

REVIEW OF THE LITERATURE UPON THE INTERNAL LOCALIZATION OF THE GONOCOCCUS.

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During the past ten years many cases have been published of internal complications of gonorrhoea. The importance of these and the desire to call attention to these observations has caused the writer to collect all of the available literature upon the subject from the time of the discovery of the gonococcus as the specific exciting agent of gonorrhoea by Neisser.

Clinicians and pathologists have been actively engaged in investigating the symptoms of local conditions of such cases of gonorrhoea as are complicated by a localization of the poison at other places in the body than in the genital organs. The fact that a form of articular rheumatism at times accompanies a gonorrhoea has been known for many years, but the question as to whether the gonococcus bore a direct relation to it has remained an open one until within recent years. Following the elucidation of this subject came the fact that localizations of this microorganism may occur in other places than the joints. Many reports appear of cardiac complications and still more recently of pleuritic, cutaneous and even osseous manifestations of gonorrhoea.

With the introduction of the Wertheim nutrient medium (blood serum agar) for the cultivation of the gonococcus, our knowledge as to the role which the gonococcus plays in these various complications has become far more exact.

Petrone (1), Kemmerer (2), Bousquet (3), Bergman (4), Smirnov (5), Sahli (6), Deutschman (7), Jacquet (8), Stern (9), Tollermer and Macaigne (10) all found diplococci resembling the gonococcus in form and in their behavior to reagents, that is decolorized with Gram's solution, in the joints. Paltauf and Lang (11) were the first to find the gonococcus in the joint effusions and to confirm it by cultivation on nutrient media. Later Lindeman (12) obtained it in pure culture from an abscess in a finger during an attack of acute gonorrhoea. He also obtained it in the joint after ophthalmia neonatorum in a culture, but there were some contaminations. Hock (13) also obtained it in pure culture from a knee joint in an infant with gonorrhoeal ophthalmia. This case and the culture were seen by the writer. Colombini (14) reports a case of gonorrhoeal inflammation of the joint in which he obtained a

microorganism resembling gonococcus morphologically and tinctorially. The fluid removed from the joint when inoculated upon ordinary media was shown to contain no ordinary pus organisms as the media all remained sterile, but upon inoculating tubes of human blood serum agar, he obtained pure cultures of the gonococcus in abundance. In order to prove its virulence and that the organism obtained was identical with the gonococcus, he inoculated two previously healthy men by inserting a small amount of pure culture into the urethra, under all possible precautions; within two days the first clinical symptoms appeared and the further development revealed typical cases of gonorrhoeal urethritis. He obtained the same results upon inoculating the urethra of dogs with a pure culture. He examined the blood of a patient who had been suffering from rheumatism and found no gonococci. He therefore believes that transmission of the virus occurs through the lymph vessels, although its transmission through the blood is by no means excluded.

Bordone Uffreduzzi (15) reports a case of a young girl of a good family suffering from gonorrhoea, who did not consult a physician at first, because she desired to keep the disease secret. Soon after this a polyarthritis developed and the physician who was called confirmed gonorrhoeal vaginitis. On account of the fact that the inflammation of the knee joint was very severe, an operation was proposed. Under all bacteriological precautions some of the effusion into this joint was removed. In the purulent and fibrinous fluid Uffreduzzi observed diplococci contained within the pus cells, which morphologically and tinctorially completely resembled those contained in the vaginal pus. He obtained the same in pure culture on blood serum agar. In order to exclude all doubt that the gonococcus was the cause of the arthritis, he inoculated a man 23 years old, who had never had any venereal disease, and who had had no coitus for four months prior to the inoculation. He had previously examined the sexual organs, made cover glass preparations and found only smegma bacilli about the genitals. He carefully washed off the glans and the urethral orifice with sterilized water and brought a small amount of pus from the second generation of the culture originally made from the joint exudate, upon the mucous membrane, just beyond the meatus, taking care not to wound it. After two days, a typical gonorrhoeal urethritis with all the clinical characteristics appeared and with the usual symptoms.



In the pus cells discharged, he found a very large number of microorganisms which microscopically and upon inoculation on blood serum (human) and calves' serum agar, showed typical colonies of gonococci which were demonstrated at the time of the reading of the paper by the author. He found that the vitality and virulence of the microorganism was soon lost.

Neisser (16) reports a case of a woman 46 years of age, admitted with acute gonorrhoeal rheumatism affecting the right middle finger and ankle. The disease began four days previously, with a marked rise of temperature. Both joints were very much swollen. Upon puncture of the ankle joint he obtained a small amount of thin, whitish fluid containing a great many pus cells. Microscopically he found a very large number of micrococci contained within the pus cells. Cultures on ordinary agar remained sterile, cultures upon Wertheim medium on plates and in tubes showed a large number of typical colonies of gonococci. He confirmed his diagnosis by the microscopic examination. There was fluctuation over the infected joint and the fluid removed from the joint also contained gonococci in a very large number. This was also confirmed by cultivation upon blood serum agar. The joint contained exuberant granulations, and microscopic examination of these revealed the presence of gonococci in them. The pus from the joint itself contained few gonococci, hence Neisser believes that this throws light upon the negative findings in gonorrhoeal joints, verifying the theory advanced by Jadassohn (17), who claimed that the growth and presence of the gonococcus is found, as a rule, in the synovial membranes, and only when the exudate is very large do we find it in the same, hence in Neisser's case there were very many present in the fluid taken from the ankle joints, which was large in quantity, while in the joint where granulations were exuberant and the fluid small in quantity there were but few.

Jadassohn (17) and Stanziale have reported such cases in which cultivation of the Wertheim media and inoculation on the human urethra have resulted negatively, yet there was little doubt but that they were gonorrhoeal in origin.

Councilman (18) in a case which will be spoken of later, found diplococci in a knee joint effusion from a case of acute gonorrhoea, which completely resembled the gonococcus in form and tinctorially, but which he was not able to cultivate, yet he regarded them as typical gonococci, the case being accompanied by cardiac manifestations.

The frequency with which effusions into the tendon sheaths occur during the course of gonorrhoea is almost as great as its localization in the joints. Jacoby and Goldman (19) report a case in which they found characteristic gonococci in the pus in a suppurative tendo-vaginitis of the tibialis anticus muscle, they decolorized with Gram's solution, their cultivation on ordinary media resulted negatively.

Bloodgood and Flexner, quoted by Thayer and Blumer (20), found the gonococcus in pure culture from a similar case of tendo-vaginitis complicating gonorrhoea. Why localization of the gonococcus occurs in the tendon sheaths and joints more frequently in certain climates is still an open question. Hehir (21) observed it as a very frequent complication combined with heart lesions in India. Undoubtedly many cases occur clinically whose gonorrhoeal nature is entirely overlooked, either that the complication occurs during a time when the urethritis is latent or in a chronic stage. The fact that the joint effusions when inoculated from such cases upon the specific medium for the cultivation of gonococcus shows no growth, does not, according to the most recent writers, exclude the fact that it may be gonorrhoea in origin. There are sufficient cases now on record in which the presence of the gonococcus has been confirmed microscopically and bacteriologically with reinoculation on the human subject to show that there is a specific form of rheumatism, due to the gonococcus. The manner in which the organism reaches the internal organs can also no longer be considered an open question, since Wertheim (22) investigated a case of gonorrhoeal cystitis, microscopically found the veins in the submucous tissue thrombosed by masses of gonococci. This shows how joint infection may occur, and that we may speak of gonococciopyemia. In the same case in which Wertheim observed this condition, a gonorrhoeal suppuration of both elbow joints had occurred. The other serous membranes are equally as well affected by gonorrhoeal inflammation. That gonorrhoeal peritonitis may occur has been well known for some years past, and its discussion will be taken up in a later article.

Talamon (23) was the first to call attention to the fact that a pleurisy with effusion might occur as a complication of gonorrhoeal urethritis. Cornil and Klippel (24) reported a case of pleural effusion occurring with subacute gonorrhoea. Souplet (25) reported several cases of such effusion accompanying an endo and pericar-

ditis. None of these cases were confirmed by microscopical and bacteriological examination.

Mazza, quoted by Bordone Uffreduzzi (26), was the first to prove bacteriologically that the gonococcus was the cause of the exudative pleuritis. The case was that of a girl 11 years old, who had been infected by a man suffering from an acute gonorrhoea under the popular superstition that the latter could be cured by coitus with a virgin. The girl soon after, had effusion into several joints and into both pleural cavities, as well as peri and endocarditis, of which clinical symptoms still exist. Mazza examined some of the fluid from the pleural cavities which he had obtained under all possible precautions, he found micro-organisms corresponding to the gonococcus in form and in reaction to stains, inclosed within the leucocytes and the endothelium. Inoculated upon blood serum agar he obtained a pure culture of gonococci.

Recent observations show that the serous membranes next to those of joints most frequently affected by gonorrhoeal inflammation are the endo and pericardium.

Malignant endocarditis as a sequel of gonorrhoea was first described by Brandes in 1844. He reported a case of gonorrhoeal rheumatism with endocarditis. The next mention of this disease is by Lorrain, in 1866, a case of fatal mitral insufficiency complicating gonorrhoea. Marty (27), Morel (28), Trager (29), Schedler (30), Leyden (31), Martin (32), Derignac (33), Velden (34), Glucinski (35), Genzinsery (36), all report cases of endocarditis complicating rheumatism. Of these Morel collected thirteen cases complicating gonorrhoeal rheumatism, and came to the conclusion that gonorrhoeal rheumatism was not a necessary intermediary between the specific lesion in the urethra and those of the mucous membranes, but this coexistence is the usual condition. Martin observed a case with general septic symptoms in which there was a pericardiac effusion, and many metastases and which ended in death under a clinical picture of septicaemia.

Souplet (25), His (38), Leyden (37), Councilman (14), Wilms (39), Leyden (40), all observed gonorrhoeal rheumatism complicated by endocarditis. The latter observed it in four cases, accompanied three times by a hemorrhagic eruption spread over the entire body and one by a recurring petechial eruption. Similar cases are observed by His. All of these cases in which septic symptoms were present, with the exception of Litten's, ended fatally and showed chiefly

an affection of the aortic valves and in the non-fatal cases the insufficiency of the mitral valves was diagnosed. Pericarditis was found by three authors and myocarditis by four. Genzinsery, who collected 31 cases, states positively that endo and pericarditis occur as a complication of gonorrhoea, with or without a preceding articular rheumatism, and that their course is the same as in ordinary ulcerative endocarditis leading to valvular defects. Post-mortem endocarditic ulcerations and vegetations were found most frequently on the aortic valves, and in some of the cases, myocarditic areas. In the infarcts of the spleen, kidney, in the liver and in the prostate and testes no microorganisms were found, in other places a microorganism resembling gonococcus in form and in its behavior to stains.

Councilman (25), reported a case of a man who first had an effusion into the knee joint, ten days after the beginning of the attack of gonorrhoea. Other joints were soon affected. He died after five and a half weeks with pains in the chest. He found in the knee and in the peri and endocardium, acute inflammatory processes, differing considerably from the usual purulent ones. There was a hemorrhagic exudation into the pericardial cavity, a gelatinous soft area in the endo and myocardium. He found the gonococcus microscopically freely, yet he did not prove it by culture. In the urethra he found a typical gonorrhoeal urethritis, with gonococci in the superficial layers of the mucous membrane.

Leyden (40), was the first to claim positively that he found the gonococci in the endocardiac vegetation. The case was one of ulcerative endocarditis, following gonorrhoea, complicated by epididymitis and urethritis. Culture on ordinary media taken from the patient's blood during life, and from the left ventricle post-mortem, gave negative results. He believed, however, that the diplococci which he had found in the thrombotic mass on the valves were gonococci; first, because they were biscuit diplococci, second, because a large number of them lay within the cells in the characteristic manner, third, because they were decolorized by Gram and by alcohol and by oil of lavender.

Amongst the more recent articles upon this subject are those of Thayer and Bloomer (20), Dauber and Borst (41), Michaelis (42), Finger, Ghon and Schlagenhauser (43). The first named reported a carefully observed case of ulcerative endocarditis occurring in a widow 34 years old, who three months previous had suffered from

"rheumatism" in the finger, wrist, knees and shoulder, apparently not severe, and wandering. Three days before her admission she became worse and the day prior to her admission there was a distinct chill. Examination of the heart showed that it was increased to the left, maximum impulse in the fourth and fifth intercostal space, there was a presystolic and systolic murmur with an intervening first sound. The urine contained a large amount of pus and epithelial cells; the patient had irregular chills accompanied by an exacerbation of her fever, the spleen was enlarged later the second pulmonic sound was accentuated, there was a pericardial rub. She died three weeks after admission. Thrombi were found on the mitral valves, a pedunculated mass was found on the aortic segment which when removed left an ulcer. Microscopically the valves showed subacute endocarditis with a very large number of diplococci, biscuit-like in shape, at times extra, but the majority intra-cellular. They did not demonstrate the gonococci by culture in any of the organs. The vagina and interior of the uterus were covered with a thin opaque exudate containing cocci having the morphological features of these of the valves and decolorized by Gram. Culture made from the blood during life showed typical colonies of gonococci ten days before death on blood serum agar and again six days before death. By the sixth day on reinoculation from tube to tube the organism died out. The blood examination made post-mortem on bullocks blood-serum agar and ordinary agar-agar resulted negatively. They concluded that the microorganism found in the heart was the gonococcus, because its form and arrangement were characteristic, because they did not grow on ordinary media, because they were decolorized by Gram and were, for the majority, intra-cellular and in the valve thrombus. They spoke of a second case in which Lazaar and one of the authors obtained the gonococcus three times during life from the blood, in a second case of ulcerative endocarditis which is soon to be published.

Michaelis (42), an assistant of Leydens, reports as a second observation to that of Leyden, a case in which there was an ulcerative endocarditis affecting chiefly the aortic valves, occurring during a three weeks old attack of gonorrhoea in which there was a systolic murmur over the aorta during life. Cultures made from the vegetations on the Wertheim media resulted negatively, yet the gonococci found in the vegetation microscopically showed typical morphological and tinctorial properties.

Dauber and Borst (41) reported a case of a young woman 20

years old affected with gonorrheal urethritis, rheumatism and tendovaginitis in which after high temperature which followed a continuous remittent type of fever, all the signs of aortic insufficiency were found several weeks after admission, the heart having been found normal upon admission. Frequent cultures during life of the blood gave negative results. The post-mortem showed an ulcerative endocarditis of the aortic valves with abscesses in the myocardium. The vegetations and the abscesses contained diplococci resembling gonococci perfectly; all of the media inoculated remained sterile. The author concluded on account of these negative findings that it is not correct to assume that the gonococci are the cause without positive culture results, yet they did not deny the possibility of gonorrheal endocarditis, for they consider in their case the urethra as the only possible infection atrium.

This fact, that the diplococci found upon the valves of the heart in such cases are not gonococci is also maintained by Wilms.

The case reported by Finger is one of the most convincing which have yet been published. He reports a case in which the sterility of the culture excluded all other microorganisms, on the other hand the microscopical findings were so characteristic that the author positively believes that the gonococcus is the cause of the endocarditis and that its lack of vitality is to be taken as the cause of the negative cultures on the ordinary and specific media. A young man, 19 years of age, previously healthy, acquired gonorrhoea in March, 1895, for the second time. On the 15th of April, 1895, had severe pain and swelling of the right knee, there was no previous history of rheumatism, cardiac disease, syphilis or alcoholism. He was admitted to the hospital on April 29, 1895. Cultures from the urethra showed typical gonococci. Upon the following day a loud diastolic murmur was heard over the aortic valve which increased in intensity. The urethra discharge ceased spontaneously on the 30th. Death took place on the third day of May as a result of pulmonary edema. The post mortem showed an acute endocarditis of the aortic valves with insufficiency of the same and hypertrophy of the left ventricle, suppurative arthritis of the knee and urethritis. Examination of the cardiac vegetations showed diplococci having all of the characteristics and taking the stain equally like gonococci from a pure culture. Cultures made from the vegetations, from the joint, from the urethra and blood gave negative results. They concluded, first, that ordinary pus microbes could not be found microscopically in the deposits on the valves, hence they were absent, and there was no mixed

infection, second, the gonococci of the endocarditis had exhausted their vitality and could not grow, and an actual culture of the gonococcus for future cases is not necessary to show that the inflammation is of gonorrhoeal origin, therefore, since the gonococci appear in the tissues in such characteristic form a microscopical diagnosis is possible and can under favorable circumstances be of the greatest value. Their conclusions are as follows: 1. There exists an undoubted malignant endocarditis caused by the gonococcus. 2. The cultivation of the gonococcus in these cases which have high temperature for a number of days before death become very difficult, because they lose their vitality. Nevertheless the gonococcus shows such characteristic features that its recognition from microscopical examination alone is justifiable. If the gonococcus is the cause of the rapidly fatal disease certain differences exist between them and pus microbes. The mode of identification is by means of their reaction to stains, their intracellular situation, the pus cocci invade the tissues more deeply, while the gonococci are only present in tissue spaces and cavities, the gonococci are killed by high temperature existing for several days before death while the pus cocci are not.

Finally, to show that the condition of gonococco-pyemia may exist, Bujwid (44) reported a case in which during an attack of gonorrhoea, after passing sounds the patient had a chill and severe pain, several days afterward abscesses formed in the popliteal space, in the right hip and shoulder, they were incised and found to be situated in the muscular tissue. On examination microscopically they showed organisms completely resembling the gonococci and in cultures only the Neisser gonococcus grew. We have absolute proof that the gonococci can invade the blood in the same manner as the ordinary pus micro-organisms, can give rise to a venous thrombosis and be carried through the blood to distant parts of the body. In other words it can give rise to a condition of pyemia producing metastatic foci of suppuration, ulcerative endocarditis and effusion of a fibrino-purulent character in the various serous cavities. It can even cause a periostitis as described by Raymond (45), which produces such a characteristic deformity as to have given rise to the name of blennorrhagic flatfoot.

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