terations of it unless salicylic acid is the adulterant. He also warns against prescribing sulphate of quinine and iodide of potassium together, lest iodine should be set free in the intestinal canal.

There is not much to be said about the treatment of the toxic effects of quinine. Usually stopping the administration of the drug is soon followed by relief of the symptoms. When it is esteemed necessary to give the medicine, although unpleasant effects are already present or may be anticipated, several means of counteracting them are recommended. The bromides, and particularly hydrobromic acid, have quite a reputation, while Lewin and others have found ergotin, given in about equal doses with the quinine, efficient. Morrow and others recommend tincture of hyoscyamus. In dangerous cases in which there is collapse, the usual measures for stimulating the circulation by external applications and friction are in order, as well as the internal use of hot tea and coffee, and perhaps the subcutaneous injection of tincture of musk.

MacGregor favors subcutaneous saline injections in treating black-water fever. *J. Haven Emerson.*

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QUINOFORM. See *Formaldehyde.*

QUINOIDINE. See *Cinchona.*

QUINOLINE-BISMUTH-SULPHOCYANATE, or **RHODANATE.** See *Crurin.*

QUINOPYRIN is an aqueous solution of quinine hydrochloride and antipyrin. It is used by hypodermic injection as an antipyretic and nerve sedative in dose of 1 c.c. (ɱ xv.) several times a day. *W. A. Bastedo.*

QUINOSOL. See *Chinosol.*

RABIES OR HYDROPHOBIA.—Rabies or hydrophobia is an acute infectious disease of the central nervous system which occurs in man as well as in other warm-blooded animals. As a spontaneous disease, as distinguished from that due to intentional inoculation, it is met with in the dog and allied species, the wolf, the fox, the jackal, the hyena. Cats are also more or less often affected. Osler states that the disease is said to prevail among the skunks of the Western States of North America. So far, no species of animal except pigeons has been found to be refractory to intentional inoculation with the rabies virus. In these birds the older individuals are not normally susceptible, but they become so on the deprivation of food, and the young birds are normally susceptible.

From the many points of analogy which exists between rabies and other acute infectious diseases, the conclusion would seem unavoidable that rabies is caused by a specific micro-organism; but all efforts to establish this by experiment and observation have so far proven futile, though several unsubstantiated claims to this effect have been made, it is true. Although the specific infectious agent is not known, it can be propagated in the central nervous system of living animals, not of dead animals. By inoculation of animals it has been shown that the poison is always present, sooner or later after infection, in the brain, spinal cord, nerve trunks, and saliva of infected animals. It is present in these situations even before any symptoms have developed, during the incubation period, while the animal is apparently well. It is usually not present at any time in the milk, lachrymal secretion, pancreas, testicle or semen, aqueous humor of the eye, cerebrospinal fluid, or in the fœtus, though it has been found occasionally in one or other of these situations.

Accidental infection usually results from the bite of a mad dog, and therefore is due to the introduction of the saliva of the rabid animal into the wounds made by the teeth. Sometimes infection results from the licking of an abrasion by a pet dog that is going through the incubation period and before any symptoms of the disease have manifested themselves in the animal. For this reason mad dogs are specially dangerous while they are going through this stage. They are not suspected of being mad, and are not avoided as they are after the symptoms appear. Novi states that midges and flies are also capable of carrying the contagium. Artificially, as already stated, the disease may be produced by inoculating animals with tissues from an infected animal. Injection under the dura mater of suspensions of the spinal cord from an animal dead of rabies in neutral beef broth, is the method very commonly resorted to, and this produces the disease very uniformly. The point of the hypodermic needle is inserted beneath the dura mater through a small trephined opening at the summit of the cranium a little to one side of the median line. With aseptic precautions and with ordinary care in manipulation, there is no immediate danger to the animal from the operation itself, either as regards the effect of the trauma or from infection with pyogenic organisms. Occasional failures to produce the disease by the method just described have been reported, it is true, but the failure was probably due, at least in most of these cases, to the use of too small an amount of material for the injection. To insure success, the amount used must not be less than one-thirtieth of a gram by weight of the cord, according to Kruse, although even smaller amounts are usually effectual. Johne, Dawson, Oshida, and others recommend injecting suspensions of the cord through the optic foramen. If this method is resorted to it is recommended to anæsthetize the animal, or to keep it perfectly still by any method, otherwise there may result a fatal trauma of the brain. Oshida has successfully inoculated rabbits by using a long needle and passing this through the optic foramen, through the brain, up to the dura mater. Similar injections into the sciatic nerve or other large nerve trunks, or into the anterior chamber of the eye, are also usually successful. Intravenous injections are also usually successful in small animals, but not in large. The same is true of intraperitoneal injections. Subcutaneous injection is very uncertain. The reason that has been suggested for the frequent failure of subcutaneous injection is that by this method the virus is not brought in contact with an injured nerve, an essential condition for successful inoculation, according to this view. Those offering this explanation cite in support of their position the facts that the disease is more apt to follow from the bite of a mad dog if the injury is situated on the hands or face where the nerve supply is specially abundant; also that injections into nerve trunks, the brain, or the spinal cord, are uniformly successful, and less so in other situations, as has been said; and, finally, that deep lacerated wounds are particularly dangerous.

Whether the abundant nerve supply renders a part specially liable to infection or no, the danger of infection from bites on the hands and face is at least enhanced independently of this by the fact that these are usually bare, whereas the clothing over the rest of the body may prevent the infectious saliva from coming in contact with the wounds. On the other hand, it has been shown that application of the infectious material to the uninjured

conjunctiva, the uninjured genital mucous membrane, or to the uninjured alimentary mucous membrane may be followed by the disease; so it does not seem necessary for the nerves of a part to be injured, in all cases at least, unless we assume that where infection follows applications of the virus to the mucous membrane there are minute abrasions too small to be detected with the naked eye. But whatever the portal of entry, the disease develops only where the poison invades the central nervous system, and all observation goes to show that the course of the poison from the seat of infection to the brain and spinal cord is not through the blood or lymph channels, which are the distributors of the micro-organisms and toxins usually in other infectious diseases, but that the virus travels for the most part, if not exclusively, by way of the nerves themselves.

In rabies, as in other infectious diseases, there is always a period of incubation between infection and the appearance of the symptoms of the disease. This period of incubation varies in rabies not only in different species of animal, but also in different individuals of the same species. In dogs it lasts for from three to five weeks, seldom more, and seldom less. Bollinger states that in one case in a dog it lasted for eight months, and that is the maximum. In human beings the period of incubation varies greatly in length in different cases; from six weeks to two months is common, though cases have been reported in which the period of incubation is said to have lasted for one or even two years; but these long periods of incubation are certainly rare, if they occur at all. The disease usually shows itself in the course of the second month after the person has been bitten, rarely in less than fifteen days, more rarely still after three months or longer. In the rabbit the period of incubation is twelve to fourteen days when the animal is inoculated with cord from a mad dog, but it becomes shorter and shorter by successive inoculations of suspensions of the cord from one rabbit to another through a series—in other words, the virus becomes more and more virulent by successive passages through rabbits. This increase of virulence, however, cannot be carried on indefinitely, for there comes a time when further inoculations do not increase the virulence, and the virulence is then said to be fixed. Pasteur's "virus fixe" is obtained in this way, and consists of a portion of cord from a rabbit dead in nine or ten days of rabies. This explanation of what is meant by "virus fixe" should be carefully borne in mind in order to understand much of that which follows, for it will be necessary to use the term frequently. It may also be noted in passing that this "virus fixe" is made use of in the production of the "vaccines" for treating persons who have been bitten by a mad dog, as explained below. By the use of large rabbits the potency of the virus may be so increased by successive passages that the period of incubation finally will be six or seven days; and by the use of small Russian rabbits the period of incubation may be still further reduced to five or six days. Successive passages of the virus through apes, on the other hand, decreases the virulence, the period of incubation becomes longer. In ducks and geese the period of incubation is fourteen days. In chickens the disease has a period of incubation of forty days. Chickens, like pigeons, are partly refractory to rabies, as shown by Dr. Paul Gibier in 1884 (Thèse de Doctorat, Paris, 1884).

But the symptoms do not appear as soon as the rabies poison invades the brain and spinal cord, for these are infectious for other animals before any signs of the disease have shown themselves in an infected animal. Roux and his pupils, and others, have found that not only the medulla, but also the saliva of infected animals is infectious for other animals for from twenty-four to forty-eight hours—sometimes for three days—before any symptoms have developed. The different parts of the spinal cord become infectious for other animals at different times; the part nearest the seat of inoculation becomes infectious first, as a rule. Högyes found that the brains of rabbits inoculated under the dura mater are fully virulent in six days, as soon as the first characteristic symptoms appear, but that the medulla is fully virulent before this time, on the last part of the fourth or on the first part of the fifth day, at the beginning of the febrile symptoms. Vestea and Zigari and others found that after subdural inoculation the medulla becomes infectious for other animals several days before the lumbar cord. By inoculation into the sciatic nerve, on the other hand, the lumbar cord usually becomes infectious for other animals before the medulla. Nevertheless, this is not always the case, for Kraus, Clairmont, and Keller have shown that the medulla is sometimes infectious after inoculation into the sciatic nerve at a time when the lumbar cord is not infectious at all. This is not the rule, however, for usually the lumbar cord is infectious for other animals in six or seven days after inoculation of the "virus fixe" into the sciatic nerve, whereas the medulla does not usually become infectious by this time by similar inoculation. On the other hand, the medulla becomes infectious for other animals in one day after intracerebral inoculation with "virus fixe," and in three days, or even in a shorter time, after subdural inoculation with "virus fixe," less than half the time required by inoculation into the sciatic nerve for the poison to accumulate in the lumbar cord in sufficient amount to be infectious for other animals. Enough of the poison, however, gets into the lumbar cord in twenty-four hours after inoculation into the sciatic nerve finally to cause the disease in the infected animal, as explained more fully below.

Kraus, Keller, and Clairmont have furthermore shown that intracerebral injection of the "virus fixe" causes the development of the poison more quickly than the subdural injection. In intracerebral inoculation with "virus fixe" the poison is present in the medulla in twenty-four hours in sufficient amount to cause the disease on inoculation into other animals. In subdural inoculation, on the other hand, it is not certain that the medulla is ever infectious in as short a time as twenty-four hours after inoculation. It is true that rabbits inoculated with the medulla of rabbits taken out twenty-four hours after subdural inoculation usually die of gradual emaciation, a sort of marasmus, but they show no symptoms typical of rabies, and the medulla of these rabbits is not infectious.

Subdural inoculation, intra-orbital inoculation, and inoculation into a large nerve trunk, as into the sciatic nerve, all have about the same effect as regards the appearance of the poison in the spinal cord. In no case does the poison invade the entire nervous system all at once; on the contrary, there is always a more or less gradual extension along the course of the nerves or the spinal cord.

Kraus and his colleagues report one experiment in which the inoculation was made with "virus fixe" into the lumbar cord in a rabbit. The cord in this case was cut out twenty-four hours after inoculation, and different portions of it were inoculated under the dura of different rabbits. The results of these inoculations showed that the lumbar portion was typically virulent; the rabbit inoculated with this died of unmistakable rabies. The dorsal portion produced no symptoms. The medulla caused the death of the rabbit in fourteen days without any symptoms of rabies, it is true, but the medulla of this animal caused death in another rabbit in sixteen days with all the symptoms of rabies. The reason why the virus in its passage through the dorsal cord to the medulla from the seat of inoculation in the lumbar cord should not have found conditions for lodgment and development in the dorsal cord is not apparent. It would seem as if this observation shows that the medulla and lumbar cord have special affinity and attraction for the rabies virus. Some of the other observations mentioned above also seem to indicate that the most favorable situations for the development of the virus are, first, the medulla, and next to this the lumbar cord; and that the rest of the central nervous system becomes invaded only after these two locations have been fully impregnated.

The source of the rabies virus also affects the length of time of the development of the disease as well as the ac-

cumulation of the poison in the central nervous system. Tests upon animals show that the virus present in the cord of a dog suffering from an ordinary case of rabies, the "street rabies," takes longer to invade the nervous system and produce the disease than the "virus fixe," the virus obtained by successive passages through rabbits. This is shown not only in the difference between the period of incubation in the disease produced by inoculation with "virus fixe" on the one hand, and that produced by inoculation with the "street virus" on the other, but also by the fact that the cord of an animal inoculated with the "virus fixe" is infectious for other animals in a much shorter time after inoculation than is the cord of an animal inoculated with "street virus." It has been stated that the medulla of an animal inoculated under the dura with the "virus fixe" becomes virulent in two or three days after inoculation. The medulla of an animal inoculated under the dura with the "street virus," on the contrary, does not become virulent for other animals before the sixth day, and usually is not virulent before nine or ten days, and the lumbar cord is frequently not virulent at any time after inoculation with the "street virus." The reason for this difference between the "virus fixe" on the one hand, and the "street virus" on the other, is not apparent. The disease without proper treatment is just as surely fatal in the one case as in the other, and the symptoms in both seem to be of equal severity. The only difference seems to be that in the one case the poison is generated more quickly than in the other.

But, although, as has been stated, the lumbar cord does not contain enough of the rabies virus to be infectious for other animals for several days after inoculation into the sciatic nerve, enough of the poison gets to the cord in twenty-four hours by this method of inoculation to cause the disease in the animal itself; for Kraus and his co-workers inoculated a rabbit in the sciatic nerve with "virus fixe," and the animal died of typical rabies in spite of the fact that a portion of the sciatic nerve was excised at a point situated between the seat of inoculation and the cord. On the other hand, Bombicci prevented the disease from developing after intra-ocular inoculation by enucleation of the eye twenty-four hours after infection, and Babes and Talasescu also prevented the disease by cauterization of the seat of infection twenty-four hours after inoculation. But Babes has shown that even comparatively late cauterization or excision of the seat of infection delays the appearance of the symptoms, even if it does not prevent the disease, an important factor in the proper treatment of the disease, as will appear in the proper place.

The virulence of the virus may be destroyed, decreased, or increased in various ways. Light, temperatures of 50° to 60° C., drying, various antiseptics, and artificial digestion all weaken or destroy the virulence. Caterina found that formalin destroys the virus in fifteen minutes, but not in five or ten minutes. Putrefaction has but little or no effect on the virulence. The virulence is retained by preserving the infectious material in neutral glycerin and in the cold. Reference has already been made to the fact that successive inoculation through certain animals weakens the virulence for other animals, it even destroys the virulence in some cases, while similar inoculations through other animals increases the virulence. In other words, the rabies virus assumes a certain definite degree of virulence, which is different and characteristic for each species of animal; and the degree of virulence peculiar to a species of animal is attained by a sufficient number of successive passages through individuals of the species. If the virus used for the first inoculation in the series has a shorter period of incubation and kills more quickly than is normal for the species of animal under experiment, the subsequent inoculations of the series will take longer and longer to produce the symptoms and death till the normal degree of virulence for the species is reached. It does not appear from the literature at hand just how many passages are necessary to reduce the virulence in a given case, probably very few. On the other hand, if the virus used for the first inoculation has a period of incubation longer than is normal for the species under observation, it will have a shorter and shorter period of incubation after each passage till the norm is reached. The acquisition of a high degree of virulence is slow; starting with the virus from a mad dog, it takes a year or more to obtain virus of the highest degree of potency in the rabbit. The virulence of the virus is in inverse proportion to the length of the period of incubation. Thus, as has been already mentioned, the virus of rabbits is more virulent than that from dogs, because the period of incubation between the inoculation and the outbreak of the symptoms of the disease is shorter in the rabbit, after a series of inoculations in these animals, than it is in the dog under similar circumstances. The virus from the dog is more virulent than that from apes for the same reason, and while it is true that, starting with the virus from a dog, this becomes more and more virulent for rabbits by successive passages through these animals, a degree of virulence is finally reached beyond which it is impossible to increase the virulence. When the period of incubation is reduced to five or six days it is impossible to reduce this any further, the virulence becomes fixed. So that for each species of animal there appears to be a normal fixed period of incubation. And although increased virulence for the animal through which the virus is passed is usually accompanied by an increased virulence for other animals, it is not always so; for recent observations tend to show that the "virus fixe," the most virulent virus for rabbits, is decidedly less virulent for man. At least human beings inoculated with this virus do not develop rabies, in spite of the fact that they are not previously prepared by inoculations with attenuated virus. It is true that in the cases of this kind so far reported, the persons had been bitten by mad wolves, but it is not clear how this could diminish the action of the "virus fixe"; on the contrary, it would seem more probable that it would increase the action of the latter. After all, it would seem hardly correct to measure the virulence of rabies virus by its relation to the period of incubation on inoculation, for the virus from an ordinary case of spontaneous rabies in a dog causes the disease apparently with just the same certainty and with equal severity as the "virus fixe," only the period of incubation is longer with the former than with the latter. The disease, if not treated, is as surely fatal with the one kind of virus as with the other. Pigeons are not susceptible to rabies, but they become so by starvation, as already stated. In chickens the disease has a period of incubation of forty days, and it can be propagated by inoculation through a series of chickens. For these birds the period of incubation is just the same with the "virus of the street," from a case of spontaneous rabies in a dog, as it is with the "virus fixe." With either virus the disease progresses slowly after the appearance of the symptoms; the fowls usually live fourteen days after symptoms appear, and finally die of progressive paralysis. In ducks and geese the period of incubation is fourteen days. Inoculation of rabbits with the brain of birds dead of rabies is rarely followed by the disease; so while the virulence of the virus by successive passage through birds is preserved for these, it becomes weakened for rabbits.

Kraus and Maresch have studied the effect upon the rabies virus of blood serum of normal animals, and of blood serum of animals possessing artificial immunity. Their results show that the blood serum of ordinary non-immune dogs and rabbits has no effect upon the rabies virus; but the blood serum of dogs and rabbits that have been given artificial immunity destroys the virulence of the virus. Of this serum 0.01 c.c. destroys 0.5 c.c. of the "virus fixe" diluted in the proportion of one part of the virus to fifty of indifferent fluid. Pigeons' blood has no effect, neither the blood from normal pigeons, nor that from pigeons that have been previously inoculated with the virus. Chicken's blood serum, on the other hand, has the property of destroying the virulence of the virus. This property is possessed by the blood serum of ordinary, untreated chickens, and it does not seem to be increased by previously producing immunity in the chickens. The serum from a normal chicken destroys the virulence of the virus in the proportion of 0.5 c.c. of the serum to 1 c.c. of "virus fixe" diluted in the proportion of 1 part of "virus fixe" to 100 of indifferent fluid. A smaller amount of the serum, 0.25 c.c., does not destroy the virulence of 1 c.c. of the virus.

Högyes found by using dilutions of various concentration that all strengths above 1 to 200 of the usual thick suspension of the cord constituting "virus fixe" kill rabbits as promptly as the undiluted virus. Even 1 to 250 kills, but less promptly than the undiluted virus. A strength of only 1 to 5,000 occasionally produces death with prolonged incubation of the disease. Very feeble preparations, 1 to 10,000, fail to produce the disease.

During the period of incubation the individual suffers no special inconvenience, not more than would be caused by a wound of equal severity resulting from the bite of an animal that is not rabid. Indeed, it is stated by Tillmann that a wound inflicted by a rabid animal heals usually with exceptional rapidity in human beings; nor are there any other symptoms during the period of incubation to indicate whether the person has been bitten by a rabid animal or no. This lack of anything to characterize the period of incubation applies to rabies in beasts as well as in man.

In dogs the first symptoms of the disease consist of melancholia and moroseness, with restlessness and irritability, loss of appetite, dysphagia, and nausea. The dysphagia is specially noticeable in the case of liquids, and the name hydrophobia is given to the disease on this account. Abnormal appetite is also present; the animal endeavors to eat straw or dirt or anything lying around, no matter how unsuitable it may be as food. These symptoms may be insignificant at first, and for this reason the animal is more dangerous at this time than at a later period when the symptoms are more manifest. This stage lasts from a half day to two or three days, and is usually followed by the stage of raging madness. This, however, is not always the case, for sometimes the morose stage is followed by paralysis affecting the muscles of the jaws and later of the hindquarters. The lower jaw drops, the mouth remains wide open, the bark is peculiar and hoarse, there are also rapid emaciation, tottering, and final complete paralysis of the hindquarters, and the animal dies in two or three days. This form of the disease is spoken of as "dumb rabies," or as "quiet or melancholy rabies," and runs a more rapid course than the "raging madness." In the latter form of the disease the animal is sullen and morose as in the dumb form; there are also the same restlessness, loss of appetite, and emaciation, but in addition to this the animal has paroxysms of maniacal rage characterized by a desire to snap and bite at everything around. Bollinger states that the great aversion to water seen in the earlier stage of the disease is lacking in the maniacal stage, and in this stage there is only exceptionally spasm of the muscles of deglutition. The maniacal stage lasts for three or four days and then passes into the paralytic stage, which is the final stage as in dumb rabies, and lasts for from three to six days. In the paralytic stage the animal has a bristling coat, the voice is hoarse, dyspnœa increases, and there are local or general convulsions. The termination is always fatal.

In rabbits inoculated with unattenuated rabies virus, either "virus fixe" or virus from "street rabies," the disease always takes the form of "dumb rabies." But Genaro has described a peculiar form of the disease in rabbits inoculated with attenuated virus. In this form of the disease the animals die with progressive emaciation, without any of the ordinary symptoms of rabies, but the brain and spinal cord of these animals produce typical rabies when inoculated into other animals. An example of this form of the disease has been noted above in the citation from Kraus, Keller, and Clairmont's result with inoculation of a rabbit with the medulla of a rabbit taken out twenty-four hours after injection of "virus fixe" into the lumbar cord. It will be remembered also that these observers noticed that some of their rabbits died of a sort of marasmus after infection with attenuated cord, but that the cord in these cases was not infectious for other rabbits.

In the human subject the first symptoms to appear after the stage of incubation are psychical. The individual is depressed in spirits, excitable, irritable, and restless. He also suffers from sleeplessness and loss of appetite, and in some cases even at this stage there is antipathy toward liquids. He is also oppressed with a feeling of impending danger. The reflexes and sensibility are often greatly increased. A noise, even loud talking, and a bright light are distressing. The injection of the larynx and consequent difficulty of swallowing, which is the most distressing as well as the most characteristic symptom of the disease in man, is included in this stage by Osler. Tillmann regards this symptom as marking the onset of the second stage. Some authors note a rise of temperature and acceleration of pulse during this period, others not. Huskiness of the voice is also present, but this symptom depends upon the injection of the larynx, and is not always included in the prodromal stage. Although the wound is usually healed by this time, there is sometimes a return of inflammation in the cicatrix accompanied by pain, burning, and itching at this point. Pain in the bitten part is often the first manifestation of the disease and may be present several days before the onset of the other symptoms.

If the injection of the larynx with its accompanying manifestations is regarded as the beginning of the second stage, the prodromal stage seldom lasts more than twenty-four hours; for the injection of the larynx, with spasm of the muscles of deglutition and inability to swallow, appears rarely later than at this time. Along with these symptoms there appear severe spasms of the muscles of respiration. These occur in paroxysms along with the cramps of the pharynx, and are brought on by the slightest excitation of the nerves; even the sight of liquids is enough to cause them. The spasms are not confined to the larynx and respiration, but soon become general, and are usually clonic, sometimes tetanic. The nerves of special sense are also affected, not only the sight and hearing, as already noted, but also the sense of smell. The salivary secretion is also increased. The mind is for the most part clear, but there are apt to be maniacal seizures from time to time. The pulse becomes gradually weaker. After a paroxysm it is greatly accelerated. The temperature is somewhat elevated; it usually runs to 38° or 38.5° C. (100.4° to 101.3° F.). Dating from the laryngeal symptoms, the second stage lasts for from one to three days.

The third stage is marked by weakness, paralysis, and exhaustion. There is abatement of the spasms and of the difficulty in swallowing and breathing. This stage lasts for from six to eighteen hours, when death takes place, sometimes with recurrence of convulsions, but oftener quietly. By some authors consciousness is said to be preserved to the last, by others it is stated that unconsciousness supervenes.

The total duration of the disease in man, from the first appearance of the prodromal symptoms to death, is rarely less than two days or more than four days. The termination is always fatal if the symptoms once develop.

The macroscopic changes shown at autopsy are not characteristic either in man or in beasts. The blood shows insufficient aëration, is dark and thick. The mucous membranes show a catarrhal condition with hyperæmia and ecchymoses, specially pronounced in the mucous membranes of the respiratory and digestive tracts. There are general parenchymatous hyperæmia and cyanosis. In dogs the stomach usually contains various indigestible substances which the animal has swallowed to satisfy the abnormal appetite. Emaciation is also pronounced. But the most marked lesions are met with in the central nervous system. Besides extensive œdema of the brain, there are very considerable microscopic changes. These consist of diffuse myelitis of both white and gray matter, accompanied by degeneration of the nerve fibres and ganglia. The axis cylinders of the nerve fibres of the central ner-

vous system are hypertrophied. The nerve cells are atrophied and contain pigment. These changes are most marked in the motor centres. The most characteristic lesions, however, are seen in the cerebro-spinal ganglia, in which there is a proliferation of the endothelial capsule of the ganglion cells and a corresponding destruction of the latter cells (Van Gehuchten and Nelis).

The diagnosis of rabies presents no difficulty. It is true that the disease is simulated by tetanus arising from an infected wound in the regions supplied by the cranial nerves; then, besides, pharyngeal spasms are also a marked symptom of this affection. But the history of the injury would suffice in most cases for a diagnosis; this would be misleading only in case the tetanus bacilli are introduced into a wound caused by a dog bite, a contingency which is not at all probable. The different lengths of the periods of incubation of the two diseases also afford a point of differentiation. But the surest method of diagnosis is the inoculation of a rabbit under the dura mater with a bit of the cord or brain (rubbed up in bouillon or glycerin) of the animal that has inflicted the bite. If this animal was really affected with rabies, this inoculation would produce the disease in the rabbit in from twelve to twenty-one days. Consequently, if this step be taken promptly after the bite has been inflicted, there will still be time enough to prevent the development of the disease by a resort to the Pasteur method, to be described later. However, in cases of bites on the head or face, the treatment must be begun as soon as possible after the accident, and it would be very unwise to wait for the result of such an experiment. A diagnosis may be reached in twenty-four hours, if the dog died of rabies or was at least in the paralytic stage, by the method of Van Gehuchten and Nelis, *i.e.*, by the microscopical examination of some of the cerebro-spinal ganglia, especially the vagus ganglia which are easily found.

If facilities for inoculating a rabbit are not at hand, material from the animal should be sent for diagnosis to some convenient laboratory. It suffices fully for all purposes to send the medulla in a small vessel containing glycerin, as recommended by Kempner. This method not only possesses the advantage of great convenience, but the material arrives at the laboratory in good condition for inoculation, which is not always the case with the other methods of shipment that are recommended.

The disease can be cured, or, rather, prevented from developing, only during the incubation period, before any symptoms have developed; after this, the treatment is only palliative, and consists in keeping the patient as quiet and undisturbed as possible in a darkened room, and in the administration of quieting drugs. Curare is strongly advised by some, while by others it is not even mentioned in the list of suitable drugs. Chloral hydrate, potassium bromide, and similar drugs are also advised by some. Osler advises resorting to morphine hypodermatically and to the use of chloroform at the start. Dr. Rambaud reports that he has obtained the best results (experience of about thirty cases) from the employment of hyoscine hydrobromate in doses of gr. $\frac{1}{100}$ injected hypodermatically. Cocaine applied locally may be used to diminish the sensibility of the pharynx so as to enable the patient to take liquid nourishment where swallowing is otherwise impossible. Nutrient enemata are also recommended.

The disease may be prevented from developing by speedy excision, or by thorough cauterization with the actual cautery or the strong mineral acids, not with nitrate of silver. These are usually of no avail when not resorted to within a short time after the bite. But cauterization or excision would seem advisable, nevertheless, even several hours after the bite, for, as stated above, the absorption of the virus into the nervous system from the seat of inoculation is sometimes delayed as long as twenty-four hours. Moreover, as already stated, Babes has shown that even when the disease is not prevented in this way, the period of incubation is lengthened by excision or cauterization, a most desirable result when the Pasteur treatment is resorted to, as it should be, and indeed now universally is.

Although the disease is altogether beyond treatment after symptoms develop, and although cauterization and excision are uncertain, the Pasteur method of inoculation affords a means of prevention that very rarely fails. The principle of this treatment, or, rather the object aimed at, is the rapid production of immunity in the patient during the period of incubation of the disease. If immunity can be established before the termination of the period of incubation, before any symptoms have developed, the progress of infection is arrested. The method consists in inoculation once a day, for from fifteen to twenty-one days, with virus of graded potency. The virus employed consists of bits of the spinal cord of rabbits possessing such potency, by repeated passages through the central nervous system of these animals, that it produces death from rabies in nine or ten days in rabbits by subdural inoculation. As indicated on more than one occasion above, this constitutes the "virus fixe" of Pasteur. The graded potency which is required if the virus is to be used upon human beings, is obtained in the following manner: The spinal cord of a rabbit that has died of rabies on the ninth or tenth day after inoculation is carefully removed and hung up in a flask, at the bottom of which are placed a few pieces of caustic potash. Protection against dust, etc., is secured by stuffing sterilized cotton into the neck of the flask which is kept in a dark room, at a constant temperature. In this way the cord is subjected to a slowly advancing process of desiccation, as a result of which the rabies virus is rendered progressively less virulent. On the day following that on which the cord was introduced into the flask, it is spoken of as cord of the second day, or No. 2. On the third day it becomes cord No. 3; and so on up to the fourteenth day. After the fourteenth day what remains of it, if not entirely used, is discarded. It is customary, at the Pasteur Institute in Paris, to use for the first injection an emulsion made from portions of the cord of both the fourteenth and the thirteenth days. In the New York Pasteur Institute, however, the first injection contains portions of the cord of the twelfth and eleventh days. An emulsion is made by rubbing up a segment of cord measuring 0.5 cm. in length in 6 c.c. of normal salt solution (sterilized) for one patient. Two separate injections are made simultaneously, one in the right and the other in the left hypochondriac region. Each succeeding couple of injections is made with a stronger emulsion, that is, with an emulsion made from a segment of the cord that has been subjected to one day less of drying than the preceding one. The most virulent cord used in Paris is that of the third day; in New York, that of the second day. The time for using this is reached somewhere between the seventh and the tenth days, and then a return is made to the cord of the sixth or fifth day, after which a gradual increase is again made until cord of the third or second day is reached. But if the treatment has been deferred, for any reason, so long that there is danger of the disease developing before the entire series of injections can be administered one day apart, the interval between the injections is shortened, and two or more injections of increasing strength are given daily instead of one each day for the first three or four days. Finally, when the case comes for treatment very late, and the necessity for such treatment is therefore urgent, it is maintained by some that all the twelve or thirteen injections should be administered in twenty-four hours, or that the preliminary injections should even be dispensed with entirely, and virus of full potency administered at the start. The procedure mentioned last, the use of unattenuated "virus fixe" without any preliminary inoculation with attenuated virus, has been practised with good results in cases of persons bitten by wolves, the most dangerous of all forms of infection. This procedure, however, is condemned by the Pasteur Institute in Paris as well as by the New York Institute, as it has caused several deaths.

Babes has advanced the theory that the reason why the

"virus fixe" does not itself produce the disease in man is that the injections are always made under the skin of the abdomen where it is not likely, owing to the presence of abundant adipose tissue, that any nerves are injured. But Marx is quoted by Babes as authority for the view that the virus becomes attenuated for human beings and for monkeys by being passed through rabbits, although enhanced in virulence for rabbits themselves.

The writer desires to acknowledge his indebtedness to Dr. George G. Rambaud, of the New York Pasteur Institute, for assistance kindly rendered in revising that portion of the text which relates to preventive treatment.

B. Meade Bolton.

RACHISCHISIS. See *Spina Bifida.*

RACHITIS.—See *Rickets.*

RAG-WEED.—Ambrosia. *Ambrosia* is a genus of the Compositæ, containing about a dozen species, mostly North American. The best-known species is *A. artemisiifolia* L., the common annual rag-weed, and one of the most abundant and troublesome of weeds. It is best known to medicine because the presence of the pollen in the nares is believed to be the principal cause or occasion of the disease hay fever. This and other species contain small amounts of amaroid and volatile oil, and have been employed, especially in domestic practice, as aromatic bitters. The idea that a preparation of rag-weed can act as a specific in hay fever is in the highest degree fanciful.

Henry H. Rusby.

RAILWAY MEDICINE AND SURGERY.—While, as a matter of course, passengers and employees have been killed and injured ever since the inception of railways, and railway surgeons have been known over fifty years (Dr. W. W. Apply was appointed surgeon for the Erie R. R. in 1849), the recognition of railway surgery as a special branch of the healing art is a matter of the last twenty years, and has reached its highest degree of development in the Western United States. It seems as fully entitled to recognition as military surgery, with which it has many features in common.

Prior to the War of the Rebellion, the mileage was mostly east of the Mississippi; skilled assistance being as a rule easily obtainable, there was little demand for systematic surgical service such as is now met with. Even at the present day in the Eastern States, where railways traverse thickly populated communities, the stations are almost in sight of each other, and cities and towns with well-appointed hospitals occur at frequent intervals. In the extreme Western States, however, perhaps several hundred miles of unsettled or sparsely inhabited territory may intervene between the locations of properly equipped hospitals. Hence during the building of the great transcontinental lines, provision had to be made for the care of employees injured during the construction of the road, all of them away from their homes and in uninhabited districts. In many instances this hospital department became a permanent feature after the roads commenced operation.

Except for the fact that it will have a larger proportion of emergency cases, the practice of the railway surgeon will not differ materially from that of his surgical brethren in general. The injuries with which he has to deal are very similar to the severe crushing injuries from machinery or heavy vulnerating bodies in ordinary surgical practice. They, however, present some special features. Thus, for example, owing to the fact that the extremities often become engaged between two unyielding surfaces—the rail and the flange of the car-wheel,—these railroad injuries are often extremely severe in character, with great destruction and laceration of the soft parts, and comminution of bones. Again, they are attended by a high degree of mortality, and their effect on the nervous system is overwhelming, shock being especially noticeable in this class of injuries. In addition to the crushing force, there should be taken into account the weight and velocity of the moving train. The weight varies from ten tons for empty flat cars to twelve or fifteen for box cars; from twenty to sixty for coaches; and it amounts to one hundred tons or more for locomotives. The railway surgeon often has to exert his skill under the most unfavorable circumstances and the most depressing surroundings, laboring at night with no light but the trainmen's lanterns, far from skilled assistance or even habitations, and amid rain, sleet, and snow.

The present mileage of steam roads in the United States is over 200,000, on which over 600,000,000 passengers were carried last year (1901–02). To operate this system required in 1895 an army of 785,000 men; in 1901 this number had grown to 1,071,000. In the Middle Atlantic States the number of employees per one hundred miles is 1,140; next come the New England States with 827; and so on, the lowest being the Middle Northwestern States with 303. For the year ending June 30th, 1902, the total number of casualties to passengers and employees reported was 42,619 (2,819 killed; 39,800 injured). Passengers killed, 303; injured, 6,089; employees killed, 2,516; injured, 33,711. (Report of Interstate Commerce Commission.)

As regards the different classes of employees, brakemen are injured most frequently, then come switchmen, firemen, and engineers in the order named. In former years the largest number of injuries resulted from coupling and uncoupling cars. In 1893 the "Safety Appliance" law was enacted, requiring the use of automatic couplers. This law went into full effect in August, 1900, and the results from this humane legislation are both surprising and gratifying. The number of employees killed in 1902 as compared with 1893 is sixty-eight per cent. less, and the diminution in the number of those injured is no less than eighty-one per cent., notwithstanding the much larger number of employees. Other frequent sources of accidents to trainmen are getting on or off trains in motion, falling from the cars, collisions, and derailment. The principal causes of accidents to passengers are collisions, derailment, and falls from the cars. According to Herrick, about fifty per cent. of injuries to employees involve the upper extremity, thirty-three per cent. the lower extremity, twelve per cent. the head and face, and eight per cent. the trunk.

To furnish relief for sick and injured employees there are four principal methods in operation at present: (1) the relief system; (2) the surgical service without a chief surgeon; (3) the surgical service with a chief surgeon; (4) the hospital system.

1. The relief system is in operation on a number of roads, among them the Baltimore & Ohio, Pennsylvania, Reading, Burlington, and Plant System. Membership may be either voluntary or compulsory. Under this plan the employee is assessed monthly according to the amount of his wages—usually from twenty-five cents to two dollars. When injured, he receives a certain sum monthly during this period of disability. Provision is also made for death, and for benefits in case of permanent disability. In some associations membership lapses if the employee quits the service of the company, in others the death benefits may be retained. In others again, additional features are found in the shape of savings, building and loan departments, and old-age pensions. The scope of such a system on a large trunk line may be gleaned from the last annual report of the one in operation on the Pennsylvania west of Pittsburg. The membership was 23,179, an increase of 2,122. The average number of members disabled per day was 778, or 35 for each 1,000. The death rate was 13 for each 1,000. Applications for membership were 11,010, while the cessations of membership were 8,868, of this number 8,090 having left the service. The total receipts for the year were $415,643, the disbursements $349,104.

2. The local surgeons are appointed by the superintendent or general manager. Local surgeons are generally located at divisional or terminal points, and along the remainder of the route,—as a rule, about fifty miles apart.

3. A chief surgeon is appointed who selects his own