vein of a rabbit, which when killed six weeks afterward showed extensive tuberculosis of the liver and of the lungs. The rabbit served to inoculate a crow, but without result. Although there is no doubt that Klencke did succeed in transmitting the disease, it in no way detracts from the credit of Villemin. Villemin (1865) showed that rabbits inoculated subcutaneously with tuberculous material from a man, from a cow, and from a rabbit became tuberculous. At the end of twenty to thirty days the animals began to emaciate and finally died in a state of extreme cachexia. The autopsies showed tuberculosis of the lymphatic ganglia and a formation of tubercles in the viscera and on the serous membranes. Cohnheim, in his celebrated address on tuberculosis, gives Villemin the credit of the discovery. He says: "At this time a discovery was made in France which not only marks an incomparable advance in the history of tuberculosis, but from which must date a complete change in the general conception of the process. There have been few discoveries which have so influenced medical thought as Villemin's proof of the transmission of tuberculosis. Wherever scientific work was carried on, head and hand were set in motion to repeat Villemin's experiments and to prove his views."