textiles which will not be damaged thereby should be subjected to live steam for a period of thirty minutes; and such as will not bear this treatment should be disinfected by the conjoint use of a vacuum and formaldehyde gas, six per cent. volume, for an exposure of one hour's duration. All textiles which have been polluted by cholera dejecta should without exception be burned, and no attempt should be made to disinfect and re-use such articles. The detained *personnel* may be released when five days have elapsed since their last possible exposure to infection.

Plague.—Measures to be taken in the treatment of a vessel infected with plague are identical with those used in the case of a cholera-infected ship, except that on account of the peculiar methods of transmission of this disease (partly through small animals), it is necessary to use a germicidal agent which will destroy animal life as well as bacteria; and for this purpose formaldehyde is not strictly reliable; consequently, all gaseous disinfection done on a plague-infected vessel must and should be done with sulphur dioxide. The segregation and careful attention to the individuals, including the adoption of stringent measures capable of preventing the pollution of either dejecta or sewage, apply to this disease as strongly as to cholera; and for the reason that small insect life has a bearing in the transmission of the disease, the screening provided for cholera and yellow fever, while not so absolutely essential, is nevertheless advisable, and, wherever possible, should be used. Manifestly the persons under detention may be released at the expiration of from seven to eight days since their last possible exposure to infection.

Smallpox.—Here we have to deal with a disease which does not require such rigid measures as have been applied to any of the other quarantinable diseases. If a person in any given apartment of a vessel has been afflicted with smallpox, it does not necessarily follow that all the persons on the vessel are to be detained in quarantine, nor that the whole ship is to be disinfected. It will be sufficient if we disinfect with scrupulous care all possibly infected personal belongings, and, in the same manner as is applied for yellow fever, all portions of the vessel which have been invaded by the disease. At the same time it is important to keep under observation those persons who have been in direct contact with the afflicted party, or who have not been vaccinated. The usual custom is to vaccinate immediately all exposed persons and hold them under observation for fourteen days; to release at once all those who have not been exposed and who are vaccinated; and to disinfect such parts of the vessel as have been in touch with the actual case, releasing the vessel at once, and holding only the suspects. Should the infection on the smallpox vessel be so general as to justify the opinion that all on the vessel have been more or less exposed, then it becomes necessary to disinfect the vessel in the same manner in which it would be done for yellow fever, and to disinfect it throughout, holding under observation for fourteen days all of its *personnel*.

Typhus Fever.—In view of the little that is known of typhus fever, *i.e.*, as to its manner of transmission, period of incubation, etc., it is exceedingly fortunate that we seldom or never find a general infection of typhus fever aboard ship. Should such a calamity supervene, all the *personnel* should be immediately segregated ashore, and the groups placed far enough apart, if sufficient ground is obtainable, to prevent the infection of one by the other, it having been claimed that aerial infection plays a part in this disease. The vessel should be disinfected in the same manner as for cholera, and the *personnel* kept under observation for a period of fourteen days from their last exposure to possible infection.

Leprosy.—The quarantine regulations of the United States demand the retention at quarantine of any alien leper, and his replacement upon the vessel when outward bound.

Minor Communicable Diseases.—There are, in addition to the diseases above discussed, several others which at times call for treatment, but which are not generally classed as quarantinable diseases. These diseases—scarlet fever, measles, diphtheria, and even some others—are as a rule passed up to the local board of health for proper handling.

When treated at quarantine, they call for the same measures as are applied to smallpox (except of course vaccination).

Land Quarantine.

Because of lack of space only brief notice can be given this subject, which after all is simply a common-sense application of maritime rules to exactly the same diseases on land. The people are to be handled in precisely the same manner as at a maritime station, and if we simply transfer our disinfecting agents from a ship to a house, the methods remain the same. The difficulties of administration are greater because, while at a maritime station the quarantine officer is practically supreme, in land quarantine he has to meet the whims and foibles of local lay authority, or even of individuals.

Joseph H. White.

QUASSIA.—*Quassiæ lignum* or *Lignum Quassiæ. Jamaica Quassia, Bitter-wood, Bitter-ash.* The dried wood of *Picrasma excelsa* (Swz.) Planch (*Quassia e.* Swz.; *Picræna e.* Lindl.; *Simaruba e.* DeC.—Fam., *Simarubaceæ*), U. S. P.

The Jamaica quassia tree is said closely to resemble a small or medium-sized ash tree. It occurs chiefly in Jamaica, but to some extent in other parts of the West Indies. Quassia was originally derived from a different plant, considered below, but was later replaced by this one. The wood occurs in billets of various sizes, dense, tough, of medium hardness, and of a nearly uniform yellowish-white color; internally porous, with a minute pith, indistinct rings, and medullary rays which, on tangential section, exhibit from two to five vertical rows of cells; inodorous and intensely bitter.

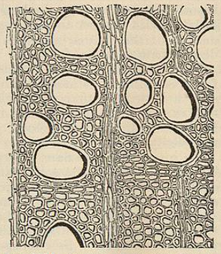

Fig. 3224.—Section of Quassia Wood. (Baillon.)

It is usually met with in the form of chips or raspings.

The powdered wood is devoid of stone cells, contains crystals of calcium oxalate, and exhibits the tangential appearance of the medullary rays described above.

Quassia contains neither tannin nor starch, and, if pure, yields not more than four per cent. of ash. Its bitter principle is the crystalline substance *quassiin*, freely soluble in alcohol and chlorofom. Although it requires 1,200 parts of water for solution, the dose is so very small that water constitutes a satisfactory menstruum. Quassiin is further resolvable into two crystalline bodies, called respectively *α-picrasmin* and *β-picrasmin*. A minute amount of alkaloid has been reported, but is probably of no medicinal importance.

Action and Uses.—Quassia is generally regarded as a pure or simple bitter tonic, like gentian, and is mostly used as such, being given, either alone or in combination with aromatics and stimulants, as a stomachic and appetizer. In debility, in convalescence from fevers, in dyspepsia, it has been, and is still, in considerable use. Its taste is, however, more bitter and disagreeable than that of gentian or quinine.

Quassiin is a powerful irritant and convulsive poison when concentrated or used in overdoses, and is apt after long administration to set up a gastric irritation. Its use is therefore better alternated with that of other medicines.

It is particularly poisonous to the lower animals, on account of which it is much used as a rectal injection for the destruction of ascarides. For the latter purpose, from a half-pint to a pint of the ten-per-cent. infusion is employed. The death of an infant has followed such use. The freedom of quassia from tannin renders it a desirable bitter for mixing, in prescription, with the iron preparations. The Pharmacopœia provides an extract (*Extractum Quassiæ*), the dose of which is 0.03–0.2 gm. (gr. ss.–iij.), but this is the least desirable preparation for use, since the patient fails to receive the beneficial effect of the bitter taste. The dose of the official fluid extract is 1–4 c.c. (fl. ʒ ¼–i.) and of the tincture, which is by far the most efficient of all preparations, 2–8 c.c. (fl. ʒ ss.–ij.). The infusion is a popular form of administration, and should be of five-per-cent. strength. Another excellent method is to introduce cold water into cups made of quassia wood. The water becomes almost at once intensely bitter, the patient receiving the full benefit of the bitter taste, with little systemic effect.

Surinam Quassia.—This, the original quassia, is still the one chiefly employed in Southern Europe, and is official in nearly all pharmacopœias. It is the product of *Quassia amara* L., of the same family, a shrub or small tree of Northern South America, whence it extends up into Central America and into the West Indies. The billets are much smaller, usually from one to three inches in diameter, crooked, and still bearing the bark, which is of an ashy gray color and nearly smooth. The wood is somewhat heavier than that of the Jamaica variety, and exhibits medullary rays only one row of cells wide on tangential section. The bark is full of large stone cells, which are seen in the powder, since bark and wood are usually ground together. The active principle of this variety is practically identical with that of the other, and the properties, uses, and doses are the same.

The same statements may be made concerning East Indian quassia and Japanese quassia, derived from other species of *Picrasma*.

Henry H. Rusby.

QUEBRACHINOFORM. See *Formaldehyde.*

QUEENS ROOT. See *Stillingia.*

QUERCIFORM. See *Formaldehyde.*

QUINAMINE. See *Cinchona.*

QUINCE SEED.—*Cydonium* (U. S. P., 1880).—The dried ripe seeds of the common quince, *Cydonia Cydonia* (L.) Lyons (*Pyrus Cydonia* L.; *Cydonia vulgaris* Pers. fam. *Rosaceæ*) together with the gum in which they are naturally embedded.

The quince is a native of Southwestern Asia and adjacent Europe, but the seeds are wholly the product of cultivated plants. They occur agglutinated in masses of eight to ten or more, being embedded in a colorless, transparent gum, of which about twenty per cent. is obtainable, and for which they are valued. One part of this gum makes about 100 parts of mucilage. This has little adhesive power, but is excellent for the ordinary medicinal uses of mucilage, such as the making of collyria, demulcent drinks, etc. When the drug was official, it was directed that the official mucilage be made by taking 2 parts of the seeds with 98 parts of water.

Henry H. Rusby.

QUINETUM. See *Cinchona.*

QUINIDINE. See *Cinchona.*

QUININE. See *Cinchona.*

QUININE, NEW COMPOUNDS OF.—In the following preparations, the dose, unless specified, is that of quinine sulphate.

Acetyl-salicylate—for rheumatism.

Arsenite—sixty-nine per cent. quinine. Dose 0.005–0.03 gm. (gr. $\frac{1}{12}$ to gr. ss.).

Bichloride—very soluble. Improvement in recurrent cancer followed daily injections of 0.5–1 gm. (gr. viij.–xv.) by Jaboulay in France and Trible in America.

Borate—a yellow insoluble powder, antiseptic.

Caseinate.

Chloro-carbonate—freely soluble, almost free from bitter taste.

Chloro-phosphate—fifty per cent. quinine; soluble in two parts of water.

Chloro-sulphate—seventy-four per cent. quinine; soluble in one part of water.

Dibromguaiacolate—guaiaquinol.

Dihydrobromate, dihydrochloride, dihydroiodate—all readily soluble and used by hypodermic injection for whooping-cough. Dose, 0.06–0.2 gm. (gr. i.–iij.).

Dihydrochloride-carbamate—muriate of quinine and urea. Seventy per cent. quinine; very soluble.

Ethyl carbonic ester—Euquinine (see Vol. IV.).

Ferri-chlorid—dark reddish-brown crystals used in two-per-cent. solution as a hæmostatic in internal hemorrhage and in uterine hemorrhage.

Glycerophosphate — kinewin, especially employed in neuralgia. Dose, 0.1 gm. (gr. iss.).

Guaiacol bisulfonate—guaiaquin, an odorless, non-caustic substitute for guaiacol.

Hydroquinone-hydrochloride—antipyretic.

Ichthyol-sulfonate—sulpho-ichthyolate, employed in tuberculosis.

Iodo-hydroiodate—insoluble in water. Used as substitute for iodides in syphilis, and in the same dosage.

Lactate—readily soluble.

Lygosinate—antiseptic compound of di-ortho-cumarketone (lygosin).

Methyl-di-hydrazin-perchlorate—compound of quinine hydrochlorate, caffeine, and antipyrin.

Phospho-hydrochloride—soluble.

Phosphoric acid ester—phosphorylquinine.

Salicylic acid ester—salicyl quinine or saloquinine (see *Saloquinine*).

Salicyl-salicylate—(see *Rheumatin*).

Silico-fluoride—soluble in water.

Sulpho-creosotate—used in tuberculosis.

Urethane—very soluble, made by mixing 3 parts of quinine hydrochloride, 1.5 parts of urethane, and 3 parts of water.

W. A. Bastedo.

QUININE. (TOXICOLOGICAL.)—Any high degree of toxicity can hardly be said to exist in the ordinary use of cinchona and its alkaloids or their salts. There are certainly symptoms very commonly associated with their therapeutic uses, even in most moderate doses, which are characteristic and indicate some functional disturbance of various organs. Such are the sense of constriction about the forehead, the ringing of the ears, and occasionally nausea. In many persons these are not sufficiently marked to attract attention unless the doses given are very large or long continued. Of these the sense of fulness and the deafness are the commonest, and are looked upon as necessary accompaniments of the administration of the drug, not giving rise to uneasiness either in the patient's or in the physician's mind, and expected to disappear promptly when the medication is stopped. They are the physiological evidence of mild cinchonism. The susceptibility of individuals varies greatly as to the amount of the drug which will produce such manifestations. Some persons are occasionally met with who suffer so promptly and acutely from these troubles that treatment to counteract them has to be instituted in order that enough of the required drug may be taken into the system to produce the desired effect upon the primary disease. Many, on the other hand, show so little susceptibility that astonishingly large and rapidly repeated doses may be given with only beneficial results.

Liebermeister (quoted by Kunkel) says: "I have up to this time employed quinine in large doses in more than fifteen hundred patients with abdominal typhus, and also in hundreds of pneumonias and other diseases. The number of single doses, of from 1 to 2, up to 3 gm.,

which I have prescribed, may run up to ten thousand, and not once have I seen any essential or lasting injury which one might seem warranted in ascribing to quinine." The cause of the disturbances produced by quinine has not yet found a satisfactory explanation.

Notwithstanding the infrequency of toxic manifestations from the use of quinine, a large number of cases can be found in the periodical literature of the last half-century, some of an acute character after minimum doses, and some in which the most inordinate quantities have been taken. It is these latter which present the most serious symptoms, and are even followed by death. The former must be regarded as due to an idiosyncrasy, which also is not infrequently hereditary, while the latter may properly be classified as cases of poisoning, whatever the action of the drug or whatever organs are specially involved. There is still another class of cases, viz., those in which quinine, given in very moderate doses, especially in certain tropical districts of Africa, to persons who are already the subjects of malarial dyscrasia, quite promptly causes a sharp advance in temperature accompanied by hæmoglobinuria—the Schwarzwasserfieber of German writers. The following may serve as illustrations:

Hare reports the case of a man of fifty-three for whom two grains of quinine, three times a day, was prescribed. It produced an intense erythematous rash, which was subsequently followed by desquamation, including the palms of the hands and soles of the feet. On learning that quinine was contained in the medicine prescribed for him, he said that he had once before had the same experience, an eruption having developed after he had taken a cocktail containing a few drops of elixir of calisaya. This man's daughter, twenty years of age, also suffered from a rose rash followed by desquamation after taking a small dose of quinine.

Husemann reports the case of a soldier in good health who took 12 gm. of sulphate of quinine in a five-per-cent. solution. He died in four hours in an access of heart weakness. A third report is by Guersant. A French physician in a rural district was in the midst of an outbreak of malarial fever. When his wife was taken ill he gave her 240 grains of quinine in the course of a short time, and she fell into a state of stupor with amaurosis, deafness, and difficulty of moving, whereupon he gave her 375 grains more, and the serious symptoms increased. Fortunately for her he was about this time taken ill with the fever himself, and she finally recovered. He administered to himself, however, 900 grains by mouth and rectum, which brought him to a condition resembling that of a man affected with pneumonia terminating in hepatization; but he managed to take in the course of eight or nine days five ounces more of quinine. When at last he came under the observation of another physician he was in a cold sweat, deaf, blind, his respiration difficult and rattling, and in a profound stupor, looking like a drunken man. Delirium and death soon closed the scene.

I. B. Yeo reports his own experience as follows: Fearing that he had taken cold, he administered to himself two doses of two or three grains each of quinine. The next morning he found upon his legs an erythema with much itching, which faded in three or four days. He repeated this experience twice at intervals of two months, the last time taking three grains and the rash appearing in a few hours. Five months later, imagining that the former doses might have contained some impurity, he took pains to get the sulphate of quinine from a druggist of the best repute, and the usual eruption in three and a half hours followed the taking of three grains. Six weeks later, a dose of one fourth of a grain, directly after breakfast, was followed by the rash in five hours.

Not to burden this paper with the details of the action of quinine in disturbance of all the various organs, it will suffice to mention those of special interest and importance, whether such toxic effect is manifested after the introduction into the system of such quantities as would everywhere be considered large if not excessive, or of such minute doses that their poisonous activity is the evidence of an individual idiosyncrasy. Of these the most prominent are the effects upon the skin, upon the eyesight and hearing, upon the kidneys, and upon the pregnant uterus. Some reference should also be made to effects upon the general nervous system.

Cutaneous disorders may arise from the local irritating action of quinine when the skin is denuded, according to Hugounenq, and it has frequently been observed that the operatives in quinine factories suffer from similar local troubles, with also a certain amount of constitutional disturbance, even when the skin is sound.

Authorities differ in their views of the pathogenesis of these eruptions, Lewin saying that no absorption of quinine takes place through the sound skin, and that the eruption occurring in quinine workers is not to be regarded as an occupation disease, but as an idiosyncrasy against quinine, which seems not a very tenable theory in view of the frequency with which such cases occur. He says also on the next page that it is the direct contact of the quinine with the skin, its excretion through the medium of the sweat glands, among other like possibilities, which chiefly furnishes the explanation of this irritation rather than a disturbance of the stomach or bowels producing a reflex irritation of the skin or any action of the drug in solution in the blood acting upon trophic or vaso-motor nerve tissues.

Morrow considers that the theory of the stimulation of the sensory nerves of the gastric mucous membrane, producing reflex dilatation of the cutaneous vessels, is applicable to only the milder and superficial forms of eruption. He also refers to the theory of an elective affinity of the sweat glands for the drug, its attempted elimination through this channel causing local irritation. He says that the toxic action of quinine upon the skin may result from electrolytic action, from its use in pomades or lotions, and from subcutaneous injection as well as from ingestion of the drug.

Writers report many forms of quinine eruption, although that resembling scarlatina is the commonest and most important from the point of view of diagnosis. It is most apt to follow the taking of sulphate of quinine rather than other preparations.

Thus there is pruritus, which is often limited to certain regions, such as the glans penis, the hands, or the legs. Erysipelatous and gangrenous forms are reported, although the latter is very rare. The urticarial form is wont to be accompanied with much constitutional disturbance. Hyde and Montgomery remark that it is hardly to be distinguished from an *urticaria ab ingestis*. The mucous membrane of the throat and fauces may be involved in this form. Eczematous and bullous forms are mentioned, and finally the petechial, which may be accompanied by bleeding from the buccal mucous membrane or by sanguinolent stools, sometimes following very small doses of the drug. Desquamation of greater or less extent is a not infrequent sequela of these various forms of eruption. In the matter of differential diagnosis the greatest interest attaches to the exanthematous form from its likeness to scarlatina. The eruption is of a vivid hue and disappears under pressure. The history of the case, as to whether quinine has been given or not, is of the utmost importance, and Morrow points out that there is usually no fever, and that the eruption subsides when the drug is discontinued. Quinine can also be easily detected in the urine.

With reference to the effects of quinine upon the sight and hearing it is observed that they are wont to be more persistent than other toxic effects of the drug, lasting often for years or permanently, while the others disappear on its discontinuance. The symptoms of its injurious action on the eye are increased lachrymation, itching and œdema of the lids, photophobia (which may be only transient, but may persist), diminished or lost pupillary reaction, and sometimes complete but usually temporary loss of sight, either in one or in both eyes. But the most typical and persistent lesion is concentric limitation of the visual field, which may exist even though the acuity of vision is little impaired, and which may be demonstrable even when the acuity of vision is completely restored. At the same time there may be a diminished sense of light, as if a veil were interposed. There may also be color blindness, which but slowly disappears. The changes appreciable by the ophthalmoscope are in the papilla of the optic nerve and the vessels of the retina, the media remaining clear. There is a high degree of constriction of all the vessels, tending to atrophy, and the optic nerve is pale (Lewin and Kunkel).

Quinine given in even very moderate doses generally causes some hardness of hearing with tinnitus or roaring in the ears. There may even be complete deafness lasting for twelve or twenty-four hours. Existing middle-ear disease may be exacerbated or an otitis externa may develop. Under these conditions may be observed a slight injection of the vessels of the handle of the malleus and some degree of opacity and retraction of the membrana tympani.

It has been observed that what has been called quinine fever sometimes supervenes upon the administration of small doses of the drug in persons who are the subjects of malarial infection, the symptoms consisting in the rather prompt appearance of chill, fever, and sweating, with sometimes disorders of the alimentary canal and bloody urine. No satisfactory explanation has been offered for these manifestations. When it is added that to quinine is attributed an occasional irritation of the urinary passages leading to albuminuria, and that sometimes the urine also contains blood, hæmoglobin, and methæmoglobin, we are very near to the condition known under the German name of Schwarzwasserfieber (black-water fever), which Kunkel describes as follows: "This is a disease of the African tropics, and is so far directly associated with malarial infection that it occurs only in men who have been infected with malarial virus. They are apt to be only apparently in good health, or have a malarial dyscrasia. There is always a chill, followed by nausea, intractable vomiting, and other signs of severe constitutional disturbance, such as diarrhœa, dulness of mind, restlessness, dyspnœa, and irregular febrile movement, as in cases of septic infection. There are indications of serious blood decomposition. The urine is of a dark reddish-black color, and contains pigment granules, renal epithelium, and casts, but no erythrocytes. The symptoms of acute nephritis are always present. The prognosis is bad and death follows with signs of heart failure or of uræmia. In cases that do not succumb kidney lesions remain, and after the seizure the blood corpuscles and hæmoglobin are enormously diminished."

Kunkel enters quite extensively into the discussion of this subject, and cites many authorities who furnish good evidence that in the course of malarial disease, when quinine has not been given, attacks of hæmoglobinuria occur, and that they seem to occur most often in regions where the local perniciousness of the disease is greatest. Thus they occur in Greece more than in Germany, and in Africa more than in India.

Again, in cases in which small doses of quinine are given to the subjects of malarial infection, but who are not seriously ill at the time, bloody urine will quite promptly appear. Thus good authorities agree that in certain persons saturated with malaria the blood corpuscles become very sensitive to the action of quinine and readily break down. The question also comes up, in this connection, regarding the similar action of chlorate of potash, of carbolic acid, and of arseniuretted hydrogen as blood poisons. There seems good evidence also that not only are small doses of quinine not curative in these conditions, but that they excite the disease, which can be cured by large doses only, 4 gm. for example. Welsford, however, is of the opinion that black-water fever is a localized disease, and that some malarious districts in Africa are free from it; also that quinine certainly does cause hæmoglobinuria, but only rarely. He reports a case in which two ten-grain doses on two occasions induced black urine.

The action of quinine as an ecbolic is based on the occasional occurrence of abortion in malarial districts after this drug has been given. It is also reported that in China it is depended on to produce abortion, and that female operatives in quinine factories frequently abort. There is by no means an agreement of good authorities on this subject, however, and the best opinion favors the belief that this action is occasional rather than regular, and should be regarded as an incidental or by-effect rather than an evidence of toxicity.

It remains to consider the poisonous action of quinine upon the central nervous system. It is by no means easy to discriminate between the effects of quinine itself and those due to the disease for which it is given, especially as in severe cases, like pneumonia, intermittent and continued fevers, where large doses might probably be used, the disease itself might present such symptoms as headache, sleeplessness, and a state of collapse with loss of consciousness, delirium, or even tetanic or convulsive manifestations, such as are said to be due to the action of the drug upon the nervous system. Therefore cases illustrative of these effects are the unusual ones in which great quantities of quinine have been rapidly taken into the system when not called for by the existing disease, or far beyond its requirements, such as some already cited in this article, or the following, reported by A. E. Roberts:

"A woman, aged thirty-five, took about 20 gm. of quinine, became insensible in an hour, and this state lasted until the next day. She was cold and cyanotic, with slow and feeble respiration, pulse 45 and very weak, pupils widely dilated and insensible. Still she recovered. Her hearing became normal in a week, but it was two weeks before she had even a slight perception of light, and this was not wholly regained for months."

Such histories are the basis for the opinions of Briquet, A. B. Palmer, and Kunkel, the former of whom says: "If 2 gm. or more are taken and continued for several days, we observe an overwhelming, an exhaustion, stupor, somnolence, weakness of sight, dilatation of the pupils, and tremblings of the limbs. Very large doses lead to complete loss of consciousness, loss of sight and hearing, and complete immobility of the limbs. The delirium or intoxication of quinine is usually gay. He concludes that quinine produces a slight and temporary excitation of the encephalon, then soon a sedative action, which gradually increases, and which may go on to the destruction of nervous power."

Palmer describes as quininism ("cinchonism," Foster's "Medical Dictionary") those disorders of the cerebro-spinal functions indicated by headache, giddiness, contraction or sometimes dilatation of the pupil, ringing or roaring in the ears, deafness, partial blindness, abnormal touch and smell, difficulty of controlling muscular acts, somnolency, sometimes delirium, at other times stupor, sometimes a severe sense of stricture about the chest. These effects are for the most part temporary, but sometimes more permanent. Kunkel concludes that with poisonous doses of quinine the central nervous system is progressively paralyzed in all parts. In case of severe acute poisoning death occurs from paralysis of respiration, artificial respiration prolonging life until paralysis of the heart occurs.

When we come to look for the lessons to be drawn in the way of prophylaxis against the possibly toxic action of quinine it is clear that the dangers due to idiosyncrasy are not serious, for its results are so soon in evidence from such small doses, and so very uncomfortable to the subject, that he will be quite apt to remember them, and to avoid the drug in the future. The injurious effects of quinine, Lewin tells us, are more apt to be observed in women and aged people than in others, while persons with delicate skins and those subject to eczema are particularly liable to quinine exanthemata. To these classes then, and especially to persons suffering from eye and ear diseases, quinine should be given most cautiously or not at all.

There is little likelihood that any impurities in the drug are responsible for the toxic effects attributed to quinine. In fact, Lewin declares that there are no dangerous adul-

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-