of the external muscles of the eye, occurs, just as in locomotor ataxia, either as a transient symptom at an early period of the disease, or as a permanent condition at a later stage. Amblyopia is also a common symptom. Generally there is only impaired vision, not complete blindness. The ophthalmoscope reveals, in these cases, a discoloration of the discs, due to a degree of atrophy of the optic nerves.

Headache and vertigo are often present, both in the early and in the later stages of the disease. The vertigo often occurs in paroxysms. Occasionally it is due to the double vision, but more frequently it is quite independent of the latter condition.

The mental symptoms often play an important rôle. Sight psychic symptoms may be manifested in the beginning of the disease if the latter first affects the brain, but the graver symptoms are, usually, late manifestations. Change in disposition, irritability, loss of self-control, a tendency to laughing and crying, are common conditions. A certain impairment of intellect—weakened memory, a degree of apathy, etc.—is also not uncommon. But a high degree of dementia is rare. It is likely to occur only when the disease begins at an early age and there is arrested development of the brain, or when the pathological process is very acute. Different forms of insanity are sometimes observed, most frequently melancholia, occasionally delusional insanity.

Apoplectiform seizures, like those seen in general paralysis, are important symptoms. They occur, according to Charcot, in one-fifth of all cases. After slight prodromal symptoms, headaches, etc., coma develops within a few hours, the temperature rapidly rises, often reaching 104° or 105° F., and at the same time the face is flushed and the pulse rapid. Hemiplegia, with flaccidity of the paralyzed muscles, is soon observed. Within a day or two consciousness returns, the temperature falls, and, within a comparatively brief period, the paralysis disappears. Such attacks may occur every few months, or very rarely. They usually leave the patient in a permanently worse condition, thus marking the progress of the disease. Sometimes the patient dies in the attack. These seizures are very much like those of apoplexy, but post-mortem examinations reveal no anatomical basis for them.

In the foregoing have been given the most common symptoms of multiple sclerosis, those found in the majority of cases. But, on account of the distribution of the diseased areas, various other symptoms may be manifested. Thus the disease may attack the posterior columns of the cord, and ataxia, pain, anæsthesia, paræsthesia, etc., will be present; or it may involve the gray matter, when atrophy and paralysis of muscles will ensue. Or the disease may involve the whole thickness of the cord and produce the symptoms of transverse myelitis. When the posterior as well as the antero-lateral columns are affected, many of the appearances of spastic paralysis are likely to be absent, especially the exaggerated tendon reflexes. Symptoms referable to the bladder and to the rectal and genital functions are also likely to appear. If the disease involve the nuclei of the facial, hypoglossal, and pneumogastric nerves, the ordinary symptoms of labio-glosso-laryngeal paralysis will be manifested, and various local cerebral symptoms may appear, according to the location of the foci of disease.

The course of the disease is a very chronic one. Charcot has divided it into three stages—a division applicable to those cases which present the common clinical picture.

The first stage is from the beginning of the disease to the period of complete disability from paralysis and contractures of the limbs. This stage may last for from two to six years or longer. The symptoms are very slow in their progress. They begin as spinal or cerebral, but both sets of symptoms appear before this stage is terminated. There is often an arrest of the symptoms, or even improvement, which indefinitely prolongs this stage, and may give rise to delusive hopes of complete restoration to health.

The second stage, that of the fully developed disease, may last also for from two to six years. There seems to be little change in the patient during this period, and, though entirely helpless, he seems not to suffer in general health.

The third stage is that of decline. The general health is affected, there are loss of appetite, wasting, etc. Cystitis, decubitus, pyæmia, etc., may hasten the end. Or the latter may be due to an increase in the bulbar symptoms, or to an apoplectiform attack. More frequently a fatal termination is caused by an intercurrent affection—pneumonia, typhoid fever, or, above all, phthisis.

The average length of the disease is from six to eight years. In rare cases it terminates in a year or two; occasionally it lasts twenty years.

Morbid Anatomy.—The pathological changes can usually be seen by the naked eye. They consist of numerous patches or nodules of sclerosed tissue scattered throughout the nervous system. The nodules vary in size from merely microscopical proportions to an object as large as a chestnut or larger; they are rounded or irregular in shape, and may often be seen on the surface as slight prominences or depressions, but are found in larger number when sections of the brain and cord are made. Their color is mostly of a gray or reddish-gray; they are translucent, and have a firm, often cartilaginous, consistence. Many of the nodules are of the same color as the surrounding tissue, and are only distinguished by their consistence. In rare instances a few may be softer than the normal tissue, probably indicating recent disease; most of the nodules, on the other hand, are firmer than the normal tissue, doubtless being of very old standing, for such cases come to the post-mortem table only after the disease has existed a long time. The nodules seem to be quite distinctly circumscribed, but the microscope reveals the fact that they merge imperceptibly into the healthy tissue. They are also quite distinct, as a rule, though occasionally they blend into one another. In rare instances there has been found, in both the brain and the spinal cord, a diffuse sclerosis which, to some extent, has united the scattered nodules. On the other hand, secondary degeneration seems rarely, if at all, to develop from the disseminated disease.

The number of nodules found in a single instance may be very small, or may run into hundreds. Their distribution in the cord is very irregular. In some sections they may be found in the anterior, in others in the posterior, columns; in still others in the gray matter, or they may involve all these parts in the same section. Usually a large number of nodules are found in the medulla, pons, and crura cerebri. It is very rare that these parts are found free from disease. In the hemispheres the walls of the ventricles, corpus callosum, and centrum ovale are favored seats of the disease. In the latter two localities the nodules are often quite large. Usually nodules are also found in the large ganglia, while the cortex generally escapes. But few nodules are, as a rule, found in the cerebellum, and these in the central white matter. Similar nodules may be found in the nerves, most frequently in the optic nerves, but occasionally in the hypoglossal, the nerves of the eye, and the roots of the spinal nerves.

The microscopical appearances are those of interstitial myelitis. The nodules are mostly new connective tissue composed of very fine wavy fibrillæ. But in this new tissue the axis cylinders of the nerve fibres can usually be found in large numbers, though their medullary sheaths have disappeared. This is especially true of the nodules in the spinal cord.

At one of the meetings of the Society of German Naturalists and Physicians, Adamkiewicz expressed the opinion that the disease is not interstitial, but develops primarily in the nervous tissue, beginning in the medullary sheaths of the nerves. He bases his opinion upon results obtained by a new method of staining the nervous tissue. His view is altogether at variance with that formerly held, and may be looked upon with doubt, at least until further corroboration is forthcoming.

Morbid Physiology.—Many of the symptoms are

easily explained by the lesions found: psychic symptoms by disease of the hemispheres, bulbar symptoms by lesions of the medulla, muscular atrophy by lesions in the anterior cornua, anæsthesia and ataxia by disease of the posterior columns, spastic paralysis by disease of the antero-lateral columns—in some instances cerebral lesions may produce the same symptoms,—while amblyopia and some other symptoms are often due to nodules in the nerves themselves.

The long retention of the axis cylinders accounts for the usual presence of paresis rather than paralysis, for the anæsthesia being slight, for the amblyopia rarely advancing to complete blindness, etc. (In locomotor ataxia there are also numerous axis cylinders in the sclerosed area, and the symptoms usually point to only a partial loss of function.) Charcot attributes the tremor to the same condition. He supposes that the axis cylinders continue to carry voluntary impulses, but, because they are bared of their medullary sheaths, they carry them in an irregular, jerking manner, and hence the oscillations in the voluntary movements. While this must be considered a mere theory, we can speak with more positiveness of the location of the lesion as a cause of the tremor. It seems to be due to nodules in the medulla and pons, or, at least, in the basilar portions of the brain. In a few cases, in which the disease was limited to the cord, no tremor was observed. On the other hand, when tremor was observed during life nodules were always found in the medulla and pons; when it was not observed, these parts were not affected to any extent.

With a considerable degree of doubt, we may attribute the nystagmus to lesions in the corpora quadrigemina, the scanning speech to lesions in the medulla, the vertigo to lesions in the medulla or cerebellum. A satisfactory explanation of the apoplectiform attacks has not yet been given.

Diagnosis.—In some instances a diagnosis is made with the greatest ease, in others it is almost impossible to make a diagnosis. The most common clinical picture—paresis of the extremities with exaggerated tendon reflexes, intention tremor, nystagmus, scanning speech, amblyopia, etc.—is so characteristic that it cannot be mistaken.* But some of the most characteristic symptoms may be wanting, and then the diagnosis is much more difficult. In this case the indications of multiplicity of lesions and the very chronic course of the malady must be the guides to diagnosis. When the disease is limited to the spinal cord one can scarcely do more than guess in distinguishing it from other forms of myelitis. In such cases one must be on the lookout for cerebral symptoms. Optic atrophy is often a valuable diagnostic symptom, not only in this instance, but in excluding hysteria or other functional diseases which may simulate multiple sclerosis.

When the sclerosis affects only the brain it may present some of the manifestations of brain tumor. Here, too, the indications of a multiple lesion and the very slow course of the disease may clear up the diagnosis. But there is another important distinction, in that brain tumors produce to a large extent general symptoms, those of intracranial pressure, such as severe headache, convulsions, and double optic neuritis; while sclerosis produces merely local symptoms, those indicating the loss of function of the part affected by the disease.

The tremor of alcohol, lead, and mercurial poisoning might be mistaken for this disease, but concomitant symptoms and the history of a cause will establish the diagnosis. The tremor of paralysis agitans, with which this disease was formerly confounded, is easily distinguished by the appearance of the tremor, its being controlled to some extent by voluntary effort and increased during rest, and its very rarely affecting the muscles of the head and neck. Furthermore, paralysis agitans is rarely found in persons under forty years of age, while multiple sclerosis rarely occurs after thirty, and, apart from the tremor, the symptoms of the two diseases are quite different.

Prognosis.—Charcot believes that the disease may sometimes be cured, but the opposite view is generally entertained, though its arrest and even improvement for a number of years have been observed. It usually runs a very protracted course. When at its inception it manifests itself in various parts of the nervous system at the same time, it is likely to run a more rapid course. The occurrence of apoplectiform seizures, cystitis, bulbar symptoms, etc., indicates the approach of a fatal termination.

Treatment.—The same treatment is applicable as in other forms of chronic myelitis. (See *Spinal-Cord Diseases* in Vol. VII.)

Philip Zenner.

* Schuler reported a case of tumor of the right hemisphere, in the neighborhood of the island of Reil, which produced the typical clinical picture of multiple sclerosis, and Westphal reported two cases with similar histories, in which no pathological changes were found post mortem. But these are such rare occurrences as not materially to impair the diagnostic value of this clinical picture.

NERVI.—The town of Nervi stands upon a narrow, shelf-like plateau which intervenes between the base of an outlying spur or side range of the Apennines and the shore of the Mediterranean Sea, at a point some six miles distant from Genoa, in a southeasterly direction. The general trend of the coast line along what is known as the Riviera di Levante, or Eastern Riviera, between Genoa and Spezia, is from northwest to southeast; but, as in the case of the Western Riviera, the regularity of the line is frequently interrupted by the occurrence of bays, which are guarded by rocky headlands, jutting into the sea from the main chain of the Apennines, just as similar headlands along the Western Riviera reach down to the sea from the Maritime Alps. The scenery along this coast is consequently very similar to that of the Western Riviera, and, as the writer can testify from personal experience, it is exceedingly picturesque and beautiful. The width of the little plateau upon which Nervi is built does not exceed a quarter of a mile; its elevation above sea-level is very inconsiderable, and probably does not exceed one hundred feet. The shore line at Nervi runs nearly due east and west; the spur or side chain of the Apennines already mentioned, consisting of three separate mountain peaks, extends parallel with the shore, immediately back of the town. The most westerly and terminal peak of this side range is only about seven hundred or eight hundred feet high, and it is covered to its top with a growth of olive trees; the other two peaks are much higher (about twenty-five hundred feet), and their summits consist of bare rock.

The town of Nervi has a population of a little over three thousand, and it is built, in the straggling fashion so familiar to travellers who have visited the Italian coasts, along the old Genoa and Spezia post road. At this point the road does not skirt the shore, but hugs the base of the hills, so that the town stands close under the shelter of their steep slope, and is effectually protected from northerly winds. From easterly winds it is, in common with all points along the Eastern Riviera, protected in great measure by the main chain of the Apennines. The northeast wind is not effectually kept out, but gains access through gaps in the hills, and is sometimes strongly felt at Nervi. "The northwest wind," says Dr. Sparks, "is also not unknown, and Dr. Thilenius says of it, 'The most dangerous wind and the wind which is always the most violent, is the cold, cutting, dry, and bitter northwest.'" The warm, damp, relaxing "scirocco" wind, blowing from the southeast, is also of frequent occurrence.

The rainfall at Nervi is heavier than along the Western Riviera. The average fall in each of the six colder months of the year, derived from seven years of observation, is quoted by Dr. Sparks from Dr. Thilenius as follows: November, 6 inches; December, 4.88 inches; January, 4.78 inches; February, 3.23 inches; March, 4.49 inches; April, 2.20 inches. In the winter of 1876–77 the number of rainy days, including days on which slight showers occurred, during the months of December, January, February, and March, was 48. At Mentone, during the same period, 27 such days occurred (Sparks). This

season is spoken of by Dr. Sparks as a comparatively dry one. The winter of 1874–75, on the other hand, appears to have been at Nervi an exceptionally wet one, for Dr. Sparks quotes Dr. Thilenius to the effect that during that season "it rained almost incessantly for three months, day and night, and the air was so saturated with moisture that there was scarcely any difference between the wet- and dry-bulb thermometers." In the comparatively dry seasons of 1875–76 and 1876–77 the mean relative humidity, measured by August's psychrometer, and quoted by Dr. Sparks from Dr. H. J. Thomas, of Baden-Weiler, was as follows:

	Dec.	Jan.	Feb.	March.	April.
1875–76	64.0	60.0	64.8	66.7	72.7
1876–77	75.0	63.2	61.4	68.5	....

Dr. Kisch[3] gives the mean relative humidity of Nervi as 62.9 to 66.6 per cent. So far as these figures go, they appear to indicate greater dryness of the atmosphere at Nervi than exists at Mentone, yet Drs. Weber[2] and Sparks[1] both pronounce the climate of Nervi to be moister than that of Mentone.

At Genoa, which, it will be remembered, is only six miles distant, the mean relative humidity is decidedly less than it is at Mentone, and during the prevalence of northerly winds it falls very low indeed, below twenty per cent.; occasionally as low as eight or nine per cent. On the other hand, when the "scirocco" blows, the air at Genoa becomes very moist. Dr. Hann, in his "Handbuch der Klimatologie," gives the mean relative humidity of Genoa, for the five months November to March, as fifty-seven per cent. Now the free exposure of Nervi to the moisture-laden southerly winds and its shelter against the cold, drying, northerly winds characteristic of the Genoa climate, would no doubt combine to effect a great modification of the mean of humidity at the former place when compared with that of the latter; a modification, namely, in the direction of a higher percentage of saturation. Yet, taking into account the close proximity of Nervi to Genoa, and the relative humidity *figures* for Nervi given in Dr. Sparks' book, it seems not impossible that this writer and Dr. Weber, in pronouncing the Nervi winter climate moister than that of Mentone, have confounded the two factors of rainfall and humidity. The rainfall of Genoa is far greater than it is along the Western Riviera; the mean relative humidity is, on the other hand, very considerably less; and no better example than this feature of the Genoa climate can be adduced in support of what has already been said in the article on *Climate* (first edition), viz., that "The humidity of the atmosphere can by no means be measured by the amount of the rainfall." Probably the variations in the atmospheric humidity at Nervi are much greater in amount and more frequent in occurrence than they are at Mentone. "In spite of its raininess," says Dr. Sparks, "the soil of Nervi —clay slate—is favorable to its rapid drying."

As to the winter temperature of Nervi, it appears to be about the same as that of Mentone. Dr. Kisch[3] tells us that the temperature of the two places is similar in respect to its mean and to its variations. The observations of General Brocchi, during the years 1849–64, give the mean temperatures of November and December for thirteen years, and those of January, February, March, and April for fourteen years; they are quoted by Dr. Sparks[1] as follows: November, 55.31°; December, 47.84°; January, 46.36°; February, 47.8°; March, 49°; April, 58.1°.

The absolute reliability of these figures is not vouched for by Dr. Sparks, as he explains that he "knows nothing of the arrangement of the instruments or hours of reading."

The following table, showing a comparison of the Nervi and Mentone temperatures for a single winter, is quoted from Dr. Sparks' book, its figures being derived from calculations by Dr. Sparks, based upon observations published by Herr Schulze, in his work on the health resorts of the Riviera, and of Middle and Lower Italy.[4]

TEMPERATURES AT NERVI AND AT MENTONE, WINTER OF 1874–75. (Sparks.)

	Nov.	Dec.	Jan.	Feb.	March.
Mean temperature at 8 A.M.					
Nervi	56.0	52.0	51.0	44.0	49.0
Mentone	54.0	48.2	50.5	44.5	49.8
Mean temperature at 2 P.M.					
Nervi	59.5	56.5	58.0	50.3	55.4
Mentone	59.2	53.6	56.0	59.0	57.5
Maximum temperature.					
Nervi	70.5	56.0	66.0	61.0	64.0
Mentone	70.5	64.0	64.0	55.0	66.0
Minimum temperature.					
Nervi	44.0	41.0	44.0	36.0	44.0
Mentone	46.0	42.0	46.0	36.0	48.0

The following data for mean temperature at 8 P.M. and for absolute minimum temperature at Nervi, during the months of December, 1876, and January, February, and March, 1877, are quoted by Dr. Sparks from an article by Dr. H. J. Thomas in the *Berliner klinische Wochenschrift*. The figures for the mean temperature are as follows: December, 51.5°; January, 49.3°; February, 47.2°; March, 47.4° F. The minimum temperature observed was 35.2° on March 2d, 1877. It is worthy of note, in connection with this last-quoted figure, that a minimum temperature of 25.5° was recorded in the "West Bay" of Mentone during this same month. Moreover, if one may judge from a table of monthly highest and lowest temperatures at Mentone which is given by Dr. Sparks in his account of that place, it would appear that this winter season of 1876–77 was not an unusually warm one on the Western Riviera, and that March, 1877, was exceptionally cold; and it is reasonable to infer that such was also the case along the Eastern Riviera. If such was the case, and if Dr. Thomas' observations were made under like conditions with those of Messrs. Freeman and Andrews at Mentone, the greater mildness, or, at least, the greater equability of the Nervi as compared with the Mentone climate would be illustrated, although not accurately measured, by these two figures alone.

On the other hand, Dr. Thomas' 8 P.M. figures, when compared with the daily mean figures of Dr. Brocchi, already quoted, show a decided discrepancy between the two sets of observations, especially if we assume, on the authority of the Mentone figures, that at Nervi the winter of 1876–77 was no warmer than the average.

It is to be regretted that no fuller, more extended, and more accurate observations respecting the various climatic factors of the place have as yet been made and recorded at Nervi. Nevertheless, so far as temperature is concerned, the climate is undoubtedly a mild one, and almost identical in this respect with that of the Western Riviera. As remarked by Dr. Sparks: "In spite of the want of really scientific observations on the climate of Nervi, there is no doubt of the mildness of its climate. The abundant subtropical vegetation, and the growth of standard lemon trees, is a proof of this." The following quotation from an article by Dr. Edward Haughton (London *Lancet*, December 13th, 1884) is interesting as illustrating the agency of mountain shelter in the production of Nervi's mild winter temperature. In February, 1884, this gentleman visited Genoa, Pegli, and Nervi, all on the same day, for the express purpose of making observations on this point. "The result," as he tells us, "was that the wind, which was bitterly cold at Genoa, was much milder at Pegli, especially in the valley behind the town, while it was perfectly calm, and even warm at Nervi, so long as the headlands which protect the place were not rounded by the visitor." The same point is further exemplified in a striking manner, although on a small scale, in what Dr. Sparks tells us concerning a sheltered coast-walk at Nervi itself; and everywhere along this part of the Italian coast we find that shelter from cold wind and exposure to the sun combine in varying degrees to cause marked elevation of temperature, even "in the dead of winter." At Nervi the railway runs between the town and the sea. "Below the railway, and just before the rocky shore takes its deep descent into the sea, a path a few feet wide has been cut along the edge of the rock for the use of the coast guardsmen, and as it accurately follows the indentations of the coast line, and is absolutely protected from the north by high garden walls, or by part of the rocky slope, or the railway embankment, while it gets all the southern sun in its full force, it is naturally an excellent promenade for invalids. Here they can walk or sit, or, if they choose, at certain points descend close to the sea, and enjoy a temperature of 64°–68° F., while in the High Street of Nervi the thermometer at the same time is not higher than 43° or 44°. Naturally great care is necessary to be provided with plenty of wraps to put on when returning from the shore to the town."

Of amusements for the invalid there appears to be a great dearth at Nervi, and the facilities for the making of excursions in the immediate neighborhood are exceedingly limited. "The neighborhood of Nervi," says Dr. Sparks, "offers but a limited field for excursions owing to the nearness and steepness of the high hills at the back of the town. There is no drive along the shore close to Nervi, though further west the road at some places nearly overhangs the sea. . . . For amusements of all kinds, except rod-fishing, Nervi presents little opportunity."

[There are three first-class hotels at Nervi and various pensions. A train runs every quarter of an hour to and from Genoa. "The mild but tonic climate of Nervi has for some years been attracting every season an increasing number of visitors."[5] English physicians are to be found at Nervi.—*E. O. O.*]

Concerning the class of invalids who should be recommended or permitted to pass a winter at Nervi, it is impossible to decide with any degree of precision until a longer and more thorough series of meteorological observations shall have given us a more accurate knowledge of the local climatic peculiarities. For the present it can only be said that the general features of the climate are those of the Italian Riviera, and that the local modifications are such as render the climate less exciting than that of the Western Riviera resorts. *Huntington Richards.*

REFERENCES.

[1] The Riviera, by Edward J. Sparks, M.A., B.M., Oxon.
[2] Ziemssen's Handbuch der allg. Therapie und Klimatotherapie.
[3] Eulenburg's Real-Encyclopädie, art. Nervi.
[4] Die klimatischen Curorte der Riviera, Mittel- und Unter-Italiens.
[5] The Riviera, by C. B. Black, 1901.

NEURENTERIC CANALS.—It is now known that during the very early stages of the development of many vertebrates there is an open communication between the posterior portion of the medullary canal (spinal cord) and the entodermic or intestinal canal. To this communication the name of neurenteric canal has been applied. The original opening of the archenteron is known as the blastopore (see Vol. II., p. 4). In mammals, as in other amniota, it is represented by the posterior opening to the exterior of the notochordal canal. It has now been observed in various vertebrates that as the neural ridges or medullary plates develop backward they terminate against the sides of the blastopore, which acquires an elongated form. By their further growth the medullary plates close over across the long blastopore, in such a manner as to divide it into an anterior portion and a posterior portion. The posterior portion remains permanently open in certain amphibia and thus gives rise to the anus, or it may close over (Fig. 5159, *bl.*, and subsequently open, thus giving rise indirectly to the anus. The anterior portion is an opening enclosed within the medullary plate or groove, and may remain open until after the groove has closed to form a canal (Figs. 5159, 5160, *ne*), the true neurenteric canal, which establishes a direct communication between the neural and entodermal tubes. It has been observed in man (Fig. 5161, *Neu. c*). It might with propriety be termed the canal of Kowalewsky, from its discoverer. Kowalewsky first found it in amphioxus, and subsequently demonstrated its occurrence in various fish types.

The canal lies in front of the true or secondary blastopore and traverses the notochord. According to Durham,[4] it can be well seen in longitudinal sections of early stages of the frog (Fig. 5159) as a short canal, *ne.*, opening widely into the entodermal cavity. Compare also Götte's[1a] description of the neurenteric canal in Bombinator. It was discovered by Gasser[6] in goose embryos. Braun[5] has shown that both canals may be present in various bird embryos at a stage when there are six or eight pairs of myotomes and the development of the tail is just beginning. The neurenteric canal lies a short distance in front of the blastoporic, which is the larger of the two. The two canals appear in some species at the same time, or in other species at slightly different stages. The posterior canal is more often obliterated in birds than the anterior. In the duck and in Motacilla flava the canals are separated both in the times and positions of their occurrence; in the Australian paroquet they are both present contemporaneously, although the neurenteric passage becomes open earliest. Fig. 5160 represents a transverse section, which passes through the neurenteric canal of the paroquet. In the common fowl the blastoporic canal appears not to be open at any period after the formation of the primitive streak.

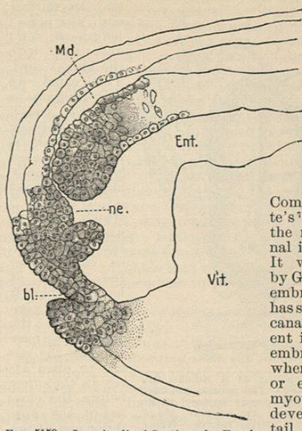

FIG. 5159.—Longitudinal Section of a Frog's Ovum shortly after the Closure of the Medullary Groove. The blastoporic canal, *bl.*, is only partially cut, but was found open in neighboring sections. (After Durham.) *Md.*, Medullary canal; *bl.*, blastopore; *Vit.*, yolk forming the floor of the entodermic cavity, *Ent.*; *ne.*, neurenteric canal.

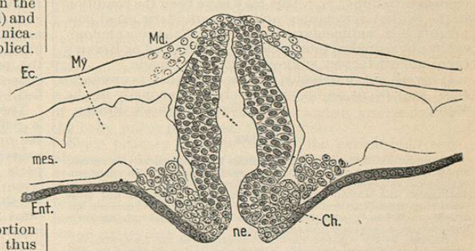

FIG. 5160.—Transverse Section of an Embryo Paroquet (Melopsittacus) to show the Anterior or True Neurenteric Canal. *Ec.*, Ectoderm; *My.* myotome; *Md.*, medullary canal; *Ch.*, notochord pierced by the short neurenteric canal, *ne.*; *Ent.*, entoderm; *mes.*, mesoderm. (After Max Braun.)

Another canal, which was first satisfactorily described by Braun,[3] occurs in older embryos. The "Enddarm" of Gasser and Kölliker becomes the "Schwanzdarm"

(post-anal gut, Balfour[1]) of older embryos, which soon becomes divided, at least in birds, into a dilated terminal portion and a narrower neck communicating with the intestine proper. The posterior section then subdivides, and its narrow end segment lengthens out and unites with the spinal cord. This canal we may designate as Braun's canal. It is not improbable that it is homologous with the amnio-allantoic canal of Gasser,[7] which Rauber[12] has nicknamed the Cochin China canal, after the breed of hens in which it seems most constant. In the one case we may suppose the canal to open after, in the other before, the closure of the posterior end of the medullary groove. If the homology is correct it may be further said that the canal is identical with Kupffer's myelo-allantoidean canal; it cannot be brought into relation with the development of the allantois, as believed by Kupffer,[10] as the allantois and Enddarm are both formed before the canal appears.

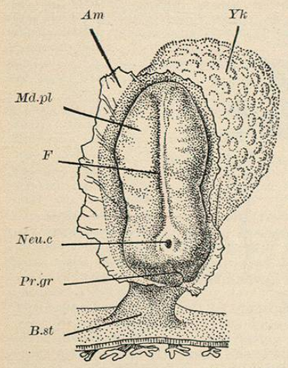

FIG. 5161.—Reconstruction of a Human Embryo 1.54 mm. Long. The amnion has been opened to show the dorsal surface of the embryo. *Yk*, Yolk sac; *Am*, amnion; *Md.pl*, medullary plate; *F*, dorsal furrow; *Neu.c*, neurenteric canal; *Pr.gr*, primitive groove; *B.st*, body stalk. (After Count Spee.) (From Minot's "Embryology," Blakiston, Phila., 1903.)

The significance of the three canals is obscure. The middle one seems unquestionably the temporarily open secondary blastopore. The first, or Gasserian canal, is distinct from the blastoporic, as the two coexist, and it seems desirable that this canal alone should be called *neurenteric*. As to its origin or significance nothing definite can be said, but it may be suggested that it was the excretory opening of the central canal of the spinal cord and that the cilia of the canal served to expel the fluid (compare Balfour[1,2]). This may have been the condition in the earliest vertebrates, and the neurenteric canal now persists as a rudimentary organ. As to the morphological or physiological interpretation of the third or Braun's canal no satisfactory suggestion has been made.

It seems not impossible that a persistent neurenteric canal may occur as an excessively rare anomaly in the adult.

Charles Sedgwick Minot.

LITERATURE.

The literature of the neurenteric canals is all comparatively recent, and is, for the most part, included in essays dealing with other embryological subjects. Great confusion has arisen from the failure to distinguish the several canals. The reader will find his way most readily by consulting first the text-books of Balfour,[2,3]; second, the article of Braun,[3]; and third, Rauber's note,[12] although Rauber's terminology is eccentric and perplexing.

[1] Balfour, F. M.: On the Early Development of the Lacertilia, etc. Quart. Journ. Microsc. Sci., xix. (1879); also in his Works, i., p. 644, with Plate 29.

[2] Balfour: Comparative Embryology, vol. ii., pp. 267–269.

[3] Braun, M.: Die Entwickelung des Wellenpapageis: ii. Theil, Semper's Arbeiten, v., 205–341. Taf. x.–xiv. (a valuable but excessively diffuse article. The most important passages on the neurenteric canals are on pp. 296, 301, and 308).

[4] Durham, Herbert E.: Note on the Presence of a Neurenteric Canal in Rana. Quart. Journ. Microsc. Science, xxvi., 509–510, Plate xxvii.

[5] Foster and Balfour: Elements of Embryology, second edition, 1883.

[6] Gasser: Der Primitivstreifen bei Vogel-Embryonen, Cassel, 1879.

[7] Gasser: Beiträge zur Kenntniss der Vogelkeimscheibe. His und Braune's Archiv, 1882, 359–398.

[7a] Götte: Entwickelungsgeschichte der Unke.

[8] Heape, Walter: The Early Development of the Mole (Talpa Europæa). The formation of the germinal layers, and early development of the medullary groove and notochord. Quart. Journ. Microsc. Sci., xxvi., 1883, 412–452, Plate xxviii.–xxxi.

[9] Hoffmann, C. K.: Die Bildung des Mesoderms, die Anlage der Chorda dorsalis, u. die Entwickelung des Canalis neurentericus bei Vogel-Embryonen, p. 109, 5 Tafeln. Amsterdam, 1883. (Abstr. in Hoffmann u. Schwalbe's Jahresber., 1883, 442–444.)

[10] Kupffer, C.: Die Gastrulation an den meroblastischen Eiern der Wirbelthiere und die Bedeutung des Primitivstreifs. Arch. Anat. u. Physiol., Anat. Abth., 1882, 1–30, Taf. i.–iv. Fortsetzung, 139–156. Taf. viii.–ix.; 2te Fortsetzung, 1883, 1–40, Taf. i.–ii.

[11] Lieberkühn, N.: Ueber die Chorda bei Säugethieren. His und Braune's Archiv, 1882, 399–438, Taf. xx.–xxi. Fortsetzung, 1883, 435–452, Taf. xix.

[12] Rauber, A.: Noch ein Blastoporus. Zool. Anzeiger, vi., 1883, 143–147, and 163–167 (*cf.* his earlier papers on the Blastoporic Canal, Zool. Anzeiger, ii., 1897, p. 499, and iii., 1880, p. 180).

[13] Strahl: Ueber Canalis neurentericus und Allantois bei Lacerta viridis. His u. Braune's Arch., 1883, 323–340, Taf. xiv.

PERITONITIS.—(Peritonæitis, Inflammatio peritonei.) The peritoneum is a thin membrane of connective tissue extremely rich in blood-vessels and lymphatics, and is covered by a single layer of flattened endothelial (mesothelial) cells (often called epithelial). These cells are chiefly polygonal, but the cell outlines are often very irregular, serrate, or wavy. By treatment with silver nitrate or by *intra vitam* staining with methylene blue, the cement lines between the cells can be made out; and by especial methods of technique the so-called intercellular protoplasmic bridges connecting the cells may be demonstrated. The connective-tissue layer consists of an interlacing network of fibrous connective-tissue bundles, numerous elastic fibres, and connective-tissue cells. Through this there runs a very abundant capillary and lymphatic network having a free anastomosis. The majority of writers hold that the lymphatics communicate directly with the peritoneal cavity by means of small openings between the mesothelial cells, known as stomata. Some of these writers regard the endothelial lining of the lymph spaces of the peritoneal basement membrane as continuous with the lining of the peritoneal cavity. This is not the case, however, and the mesothelial cells form a probably unbroken layer over both the blood and the lymphatic vessels, the processes of absorption and secretion being carried on through the two layers of cells, endothelial and mesothelial. The absorption capacity of the peritoneal surface is very great, being fully equal, in the case of experiments with certain poisons, to that of direct intravenous injections. Gases, fluids, and even morphological elements may be quickly removed from the peritoneal cavity. On the other hand, the secretory activity of the immense vascular surface of the peritoneum is very great, and in disturbances of the vascular secretion an immense amount of exudate may pass through the peritoneum into the peritoneal cavity. The endothelial and connective-tissue cells of the basement membrane respond very quickly to "irritation" of any kind, and fibroblastic activity is set up more quickly in the peritoneum than anywhere else in the body. The course of peritoneal inflammations is considerably modified by these factors.

The peritoneum lines the entire abdominal cavity, and is reflected over the organs contained within it. Over the organs it forms the serous coat or capsule (*tunica serosa*). The membrane is attached to the underlying parts by a subserous coat of adipose tissue, connective-tissue bands and elastic fibres. Over the organs the subserosa is but slightly developed. The anatomical relations of the peritoneum to the abdominal wall, its investiture of the abdominal organs, the intimate relations of the peritoneal cavity to the female genital tract, etc., in connection with its very vascular structure, peculiarly predispose this membrane to the occurrence of inflammatory processes. Such a predisposition is shown by the fact that peritonitis is one of the most common and important clinical conditions. It is also one of the most serious. The high mortality of acute general peritonitis makes it one of the most dreaded affections. Even in these days of aseptic surgery when so many operative procedures have been divested of their chief dangers, peritonitis still remains to the abdominal surgeon and gynecologist one of the complications most feared and most carefully to be avoided.

The occurrence of peritonitis is not dependent upon climatic, seasonal, or meteorological influences. Females are more frequently affected than males, this fact being dependent upon the important rôle which diseases of the female genital tract play in the causation of peritonitis. It is therefore seen more often during the years of sexual activity, but may occur at any age. It is of not infrequent occurrence in young children. The relation of peritonitis as a complication to many of the acute infections makes its occurrence to a certain degree associated with epidemics of these diseases. Alcohol is regarded as a predisposing factor.

ETIOLOGY.—Peritonitis may be *primary* or *secondary*.

Primary peritonitis is, if we except the surgical form, of much more rare occurrence than the secondary. It is usually *traumatic*, more rarely, *idiopathic*, *spontaneous*, or *rheumatic*.

Traumatic peritonitis is most commonly due to perforating wounds of the abdomen. Abdominal injuries in which the wall is not penetrated rarely, if ever, directly cause peritonitis. Nevertheless, blows, kicks, falls, etc., are often adduced as causes of peritonitis. The more severe the injury, the more likely is the occurrence of peritonitis. Hemorrhage into the peritoneal cavity is usually followed by inflammation of the peritoneum. Likewise, trauma may indirectly cause peritonitis through the perforation, laceration, tearing, or bruising of the stomach or intestines, rupture of the gall bladder, pancreatic duct, urinary bladder, etc., these lesions permitting the entrance of micro-organisms into the peritoneal cavity. The perforation of the œsophagus or stomach by the careless passage of a sound or stomach tube may also be a causal factor in the production of peritonitis.

Operative or *surgical* peritonitis may be mentioned in this connection. Before the days of antisepsis and asepsis a large proportion of laparotomies were fatal from the peritonitis following the operation. Even at the present day the chief anxiety attending operations involving the peritoneal cavity is the possibility of peritonitis. The vast improvement in surgical technique has, however, greatly reduced the number of cases of post-operative peritonitis, and in certain operations in which there is, with proper methods, no opportunity for infection the peritoneal cavity is opened with a certain degree of impunity. The occurrence of surgical peritonitis is dependent upon several factors: the character of the operation and the possibility of infection during the operative procedures, the amount of damage done to the peritoneal tissues, the state of the general resistance of the membrane to infection, etc. Surgical peritonitis is due to the introduction of bacteria into the peritoneal cavity. But not all bacteria which gain an entrance into the peritoneal cavity set up an inflammation there. It has been shown experimentally that rather large quantities of bacteria, even of the pus cocci, may be introduced into the peritoneal cavity of animals without causing peritonitis, the bacteria entirely disappearing after a short time. The presence of a tissue lesion, even though very slight, or the simultaneous introduction into the cavity of irritating substances, furnishes the conditions requisite for the growth of the bacteria and for the production of an inflammation. The peritoneum therefore when uninjured must possess a certain protective power against bacteria. This resistance is found to be lowered in the case of hemorrhage into the cavity, after the removal of ascitic fluid, and in cases of pseudomyxoma peritonei. The general condition of the body, conditions of intoxication, cachexia, etc., also play a rôle of importance. Fatal peritonitis may follow the tapping of the abdomen in ascites, the small number of bacteria introduced by means of a septic trocar being sufficient to overcome the lessened resistance. When modern methods of asepsis are properly carried out the dangers of surgical peritonitis are relatively slight in all cases in which the contamination of the peritoneum with septic material can be avoided. Even when this contamination does occur, the modern procedures of thorough irrigation have greatly reduced the chances of infection.

The existence of a *peritonitis rheumatica* (*refrigeratoria*) has been denied by many writers. While the effects of cold as a factor in the etiology of peritonitis were formerly greatly exaggerated, there can be no doubt, from the large number of observations made by reputable clinicians, that attacks of peritonitis may follow the sudden chilling of the overheated body, prolonged exposure to cold or wet, lying upon the cold damp ground, etc. The effects of such chilling of the body are especially noticeable when the abdominal vessels are overfilled with blood (*physiological congestion*). In women, particularly in girls at the time of puberty, a wetting or chilling of the body at the menstrual period is not infrequently followed by peritonitis. In all of these cases the effect of the refrigeration is not directly to excite the peritonitis, but to render the membrane less resistant to infection. The chilling plays the same rôle here as in the case of the mucous membranes. Diplococci have been demonstrated in the exudate of cases of so-called rheumatic peritonitis; and it is very probable that all such cases are infections following and dependent upon a lessened resistance of the body.

Cases of *idiopathic* or *spontaneous* peritonitis have also been reported clinically.

The autopsy findings in such cases show the presence of an infection proceeding from the female genital tract, the appendix, or some other of the abdominal organs. Such cases occur most frequently in females and in very young persons. In the former the infection is nearly always secondary to some unsuspected condition of the internal genitals. The gonococcus plays an important rôle in such cases, particularly in very young girls. It has been said that the peritonitis apparently arising spontaneously in young girls is usually gonococcal, a gonorrhœal infection of the genital passages existing at the same time. In young male children cases of apparent spontaneous peritonitis are usually found to be due to appendicitis. Further, spontaneous cases of peritonitis have been found at autopsy to be ambulatory typhoid, acute tuberculosis of the peritoneum, etc. On the whole it may be said that the existence of a true idiopathic peritonitis, while probable, has not yet been definitely demonstrated. A *cryptogenic hæmatogenous* infection of the peritoneum is of course possible and certainly occurs in tuberculous peritonitis, but has not yet been shown positively to occur in the case of the pyogenic organisms.

Likewise the existence of a toxic peritonitis, though assumed by some writers, has not been demonstrated. The occurrence of so-called *nephritic* or *uræmic* peritonitis seen in the late stages of Bright's disease is to be regarded as of the nature of a terminal infection, and similar to the pericarditis and pleuritis occurring in the same disease. The occurrence of peritonitis in association with or following various forms of intoxication is to be explained in the same way as the rheumatic—the lessened resistance of the body tissues and the pathological alterations of the body juices predispose to infection.

Since primary inflammations of the pericardium and pleura are of relatively more frequent occurrence, the greater rarity of primary peritonitis may be explained by the assumption that the peritoneum possesses a greater resistance and protective power than the other serous membranes. This relative greater immunity of the peritoneal cavity has been demonstrated experimentally.

SECONDARY PERITONITIS.—It should be noted at this point that various writers upon the subject of peritonitis are not agreed in their conceptions of primary and secondary peritonitis. In a very broad sense the term primary may be applied to those forms of peritonitis which are not secondary to, or do not occur in association with, any other acute or chronic disease, hence not metastatic; and, further, which do not arise by contiguity from any of the organs or structures covered by the peritoneum. Terminal infections should then be classed as secondary rather than as primary. A number of recent