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The work of Schaudinn is, perhaps, not very familiar to [169] the reader of medical literature, although the discovery of the syphilis organism gave him considerable prominence even in the minds of those who confine themselves to the reviews of purely medical matters.

Fritz Richard Schaudinn was born on the nineteenth of September, 1871, at Roesiningken, a village of East Prussia. He obtained his degree of Doctor of Philosophy on the third of March, 1894. He died on June the twenty-second, 1906. Into this short life of less than thirty-five years, into a working period of twelve years, there was crowded a wealth of work, which, judged by the standard of quantity alone, must stamp the author as a remarkably indefatigable worker. Judged by the higher standard of quality, his work makes of him a genius, one of those truly wonderful master-minds that appear only once in a long period of time. When he died scientific medical research lost its most brilliant exponent, a man destined by training and ability to carry us far along certain lines of work. Although much progress will undoubtedly be made along the paths marked out by him the fullest possible measure of that progress will not be realized until there shall appear another with the trained technic, the keen observation, and the intellect of Fritz Schaudinn.

[1] Read before the Experimental Medicine Section of the Academy of Medicine of Cleveland, January 10, 1908.

[169] Concerning his early education little need be said. He has been dead too short a while for time to have had an opportunity to cast about his life that haze which makes it possible for historians to quarrel as to which teacher or which particular event is of chief importance in determining the mind's development. As a youth he attended the Gymnasium at Insterburg and at Gumbinnen, leaving the latter place in 1890 to enter the University of Berlin. His original intention was to take up the study of philology. His interest was soon transferred, however, to zoölogy, and it was in this latter subject that he obtained his Doctor's degree. His thesis was a description of *Myxotheca arenilogа,* a new species and new genus of the Foraminifera. In July, 1894, he went to Bergen, Norway, for the purpose of collecting material, returning to Berlin in October as Assistant in the Zoölogical Institute.

During the year 1894 there appeared a number of papers which mark the beginning of Schaudinn's interest in the variations of the reproductive process among the protozoa. For Calcituba and several other marine Foraminifera he described, as a new type of nuclear multiplication, the loss of the membrane of the adult nucleus, the distribution of the chromatin throughout the cytoplasm, and the formation of multiple daughter nuclei from the scattered chromatin granules. Nine years later Richard Hertwig described a similar phenomenon of chromatin diffusion in *Actinosphærium eichorni* and gave to it the name of chromidium formation. In the case of this latter organism, however, Hertwig showed that the process is associated with certain of the vegetative functions of the cell and not with reproduction. Further work, particularly by Schaudinn, by Hertwig, and by Goldschmidt, established the important rôle that chromidium formation plays in the reproduction and the nutrition of many protozoan cells. In this doctrine, which forms the major part of Hertwig's kern-plasma relation theory, we have a light which must lead us through the darkness that marks the present state of cellular physiology and pathology.

Another of Schaudinn's contributions of 1894 was the description of *Camptonema nutans,* a multi-nucleated rhizopod supplied with radiating pseudopodia. The latter, besides the

already well-known movements due to flowing of the plasma, [169] have the power of rotation and of flexion and extension. The axial fiber of each pseudopod passes into the cytoplasm and its inner end becomes attached to a nucleus by a cap-like enlargement. This intimate relationship of external organelle and nucleus Shaudinn believed to be an expression of such a controlling influence of the latter over the former as exists in metazoan spermatozoa. The correctness of this view was proven by his later work upon the development of the locomotory apparatus of *Trypanosoma noctuæ,* and the idea constitutes an important addition to our knowledge of the functions of the nucleus.

In 1894 there appeared, also, the description of multiple division of the shelled amœba, *Hyalopus dujardinii,* with the formation of flagellated young forms. This observation, that an adult protozoan with the organelles characteristic of one class may produce young with the organelles supposed to be specific of an entirely different class, may be considered the beginning of Schaudinn's long series of additions to our knowledge of the protozoan life cycle. The importance of the recognition of the various changes that a protozoon may show in its life history has been justly insisted upon by Calkins. He would make the presentation of the entire cycle of a protozoon the prerequisite for its acceptance as a new species. He demands some ground principle which shall unify the science of protozoölogy. Concerning Schaudinn's part in supplying this principle Calkins says: "It was the genius of Schaudinn to establish such an unifying foundation, and in his clear perception of the importance of the life cycle we have the keynote of our present-day conception of the protozoa." In my attempts to teach to students an outline of protozoölogy I, likewise, have been struck by the large share [170] that Schaudinn has had in the advancement of this side of the subject. I have been accustomed to consider the reproduction of the protozoa the most important chapter in protistology. In looking over the notes in which I have tried to summarize the nuclear and morphological variations that make up protozoan life histories I find that the chapter is largely a recapitulation of Schaudinn's work.

[170] Dimorphism of adult organisms has long been known among the Foraminifera. It remained for Schaudinn and Lister, in 1895, independently of each other, to explain the genesis of this condition in *Polystomella crispa,* and to show that the dimorphism is part of a life cycle in which one form, multiplying by flagellospore formation, alternates with the other form, which multiplies by the production of amœbospores.

Work upon *Amœba crystalligera* in 1894, and the discovery of *Amœba binucleata* in 1895, and of *Paramœba eilhardi* in the following year, resulted in observations upon the finer occurrences in the processes of direct and indirect nuclear division. For Paramœba Schaudinn described a cycle much like that of Hyalopus. The point of chief importance in the former organism is the possession of a nucleus-like body in addition to the true nucleus, both being present in all the stages of the cycle. The true function of this " nebenkoerper " appeared during the division of the flagellospores. During this stage the body acts exactly like a centrosome. Similar conclusions as to the function of the centralkorn of the Heliozoa were arrived at from a study of *Acanthocystis aculeata,* published in 1896. Furthermore, proof of the primary intra-nuclear origin of a centrosome which later becomes permanently extra-nuclear, was furnished. In this respect Acanthyocystis seems to be intermediate between those flagellates possessed of nuclei in which the division material is permanently intra-nuclear and *Paramœba eilhardi* and *Noctiluca milaris,* in which, as in metazoan cells, the centrosome is permanently extra-nuclear. In Acanthocystis there is much the same relationship between the axial fibers of the pseudopodia and the centralkorn as exists between the fibers and the nuclei in Camptonema. The establishment of the kinetic nature of the centralkorn, its control not only of the energy of nuclear division but also of the movements of the external organelles, was confirmed and amplified by later work upon the nature of the blepharoplast of the trypanosomes.

An important fact brought out during the same year in a study of *Actinophrys sol* was the occurrence of fertilization at one stage of the life history by a process intermediate between

the partial karyogamy or conjugation of the ciliates and the [170]
complete karyogamy or copulation of other forms.

In 1897 Schaudinn, in association with Siedlecki, showed that in certain of the Coccidia there occurs a copulation of sexually differentiated gametes, a process strikingly like the fusion of ovum and spermatazoon. Further results of this work appeared in 1900, when the complete life cycle of *Eimeria schubergi* was published by Schaudinn. This paper is an example of the ideal in research. The array of facts presented indicates the possession of remarkable technical perfection of hands and of eyes, experimental resourcefulness, an intuitive knowledge of what to look for, and the intellect necessary for the proper interpretation of the findings. And above all, the facts are recorded in language that is fascinating.

In 1898 Schaudinn was promoted to Privatdocent in the University of Berlin. The greater part of this year was spent in a collecting trip to the Arctic Ocean. The results of this journey appeared under the combined editorship of Schaudinn and Roemer in a collection entitled "Fauna Arctica," four volumes of which have appeared.

The description of the complete life cycle of the newly-discovered rhizopod, *Trichosphærium sieboldi,* appeared in 1899. So thorough was this piece of work that not a single fact remains to be added to the life history as published by Schaudinn. The cycle of Trichosphærium is not quite so complicated as the coccidian cycle published during the following year, since in the former the copulation is isogamous.

During the same year he was able to report a confirmation of the work of Ross and of Grassi upon the cycle of the malarial parasite, and pointed out the analogies in the life histories of this organism and of the Coccidia.

The extreme biological importance of Schaudinn's observations had become quite evident. The German Government, to whose fostering spirit is due much of the scientific eminence of the Germans, was quick to realize the aid that a man of his training and ability might bring to protozoölogy as applied to medicine. In 1901 he was sent by the Kaiserliche Gesundheitsamt to Rovigno for the purpose of devoting himself

[170] more particularly to the pathogenic protozoa. He remained in Rovigno until 1904. This period was marked by the appearance of a number of observations of direct value to medicine. Of these, two very important ones concern the malarial parasite and the intestinal amœbæ. He was able actually to see the entrance into the red corpuscle of the malarial sporozoite, the end stage of the sexual cycle in the mosquito, and of the merozoite, the end stage of the asexual cycle in the human being. Furthermore, he established the fact that the relapse in malaria is due to a peculiar biological modification of the normal cycle of the parasite. He showed that the makrogametocytes, which normally are destined to fertilization in the mosquito's stomach, may remain in the human blood and fail to be fertilized. In the internal organs they reduce their chromatin. Parthenogenetic division results in the establishment of a fresh series of asexual generations, manifested clinically by the relapse.

In 1860 Lambl, and in 1870 Lewis and Cunningham, noted the occurrence of a new species of amœba in the intestinal contents of persons ill with tropical dysentery. This organism was more accurately described by Loesch in 1875 and named *Amœba coli.* For many years there has been considerable controversy between medical men, on the one hand, and biologists, on the other, concerning this protozoon. In amœbic dysentery clinicians saw a fairly well characterized disease. For pathologists, the anatomical findings in this
[171] condition were even more specific. Medical workers became convinced of the etiological relationship of the organism to the disease. The occurrence of an amœba, not to be distinguished from *Amœba coli,* in the intestines of healthy persons caused the biologists to maintain a rather skeptical attitude as to the pathogenicity of *Amœba coli.* For some of them it was only a harmless secondary invader. Others considered it pathogenic, but only after the lesions had been started by bacteria. Before one could state that dysentery is due to an amœba biologists justly demanded morphological differences which would permit one to distinguish between the organism associated with disease and that found in the healthy intestine. It remained for Schaudinn to describe

such differences. He showed that in the human intestine [171] there may be present at least two species of amœbæ, very much alike at first glance, but showing marked differences in their modes of reproduction. To the species found only in association with dysentery and its complications he gave the name *Entamœba histolytica*. The other, the one found in the healthy intestine, the one which corresponds more nearly to Loesch's description, he called *Entamœba coli*. There are morphological differences which, now that they have been pointed out, permit us to differentiate the two. Concerning the modes of reproduction, Schaudinn showed that the pathogenic amœba gives rise to a number of small encysted amœbæ whose nuclei are derived from the chromidial network of the parent organism. In the reproduction of *Entamœba coli* a single amœba encysts and two daughter nuclei are formed from the original single nucleus. These undergo reducing divisions, then fuse and fertilize each other. Of the eight daughter amœbæ which are finally formed within the mother cyst each receives a single nucleus produced by the division of the synkaryon.

In the establishment of autogamy among the true fertilization processes we have an hypothesis rich in possibilities for biological research. The work of recent years upon the reproduction of the protozoa, the work of Schaudinn in particular, has completely overthrown whatever last vestige of possibility there may have been in the once famous doctrine of the immortality of the protozoa. Although for many of these unicellular animals no phenomenon of fertilization is known this must be ascribed to a lack of sufficient research, and there does not seem to be any probability that there can be any exception to the general rule that fertilization is necessary for the continued multiplication of every animal cell. In cells of only one kind is there an apparently unlimited proliferation without fertilization. I refer, of course, to the cells of malignant tumors. The gametoid theory of Farmer, Moore, and Walker has not received confirmation, and Bashford and Murray's conjugation of tumor-cell nuclei can be more satisfactorily explained as something else. The continued multiplication of tumor cells without fertilization seems improb-

[171] able. If fertilization does occur, so primitive a process as autogamy must be borne in mind, and the proof of its occurrence would place one phase of the tumor question upon a firm biological basis.

While at Rovigno Schaudinn published the results of work upon two new species of bacteria. That upon *Bacillus bütschlii,* a parasite of the cockroach's intestine, is extremely important. The organism is characterized by its unusually large size and by the fact that it forms two endogenous spores. In this case, therefore, spore formation is not merely a protective arrangement, but it is also a true reproductive process which results in an increase in the number of individuals. Schaudinn showed that *Bacillus bütschlii* is made up of an alveolar protoplasm, in the interalveolar spaces of which lies a network of granules which are stained by the chromatin dyes. In the division during the vegetative state some of these granules become aggregated at the center of the bacillus, and division occurs through this central mass. In spore formation the greater portion of the granular material becomes collected at each pole into a large mass, which has the morphological characteristics of the nuclei of higher plant and animal cells. Autogamous fertilization then occurs between these two nuclei, followed by the final formation of a spore at each end of the bacillus. Grassi, in 1900, made the statement that the complete life history of not a single bacterium was known. That division could continue indefinitely without a sexual act he considered improbable, and he explained the dying out of certain bacterial epidemics upon the supposition that the conditions necessary for this sexual act were wanting. In view of Schaudinn's work upon *Bacillus bütschlii* in 1902 Grassi's words appear prophetic.

The work upon *Bacillus sporonema* is interesting chiefly because spore formation occurs after an abortive attempt at the ordinary vegetative division. It would seem that sporulation does not happen until the energy necessary for transverse fission is completely dissipated. In a review of Schaudinn's publications upon *Bacillus bütschlii* and *Bacillus sporonema* Mesnil says: "Their importance is very great, at once for the comprehension of the morphology of the Bacteriaceæ, for

the general significance of sporulation in the lower organisms, [171]
and for the phylogenetic seriation of the phenomena of sexuality."

In 1904 Schaudinn was recalled to Berlin by the Kaiserliche Gesundheitsamt and was made director of the newly-established division for protozoölogy. The first work undertaken after his return was an investigation into the modes of infection in ankylostomiasis, with the object of devising means for the prophylaxis of this disease. Looss had shown that the larvæ of *Ankylostomum duodenale* may enter the body by way of the skin. van Durme had shown the same thing for *Strongyloides intestinalis*. Their views were attacked by the Italian, Piéri. By experiments upon monkeys Schaudinn established beyond controversy that the larvæ of *Ankylostomum duodenale* may penetrate the normal skin and give rise to an intestinal infection.

During 1904 Schaudinn published two further papers, the results of work done while at Rovigno. Of these, one was purely practical in nature, like the Ankylostomum work. By the prophylactic treatment with quinine he freed the village of St. Michele di Leme, in which malaria was endemic, of [172]
this disease.

The other, upon the alternation of generations and of hosts of two of the blood parasites of a species of owl, may be considered the most important of all of Schaudinn's researches. This paper is too rich in valuable ideas to permit of adequate condensation. Only three of the more epoch-making points may be stated.

Firstly, he showed that *Halteridium noctuæ,* a parasite of the red blood corpuscles, and *Trypanosoma noctuæ,* a parasite of the plasma, are portions of a single cycle, the sexual part of which occurs in a mosquito. In other words, he established the intimate relationship of the Hæmosporidia and the Trypanosomidæ, two groups which had previously been widely separated in the zoölogical classification of the protozoa. Of the four classes of the protozoa three were fairly sharply characterized by their external organelles. The members of the remaining class, the Sporozoa, had in common only their obligate parasitism and their reproduction by multiple fission.

[172] Recent work has shown that the latter process is not at all limited to the Sporozoa. Schaudinn's work, therefore, was revolutionary. Based upon it and upon the confirmation that it has received Hartmann very recently has proposed a classification from which the Sporozoa, as a class, have been removed, and in which the Hæmosporidia and the Trypanosomata have been united to form a new flagellate order, Binucleata.

Secondly, Schaudinn traced the derivation of the blepharoplast of the trypanosomes from the nucleus by a heteropolar mitosis, and the development of the motor apparatus from the former by a second mitosis.

Thirdly, he established certain points of fundamental importance for our conception of the process of fertilization.

One portion of the owl parasite research illustrates the thoroughness that marks all of Schaudinn's labors. In following out the life cycle it was necessary for him to work with the mosquito. He added a number of new facts relating to the anatomy and physiology of this insect.

In May, 1905, Schaudinn, working in collaboration with Hoffmann, announced the presence of a characteristic spiral organism in certain of the products of syphilis. This organism they called *Spirochæta pallida*. Several other short papers followed in rapid succession, all dealing with syphilis. In these earlier papers it was not claimed that *Spirochæta pallida* is the cause of syphilis. Schaudinn and Hoffman contented themselves with a description of the organism and with statements of the lesions in which it had been found. In two years there has appeared an immense literature dealing with the relationship of *Spirochæta pallida* to syphilis. It is unnecessary here to go into the arguments which favor the etiological relationship of the organism to the disease. They may be summarized in the brief statement that in the minds of competent observers such a relationship has been established. The final solution of the much-discussed question of the etiology of syphilis, important as it was, brought into play only one of the many qualities which made Schaudinn preeminent. I refer to his extraordinary training in the use of

the microscope, a training which permitted him to see what [172] had for so long entirely escaped numerous investigators.

In a paper published in October, 1905, Schaudinn described the morphological characteristics of several species of spirochætæ. He showed that the outline of a cross-section of the body is flattened because of the presence of an undulating membrane, that there is present a condition of nuclear dualism, and that the body form is flexible rather than fixed. He concluded that the spirochætæ are protozoa and that the genus is closely related to the Trypanosomata. For *Spirochæta pallida* he could not certainly demonstrate an undulating membrane. He stated, further, that the body outline in cross-section appears circular, and that at each end there is a flagellum-like prolongation of the periplast. These characteristics warranted the establishment of a new genus, Treponema, for the syphilis parasite.

In the wealth of material published by Schaudinn up to this period he had confined himself to terse presentations of actual observations. He neglected the theoretical considerations of his work. For this he has been criticised. He was only thirty-five at the time of his death. He was not permitted to live to that Oslerian age when a man may cease active productive work and may properly begin philosophical theorizing. However, on the thirteenth of June, 1905, in a paper entitled "Neuere Forschungen über die Befruchtung bei Protozoen" and presented before the Deutsche Zoölogische Gesellschaft, he did state some of the theoretical conclusions to which his work had led him.

Nuclear dimorphism is the rule among the highly-organized Infusoria. In the members of this class the relationship of the micronucleus to division and to conjugation, and that of the macronucleus to the vegetative functions of the cell have long been known. In the work upon *Trypanosoma noctuæ* Schaudinn had established the origin of the blepharoplast and of the nucleus from a single nucleus. He had shown, also, that the function of the blepharoplast is a kinetic one, controlling the energy of mitosis and the movements of the motor apparatus. He postulates, therefore, that nuclear dualism is a condition common to all protozoa; in some, evidenced by the

[172] presence of two distinct nuclei, as in the Infusoria and the Trypanosomata; in others, only by physiological differences at some stage of the life cycle. The possession of nuclear properties, some of which are somatic or vegetative in nature, the remainder reproductive or animal, gives to every protozoan cell two forces which are constantly antagonizing each other. There is a perpetual tendency for one or the other of these forces to become predominant. If the vegetative chromatin gains the upper hand, sexual differentiation into a female cell occurs. If the animal characteristics win out at the expense of those of a somatic nature, differentiation into a male cell results. When sexual differentiation has been produced the antagonism is at its height and will lead to cell death because of the final complete loss of the characteristics of the weaker nature. The death of the cell is inevitable unless there is
[173] produced a balance between the antagonistic nuclear forces. This is accomplished by fertilization, and the result is an indifferent cell in which the warring nuclear properties are approximately balanced and in which the struggle can begin anew. The fertilization, when it occurs, is a double one. The propagatory chromatin of one cell fuses, finally, not only with chromatin of a like nature in the other cell, but also with the somatic chromatin.

The correlation of Schaudinn's views upon nuclear dualism and upon its relationship to fertilization and of Hertwig's kern-plasma relation theory and its bearing upon fertilization need not be attempted at this time. I do not think that they are at all antagonistic. They harmonize with each other and complete each other. If both are borne in mind they form a combination which makes a working hypothesis that ought to yield results in the investigation of a number of problems of interest in pathology and physiology.

Early in 1906 Schaudinn was called to Hamburg by the Institut für Schiffs- und Tropenhygiene to become the head of the division for protozoölogy which he was to organize. Here he continued his work upon syphilis. Several short papers upon this subject were published after the author's death by von Prowazek. From a study of sections treated by the silver nitrate method Schaudinn had become convinced of

the etiological relationship of *Treponema pallidum* to syphilis. [173] He also adduced further facts to establish the longitudinal division and the protozoan nature of the parasite.

In the twelve years of his working life Schaudinn saw protozoölogy become a very important branch of zoölogy, and, largely through his own work, saw it add much to general biological knowledge. He saw protozoa study become a science of great value to medicine, not only through the results it has yielded in investigations of the etiology of disease, but also through the help that it offers toward the solution of many general problems. He saw the contributions to the literature of the subject reach such numbers that they demanded a publication devoted to them alone. This journal, the Archiv für Protistenkunde, he founded in 1902.

What would have been the ultimate results of Schaudinn's labors, had he lived to complete them, cannot be imagined until they shall be taken up by another equally gifted. In the development of his own work, his earlier purely biological researches and the transition to the later ones more directly applicable to pathology, is foreshadowed the path which pathological research must take in order to add anything fundamentally new to our knowledge.