the œsophageal diverticulum, embedded in an albuminoid mass of unknown character. This becomes mature and breaks up into numerous (thirty to forty) elongated oval bodies (sporoblasts?), 0.003 mm. long by 0.002 mm. broad, which enter the cells of the salivary gland, and then coming to rest (sporocysts), divide into numerous very minute bodies (sporozoites?).

The parasite was found in the yellow-fever mosquito (*Stegomyia fasciata*) from Vera Cruz, Mexico, by Drs. Parker, Beyer, and Pothier, Working Party No. 1, Yellow-Fever Institute of the United States, Public Health and Marine Hospital Service. According to these authors the mosquitoes used were fed on the blood of a yellow-fever patient, and with due precautions against infection from any other source were killed at stated intervals from the second to the thirtieth day. A careful study of sections of these mosquitoes in which the Working Party mentioned received valuable assistance from Mr. J. C. Smith, of New Orleans, resulted in the demonstration of the life history of the organism somewhat imperfectly as outlined above. More recently, however, Carroll has maintained that the fusiform stage is actually a wild yeast.

The Working Party also states that yellow fever was produced experimentally with mosquitoes from a case that harbored this parasite, and the parasite was found again in mosquitoes fed on this case. Furthermore they permitted this same species of mosquito to feed on a case of malarial fever of the malignant type, on normal blood, and on other nutritive materials, and in none of these mosquitoes were found the parasites described above.

From the account given it appears that there was present in these mosquitoes a parasite, the development of which bears close resemblance to that of the malarial organism in the sexual cycle (sporogony). On the analogy of the latter parasite there should also occur in this case a non-sexual cycle (schizogony) in the blood (?) of the yellow-fever patient. Yet Sternberg, Reed, Carroll, and many others have sought in vain for such an organism; nor was the Working Party more successful. The further life history of *Myxococcidium stegomyiæ* lies even beyond conjecture, and it can only be said that negative evidence raises a strong presumption in favor of its etiological relation to yellow fever.

Quite recently Councilman, Magrath, and Brinckerhoff have made known the results of studies on the organisms of vaccinia and of variola, which go far toward establishing the nature of these oft-reported and much-questioned bodies. Much is needed to confirm these reports and to elucidate further details in life history, as well as the general relationship of these bodies. They may be considered briefly here without prejudicing the results of further study on these points. Before vesicle formation in the diseases noted, small, structureless bodies (0.001–0.004 mm. in diameter) occur in vacuoles of cells in the lower layers of the dermal epithelium. With increase in size the body shows granules lying in a reticulum, and becomes irregular in form as if amœboid. No nucleus was demonstrated. Formation of small round bodies, 0.001 mm. in diameter, closes the first stage in the life cycle. Following this oval or ring-like intranuclear bodies appear. In them several vacuoles are seen grouped around a central vacuole. They enlarge and destroy the nucleus, and come to lie in a completely degenerated cell. The vacuoles become less evident, and there appear multiple circular bodies with a central dot. These bodies measure only 0.0015 mm. in diameter, and are seen with great difficulty.

The intranuclear bodies represent the second stage in the life history, which is believed to be the sexual cycle, and produce spores which are the infecting agents. In the opinion of these authors the first cycle may exist without the second, and such is the case in vaccinia.

Apparently these are the same structures seen by L. Pfeiffer, Guarnieri, and others, who were not successful in working out the life history as it now stands, although they also did not hesitate to bring them into etiological relation to smallpox. One of the most recent of these (Govini) has even described and figured both extranuclear and intranuclear bodies in vaccinia. Questionable intranuclear bodies have also been reported by several investigators for sarcoma cells in man, but there are also other parasites belonging to this group and affecting lower animals in which an intranuclear existence is well known, *e.g.*, *Eimeria salamandræ* (= *Caryophagus salamandræ*), parasitic in the intestinal epithelium of one of the salamanders, and most frequently in the nucleus of the cell parasitized.

Hæmatozoa have been described by various authors as characteristic of beri-beri or kakki, an endemic form of polyneuritis particularly prevalent in Japan and the Dutch East Indies. The infectious nature of this disease seems to be generally accepted, and at different times various forms of possible pathogenic significance have been reported from the blood. The most recent of these are amœboid bodies resembling malarial parasites, which have been studied and described at length by Glogner, and especially Fajardo. The latter demonstrates their presence in the blood in peripheral as well as inner organs, and their production of pigment and formation of spores of some sort; and yet the possible confusion with malarial or other hæmatozoa and the lack of proof concerning the distinct etiological relation to beri-beri have prevented any general acceptance of the rôle assigned to the organism.

In leukæmia also Löwit claims to have discovered amœboid organisms in the leucocytes, and to have followed their development even to sporulation, *i.e.*, schizogony. (For further details see *Leukæmia*.) The parasitic nature of such structures cannot be regarded as established until they have been studied in life and not merely in preparations of fixed blood.

In dengue, an infectious disease epidemic in hot climates, and treated at length in an earlier volume (*q.v.*) good evidence has recently been furnished that the cause is a protozoön analogous to the malarial organism, and like it transmitted by the mosquito. It is an unpigmented pyriform body found in the erythrocytes though not abundantly, and is present in second and third attacks as well as in the first. The development is slow, requiring four to eight or even ten days, and in general appearance the organism suggests *Piroplasma bigeminum* of Texas fever in cattle or the organism of spotted or tick fever in man noted above. The discoverer, Graham, also found spores in the walls of the stomach and salivary glands of the mosquito, though this portion of the life history has not yet been clearly described; in one case the time required for it was, however, only forty-eight hours. In this case it is *Culex fatigans* which harbors the organism and transmits it, although other species may also be responsible. Graham has recently reported inoculation experiments, the results of which leave little doubt as to the cause of the disease and the method of transmission.

A long series of contributions concerns objects of supposed protozoan character which have been brought into etiologic connection with various pathological conditions by investigators of the most diverse type. Such are the pseudococcidia of epitheliomata, of sarcomata, of molluscum contagiosum, etc. Three views obtain as to the nature of these bodies, according to which they are blastomycetes or myxomycetes, sporozoa or other protozoa, and finally degenerative cell products. It cannot be said that their animal nature has been at all clearly demonstrated, and beyond the mere mention they have no right to consideration in this article.

In the subclass Neosporidia are included forms which in the adult condition are multinuclear, and which produce spores during the entire vegetative period. Spore formation is very characteristic. The organism forms a number of pansporoblasts, which divide again to form sporoblasts. The latter acquire a membrane and transform themselves with somewhat complicated changes into sporocysts, each of which develops within itself only a single sporozoite. Of the two orders only the

Sarcosporidia are of importance here, and they are but imperfectly known.

The Sarcosporidia possess an oval, elongate, or sacculate body (Fig. 5189), in which pansporoblasts are formed at a very early period. They parasitize at first intracellularly the muscle fibres, but by the degeneration of these come to lie in connective tissue and develop to oval or spherical bodies of considerable size. In the youngest stages yet found uninuclear spheres 0.004–0.005 mm. in diameter with relatively large nuclei (0.002–0.003 mm.) occur in the endoplasm. The protoplasm forms a frame-work between these young pansporoblasts, which increase in size with age and become also multinuclear. While at the ends of the sacculate body new pansporoblasts are continually being formed, in the older ones nearer the centre the contents divide into many finely granular pale spheres, the sporoblasts.

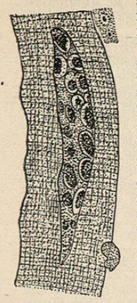

FIG. 5189.—*Sarcocystis tenella*. Longitudinal section of young stage with newly formed uninuclear pansporoblasts. Magnified. (From Wasielewski, after Bertram.)

In each of the latter is formed a single sporozoite which gradually assumes the definitive form (Fig. 5190, *a–d*). These sporozoites are usually reniform, sickle-shaped, or crescentic and very small. Some investigators claim to have discovered a polar capsule, and this has been partly confirmed by some later observers. Polar filaments are present in some cases (Fig. 5191, *b*). Theobald Smith has observed the movements of the sporozoites, and finds that in *Sarcocystis muris* there is a peculiar gliding with sudden revolutions on the long axis. This is carried out without the assistance of flagella. Smith's experiments, which were very painstaking and extended over three years, demonstrate for this species direct infection by feeding muscle tissue in which was present the parasite with ripe, mobile sporozoites. Sarcosporidia are parasitic in vertebrata, chiefly mammalia, and are common in many domestic animals.

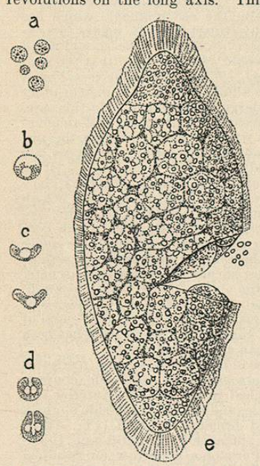

FIG. 5190.—*Sarcocystis miescheriana*. *a–d*, Development of sporozoites from sporoblasts; *e*, full-grown sac, dissected out from muscle fibre, the radially striated capsule torn on the right to show the pansporoblasts within. Magnified. (From Wasielewski, after Manz.)

Miescher in 1843 found these parasites first as cylindrical sacs in the voluntary muscles of the house mouse. Some years later Rainey found similar structures in the muscles of the pig, and the common names of these structures, often visible to the naked eye, are associated with these two investigators. The group has been but little studied, and the system is so imperfectly developed that it is advisable to omit all further mention of it, and to pass at once to a consideration of the one species which has been certainly obtained from the human body.

Sarcocystis Lindemanni (Rivolta 1878).—(Syn.: *Gregarina Lindemanni* Rivolta 1878; *Sarcocystis hominis* Rosenberg 1892; *S. Lindemanni* Labbé 1899.)

Protoplasmic body from the muscle fibres of the vocal cords, from 0.15 to 1.6 mm. long and from 0.077 to 0.17 mm. thick; membrane delicate, somewhat thickened at the ends (Fig. 5191, *a*), body distinctly chambered (Fig. 5191, *e*). Sporozoites (*d*) banana shaped, exceedingly numerous, 0.008–0.009 mm. in length.

The most certain case is that of Baraban and St. Remy, who found this form in the body of a criminal executed at Nancy. All the specimens of the parasite were in the same stage of development. The infected muscle fibres were swollen to fourfold their normal thickness. Several other uncertain cases are on record. As Theobald Smith remarks, the muscular system is not subject to the scrutiny which the viscera undergo in pathological investigations, so that the presence of these forms may be much more frequent and important than appears as yet. In the case of *S. muris* Smith has shown that the feeding of muscle tissue containing ripe mobile sporozoites to gray and white mice is followed by an invasion of the muscle fibres by the parasites, which readily become recognizable after the forty-fifth day. Nothing is known regarding the development of *S. Lindemanni*.

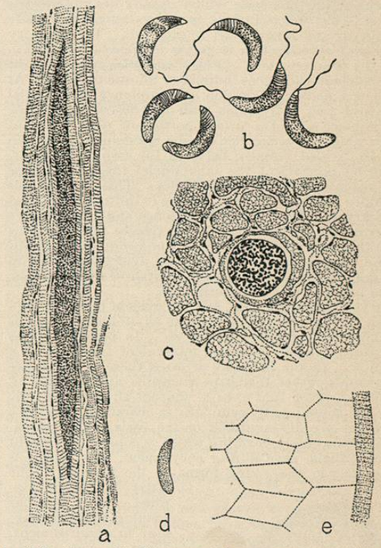

FIG. 5191.—*Sarcocystis Lindemanni* from Human Larynx (except *b*). *a*, Longitudinal section of muscle fibre with fully developed sac. × 250. *c*, Transverse section of same. × 250. *e*, Section showing chambers emptied of pansporoblasts. × 565. *d*, Sporozoite. × 1,350. *b*, Sporozoites of *S. Blanchardi* with polar filaments. × 875. (*b*, From Wasielewski, after van Ecke; other figures from Doflein, after Barbaran and St. Remy.)

The class Infusoria holds the highest rank among Protozoa, and its members are at once distinguished by the presence of peculiar organs of locomotion in the form of fine hair-like protoplasmic processes, the cilia, which are present in at least some part of the life history of all individuals in the group. By virtue of the greatly inferior length, the much larger number present on each animal, and the simple synchronous movement cilia are easily distinguished from flagella. The external zone or ectoplasm is more highly differentiated than in the forms of

Protozoa thus far considered, and the body has in consequence a more permanent form, which tends to acquire in all free species a bilaterally symmetrical structure. In the ectoplasm one finds special contractile fibrils, or myophanes, and peculiar unexplained bodies known as trichocysts. The cilia are arranged in rows, and occasionally fuse into vibrating membranes or stylet-shaped masses, cirri, in furtherance of the motor function. The firm ectoplasm forms at the mouth opening (cytostome) a groove (peristome), or a peculiar funnel-shaped pit (cytopharynx), which serves to admit food particles to the interior of the body. A differentiated anal orifice (cytopyge) is only rarely found. The contractile vacuole is always present, and often two or more occur with a more or less extended canal system branching in all directions.

One of the most striking peculiarities is found in the nuclear conditions. Typically two nuclei are present; a large somatic nucleus or macronucleus, and a small sexual nucleus or micronucleus, which usually lies close to the former. The macronucleus is always single, but there may be several micronuclei to each cell. The ordinary process of reproduction is fission or gemmation, and in this the macronucleus divides amitotically while the micronucleus undergoes indirect or mitotic division. At times one finds conjugation, or temporary and partial fusion of two individuals with the destruction of the macronuclei and of a certain portion of each micronucleus, while the remainder of each micronucleus on each side is divided equally between the two individuals. From the portions of the micronuclei fused there arise new macronuclei and micronuclei. This process has generally been looked upon as one of rejuvenation, and necessary for the continued existence and reproductive power of the individual. Certain recent investigations leave this somewhat uncertain. The complicated details of the process find, however, an evident parallel in changes connected with the fertilization of higher forms, or the union of egg and sperm cells.

Encystment is frequent, and the evident means of providing for unfavorable changes in environment, such as drought, temperature changes, etc. In parasitic forms it is related to the necessary interval of transport to a new host. In the majority of cases these protozoa are commensals rather than true parasites, and in some instances are even said to be of mutual advantage to the host, and consequently symbiotic in character. The two subclasses are distinguished on the basis of the permanence of the ciliary covering which is constantly present in the Ciliata, save during encystment, but which is found only in the young forms of the Suctoria. The latter are also supplied with peculiar sucking tubes for taking in nourishment. They do not furnish any forms found in the human body.

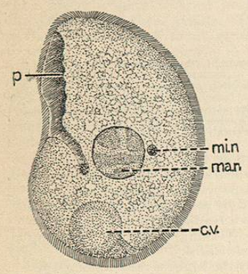

Fig. 5192.—*Nyctotherus faba*. Living. *c.v.*, Contractile vacuole; *ma.n.*, macronucleus; *mi.n.*, micronucleus; *p*, peristome. Magnified. (After Schaudinn.)

The Ciliata are present in large numbers in all fresh-water bodies, and manifest great variety of structure. They furnish many ectoparasitic species on water-living vertebrates and a few endoparasitic in higher forms, including man. The various orders into which the Ciliata are divided are based upon the number and arrangement of the cilia in the adult form. Only two of these orders call for attention here. In the Holotricha there is no spiral zone of prominent cilia or membranellæ leading to the cytostome, and the body possesses only small cilia which are more or less generally distributed. The Heterotricha have an adoral spiral zone of larger cilia, but the remainder of the body is uniformly finely ciliated.

Of the Holotricha one species has been reported from man. It belongs to the genus *Chilodon*, the distinctive features of which are included in the description of the species which follows.

Chilodon dentatus (Dujardin 1841).—(Syn.: *Loxodes dentatus* Duj. 1841; *Ch. dentatus* Guiart 1903.)

Oval, 35–55 μ long by 25–35 μ broad, flattened in ventral face, dorsal aspect strongly arched. Anteriorly a flexible membranaceous projection curved toward the left and carrying several rows of cilia on the lower aspect. Granular endoplasm confined to posterior inflated region; ectoplasm in a thin peripheral layer and forming the anterior projection. Mouth ventral, in anterior portion of the endoplasmic region, normally contracted and hardly visible, cytopharynx directed dorsally and recurved ventrad so as to form almost a complete circle. Two contractile vacuoles, macronucleus large, spherical, in posterior region.

This infusorian has been found once by Guiart, as a parasite of the human intestine in Paris, France. The animals were present in large numbers in the mucus from dysenteric stools. Care was taken to control the source of the parasite and to avoid contamination from external sources, with the result of obtaining from the dejecta on the second day after passage pure cultures of the infusorian. It is a common free-living species, and must be classed in this instance merely as an accidental parasite. Close examination of fæcal discharges will undoubtedly show the occasional occurrence of many such, especially when the resting spores happen to be abundant in the local supply of drinking-water. In this case there is nothing to show that the resting spores did not simply make the passage of the canal, and then develop almost at once in the discharges. The extreme sensitiveness of the species to changes in the environment, which has been commented upon by Guiart himself, makes this explanation of the case more probable. One should recall in this connection the record of Schaudinn, that the resting spores of a Rhizopod, *Chlamydophrys stercorea*, must make the passage of the alimentary canal in man or other animals in order to undergo development. In this case, indeed, the resting spores open in the colon and an amœboid organism emerges which does not assume the testaceous form of the adult until after the fæces are discharged from the body.

The order of the Heterotricha, already generally characterized, includes three species under two genera, which have been reported from the human host. The first belongs to the genus *Nyctotherus* Leidy 1849, which contains flattened reniform species with a peristome along the concave side from the anterior pole to the cytostome at the centre. The cytopharynx is more or less arcuate. The macronucleus is large and nearly central in location. A single contractile vacuole is present. The species of this genus occur as parasites in the alimentary canal of Anura, Myriapoda, and Insecta. A single form has been found twice in the human alimentary canal.

Nyctotherus faba Schaudinn 1899.—Body reniform, somewhat flattened dorsoventrally, left side convex, right concave and notched in the centre. Anterior end bent to the right a little, and on the right side slightly cut out; posterior end broadly rounded (Fig. 5192). Length 0.026–0.028 mm., breadth 0.016–0.018 mm., thickness 0.01–0.012 mm. Peristome a narrow longitudinal slit just at right margin of body, extending from near anterior end to middle of body. Cytopharynx tubular, short, and without guide spine at entrance. Cilia very fine and delicate as well as short. Ectoplasm thin, endoplasm granular, alveolar and without food vacuoles. Contractile vacuole large, located left of middle, near posterior end, emptying through the special anal tube. Macronucleus spherical, 0.006–0.007 mm. in diameter, with chromatin in four or five solid masses near periphery, leaving the intervals filled by a non-staining linin network. Micronucleus 0.001–0.0015 mm. in

diameter, spherical or oval, ordinarily next the macronucleus. Fission and conjugation were not observed. Encysted form oval, easily recognized by the strange macronucleus.

This species has been found only once in Berlin in a patient suffering alternately from diarrhœa and constipation. It occurred in large numbers in the fæces taken direct from the intestine, and was accompanied by *Balantidium minutum* and eggs of *Anguillula* (?) and *Anchylostoma*. The species has an especial interest here since the German physicians suggest from the history of the case that the infection may well have been attained in the United States, where the patient had lived for some time previously. A pathogenic rôle has not been attributed to the species.

Stiles reports in recent correspondence that he has encountered several cases of ciliate infection which could not be identified and at the time more exact study was impracticable. The attention of physicians should be directed more carefully to this group of organisms.

The genus *Balantidium* includes species of oval or ellipsoidal form, circular in transsection, with the anterior end somewhat tapering. The peristome has the form of a flattened funnel with the cytostome at its base. Two contractile vacuoles on the right side, sometimes two others on the left. Cytopyge terminal; macronucleus oval or reniform. The five known species are parasitic in the alimentary canal of man (two species), pig (one species), and amphibia, and in the body cavity of polychætous annelids. For the distinction of the human parasites a key to all five species is necessary. That given here is taken from Schaudinn.

1. Peristome extends to equator of body or further, cytopharynx present 2
   Peristome much shorter, cytopharynx wanting 3
2. Four contractile vacuoles, macronucleus reniform, cyst spherical ..... *B. entozoon* Clap. and Lachm.
   One contractile vacuole, macronucleus spherical, cyst oval ..... *B. minutum* Schaudinn
3. Two contractile vacuoles 4
   One contractile vacuole macronucleus oval, cyst spherical ..... *B. duodeni* Stein
4. Body elongated, spindle-shaped, or cylindrical, *B. elongatum* Stein
   Body oval ..... *B. coli* Stein

Balantidium coli (Malmsten 1857).—(Syn.: *Paramœcium coli* Malmsten 1857; *B. coli* Stein 1867.)

Form oval, slightly truncated anteriorly with very short infundibuliform peristome which lies just to the right of the anterior tip and leads to a short cytopharynx (Fig. 5193). Body 0.07–0.1 mm. long by 0.05–0.07 mm. broad. Ectoplasm and endoplasm distinct; latter with drops of oil and mucus, and according to some observers red and white corpuscles from the host. Macronucleus bean-shaped or reniform, with the small spherical micronucleus adjacent to it. Two contractile vacuoles located on the right side, but no permanent cytopyge. Fission of the free form has been observed. Conjugation has also been seen. Cysts are spherical and possessed of impervious membrane.

This species inhabits the colon of man and the pig. In the latter it occurs also in the rectum and cæcum, and is present regularly in large numbers. The pig may be regarded as the normal host, and in it this species excites no abnormal symptoms. The encysted forms evacuated with fæces are supposed to bring about the transfer of the species all the more easily that the pig is coprophagous; and yet experimental infection has been unsuccessful even in the pig. Grassi and Calandruccio have demonstrated that experimental infection of man is not successful in the case of healthy individuals. The occasional introduction of encysted forms may, however, bring about successful colonization of the canal whenever any pathologic conditions exist in the colon, although Grassi and Calandruccio argue from the slight difference in size and the failure of their experiments that the forms found in man are not of the same species as those from the pig. These conclusions do not seem to have found even limited acceptance.

Malmsten discovered *Balantidium coli* in 1857 in a man who had recovered from an attack of cholera two years before, but had since suffered from diarrhœa. The parasites were abundant in the bloody discharge of a rectal abscess, and even after its disappearance persisted in the fæces, from which they finally disappeared as a result of the use of acid enemata. In the necropsy of a subsequent case the exact seat of the parasite was determined as the anterior region of the large intestine.

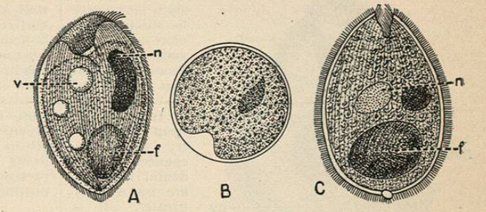

Fig. 5193.—*Balantidium coli*. *A*, *C*, Free; *B*, encysted; *n*, macronucleus; *v*, contractile vacuole; *f*, food mass. Magnified. (*A*, After Leuckart; *B*, *C*, from Braun, after Casagrandi and Barbagallo.)

Many cases have been reported from man since then. Shegalow lists sixty-three in all from Russia, Germany, Scandinavia, Finland, Italy, Cochin China, Sunda Islands, and the United States of America. Strong and Musgrave have added the Philippines to this list. While this parasite has been observed regularly in obstinate diarrhœa, its disappearance is not accompanied with the cessation of the symptoms in all cases, and Balantidia have been found after the diarrhœa has stopped. The earlier idea that these protozoa were the exciting cause of the intestinal disturbances has accordingly given way in part to a view that these protozoa continue and extend the diseased condition, but are not sufficient to cause it. Some authors report, however, that the species penetrates the intestinal wall and causes abscesses in the deeper layers. Solowjev claimed even to have demonstrated them in the blood and lymph vessels of the intestinal wall. This has recently been confirmed by Strong and Musgrave.

These authors, together with several other very recent contributors to this subject, contend very strongly in favor of the pathologic rôle played by the parasite. In most post-mortems lesions have been found similar to those of amœbic dysentery. Brooks found in apes in New York extensive ulcerations in the cæcum, irregular in contour with undermined borders. The mucous and submucous coats were destroyed and the parasites were present in great numbers in the ulcerations, especially on the floor and along the sides. They even pass beyond the limits of the ulcers, apparently following the course of the lymphatic and blood-vessels. It was surmised that the parasites entered the submucosa from the crypts of Lieberkühn, in the depths of which they were often found. The Balantidia were found in the diarrhœtic stools, but disappeared with recovery of the host. But relapses were frequent, and each time the parasites reappeared in the fæces. This is explicable on the basis of their position deep in the glands of the intestinal wall, and emphasizes the difficulty of completely destroying them and preventing a recurrence of the disease.

It is difficult to avoid the conclusion that positive proof of the etiologic significance of these forms is given by the presence of abundant parasites in the lesions and in the tissues in advance of the pathologic changes, and also by their occurrence in the depths of glands and in the submucosa before the start of such lesions at these points. The opponents of this view regard the rôle of the pro-