The Gonococcus

The discussion upon the very existence of a virulent gonorrhea has been active of late years. Ricord did not believe strictly in it, thinking that one could give himself a gonorrhea. Bumstead decided against it. The German school declared the inflammation to possess no virus *sui generis*, and matters were rapidly approaching a position that would make untenable the assumption of any difference between gonorrhea and urethritis, when Neisser claimed to have discovered the essential causative element of gonorrhea to be a peculiar vegetable parasite which he likened to sarcina and christened *gonococcus*. This announcement naturally challenged controversy, and there has been no stint of investigation.[1] Pure cultures of the vegetable organism have been difficult to obtain, and much confusion in the long discussion to which this question has given rise is due to the fact that there are other cocci, diplococci much like the gonococcus, which may be found normally in the urethra. Indeed, a similar organism has been found in the normal secretions of other membranes (mouth) and even in the pus of an acute abscess.

Lustgarten and Mannaberg[2] have made an admirable study of the micro-organisms found normally in the healthy urethra. Some of them are pathogenic, and capable in co-operation with the gonococcus of intensifying the mischief occasioned by the latter and of modifying the clinical picture. Rovsing[3] has contributed an excellent chapter upon the same subject in his book on cystitis, and Petit and Wassermann[4] and H. Heiman[5] have added precision to our knowledge.

But in spite of other microbes and other secretions, the specificity of gonorrheal pus is splendidly demonstrated by Welander,[6] who inoculated the male urethra five times without success, using pus containing small bacilli and derived from putrid balanitis; sev-

---

[1] Among the ablest articles may be instanced: A. Neisser, Ueber eine der Gonorrhoeae eigenthümliche Mikrococcusform, Centralbl. f. d. medicin. Wissenschaften, Nr. 28, 1879, which introduces the gonococcus to the world; Ernst Bumm, Der Mikroorganismus der gonorrhoischen Schleimhaut-Erkrankungen, Wiesbaden, 1885; Bosc, from the historical standpoint, Le Gonocoque, Thèse de Montpellier, 1893, and in every particular the masterly essay of Marcel Sée, Le Gonocoque, Paris, 1896, p. 354; and a contribution upon successful cultures from Cases of Arthritis, etc., by Hugh H. Young, J. of Cut. and Gen.-Urin. Dis., 1900, xviii, 240.

[2] Vierteljahresschrift f. Derm. u. Syph., 1887, S. 905.

[3] Berlin, 1890. A. Hirschwald, S. 60.

[4] Guyon's Annales, 1891, ix, 378.

[5] N. Y. Med. Record, June, 1895, p. 769.

[6] Cited in Thesis of Bosc from Gaz. méd. de Paris, 1884, p. 267.

eral times with vaginal secretions containing a variety of microbes; three times with vaginal secretions containing several rounded and bacillary microbic forms; three times from a putrid and purulent vaginal flow containing moving bacilli; three times with *vaginal secretion* containing *no gonococci* from women whose urethras *did contain these microbes*, and then he gave a typical gonorrhea to these last three subjects by inoculating them with the above-mentioned *urethral pus from the same women, which pus did contain gonococci.* What more is needed? Surely there is justification in the modern French retort to Ricord's famous recipe for catching a gonorrhea—the answer being "*La plus belle femme du monde ne peut donner que ce qu'elle a*" (Sée).

The gonococcus, then, is the cause of gonorrhea, and is always found in the infectious discharge: not in all the secretions of an infected person, as Welander's experiments show, but only in the infectious secretions—urethral, prostatic, etc. An accurate diagnosis of the presence or the absence of the gonococcus is therefore absolutely essential to the comprehension of urethritis.

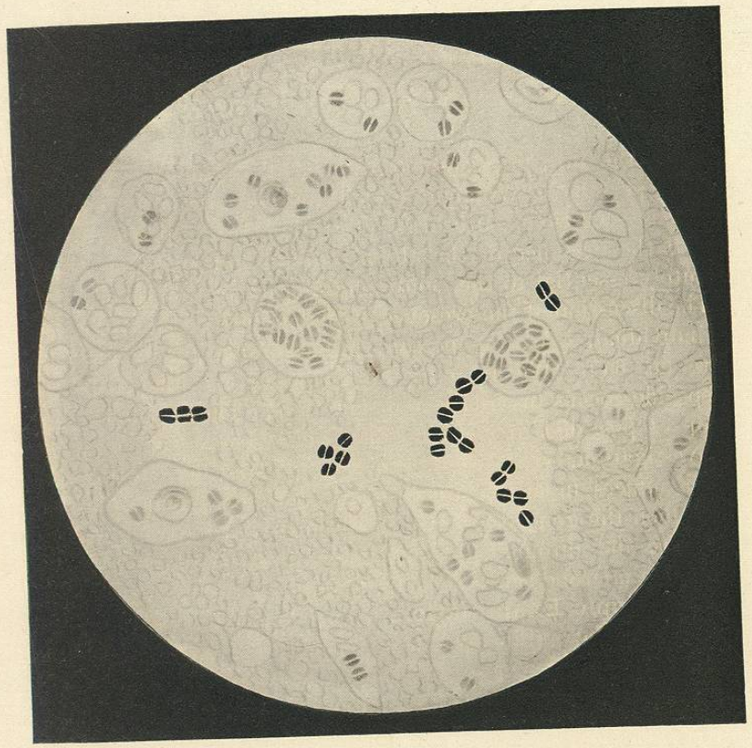
The discussion of the presence or the absence of the gonococcus in the individual, i. e., the person's infectiousness, is taken up elsewhere (p. 64). We are only interested here in the discovery of the specific coccus in a suspected secretion. The problem is: given a drop of pus, does it contain gonococci? There are two methods of investigation, viz., by the microscope and by cultures. The former suffices in any acute case and for any purulent discharge from which the gonococci have not been driven by treatment. But in obscure and chronic cases cultivation must be resorted to before the specific microbe can be declared absent.

Microscopic Examination.—The gonococcus may be stained with the familiar anilin dyes, such as methyl violet, gentian violet, and fuchsin. For purposes of study a minute drop of pus may be spread between two cover-glasses and dried, fixed, and stained in the usual manner (see below). Examined under an oil-immersion lens (magnifying 2,000 diameters), the gonococcus then presents the following characteristics (Plate I):

1. It is a diplococcus. Each individual of a pair is D-shaped (coffee-bean shaped) with the flat (or slightly concave) border opposed to its fellow, so that the couple form an ovoid made up of two separate hemispheres. The length of the pair averages about 1.25 μ (Bumm), and the interspace is about half as wide as either segment. Yet such is the divergence of size in the gonococcus that the figures of no two observers agree exactly.

2. The diplococci are found grouped in pairs, fours, and other

PLATE II



GONORRHEAL PUS.

Gram stain after washing with alcohol. Cells and gonococci decolorized and pseudo-gonococci stained black.

multiples of two, showing a tendency to rectangular disposition, in marked contrast to the irregular massing of staphylococci and the linear arrangement of streptococci. This characteristic grouping is due to the fact that the multiplication of gonococci occurs by fissure at right angles to the central interspace.

3. The gonococcus, when it occurs in pus, is found both within and without the pus and the epithelial cells.[1] Indeed, the most characteristic groups are met with inside the cells. The extracellular gonococci may be scattered or irregularly grouped, but the intracellular specimens present a greater regularity of arrangement. Without being mathematically distributed, there is still a certain symmetry in the grouping, an absence of jumbling, which the observer soon learns to appreciate at a glance and which the plates attempt to reproduce.

Such are the characteristics of the gonococcus. It is a double D diplococcus occurring intracellularly and in typical groups. But these characteristics are sometimes shared by other bacteria met with in urethral pus. We must look further for a distinguishing feature. This we find in the reaction of the gonococcus to the Gram stain.

Gram Reaction.—Gonococci do not take "the Gram." This means that if these cocci are stained first with an anilin dye and then with Gram's reagent (see below) the resultant stain may be washed from them, from the cells, from many other bacteria, but *not from pseudo-gonococci*, i. e., those microbes which, under the microscope, resemble true gonococci. Hence, when the Gram stain is applied, a thorough washing with alcohol leaves the cells and gonococci colourless, while the pseudo-gonococci stand out in bold relief, stained darkly by the combined colour of the anilin dye and the Gram stain (Plate II).

In order to make the effect of the Gram stain more apparent, it is customary to restain the cells and gonococci with a contrasting colour, in order that the true gonococci may be visible for direct comparison with the false (Plate III).

Preparation of the Specimen.—From what has been said in the preceding paragraphs, it is clear that recognition of the gonococcus depends upon the proper preparation of the specimen—the proper performance of the Gram test—and while I cannot say that

[1] I have never been able to ascertain any relation between the intracellular or the extracellular position of the gonococci and the grade or the stage of the inflammation. Every specimen contains gonococci both inside and outside the cells, and in no definite proportion.

the test is complicated, it is delicate, and, like so many other laboratory methods that appear entirely simple when one is familiar with them, it does not succeed at the hands of the beginner. Hence every practitioner is by no means competent to perform and interpret the Gram stain; but any one who can smear a cover-glass and focus a microscope may become competent by practice.

I shall not attempt to describe the methods of others, but only the one that I have employed for over two years. For the development of this method I am indebted to Dr. Chetwood.

I. *The Smear.*—A very small drop of the pus to be examined is placed upon a clean cover-glass. Upon this another cover-glass is dropped, the two pressed together and slid apart. This leaves each covered with a thin film of pus (the thinner the better). Each is then dried by evaporation at a gentle heat and fixed by rapidly passing it three or four times through the flame of a spirit-lamp or a Bunsen burner.

II. *The First Stain.*—One of the films is now covered with the following solution:[1]

Saturated alcoholic solution of gentian violet	1 part
2% carbolated water	9 parts.

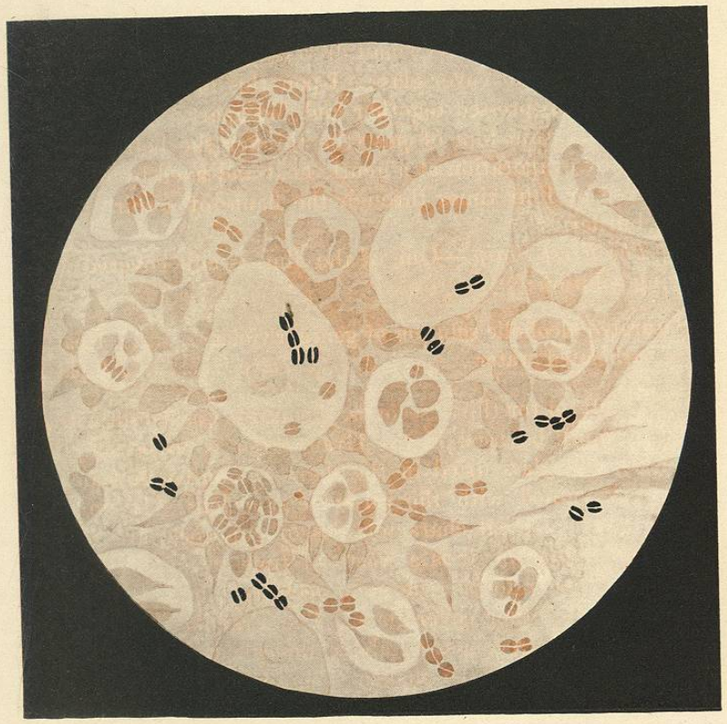
This is left on for thirty seconds, the excess washed off with water (no water must be used if the Gram stain is to be employed—see below), the glass dried in the flame, mounted in Canada balsam, and examined with the oil-immersion lens. If no bacteria with the morphological characteristics of gonococci are seen after a careful examination, it is a waste of time to employ the Gram. But if what appear to be true gonococci are found, the Gram test is applied to the other cover-glass. The Fraenkel-Ehrlich stain is applied for thirty seconds, as above described, but this time the excess of solution must be shaken from the specimen. *No water nor alcohol* may be applied at this juncture. The cover-glass is immediately floated "butter-side down" on a dish of Gram's solution.

III. *The Gram.*—Gram's solution is made up as follows:

Iodin	1 part
Potassium iodid	2 parts
Distilled water	300 parts.

[1] Fraenkel's modification of Ehrlich's gentian-violet solution. This solution has the advantage of resisting decomposition. It may be kept in stock for six months at a time without suffering any deterioration.

PLATE III



GONORRHEAL PUS.

Contrast stain: Bismarck brown. Cells and gonococci take the brown stain, while the pseudo-gonococci remain black.

The cover-glass is allowed to float upon this for four or five minutes.

IV. *The Alcohol.*—As soon as the cover-glass is removed from the Gram solution it should be washed with alcohol until all the stain has, apparently, been removed from it, and it presents much the same pearly white appearance as before the staining was begun. This requires a half minute to a minute.

V. *The Water.*—It is absolutely essential that up to this time no water shall have touched the film. Now the alcohol is washed away in running water, the film is roughly dried and submitted to the second or contrast stain.

VI. *The Contrast Stain.*—After using various more or less satisfactory counter-stains I now employ only the following:

Carbolic acid	2 parts
Saturated aqueous solution of Bismarck brown	98 parts.

If the decolourized smear is covered with this solution for four or five minutes and then rinsed in water it acquires a light-brown tint and, under the microscope, the cells and gonococci appear yellowish and in marked contrast to the deep purple, almost black pseudo-gonococci. A more prolonged staining with the brown gives the gonococci a deeper colour, which is not so readily distinguished from that of the pseudo-gonococci.

Such is the technic of staining the gonococcus, which may be employed by any one having an elementary familiarity with medical microscopy, and which may be depended upon to furnish accurate results when once one has familiarized himself with it. But let me repeat: its positive evidence is final; its negative evidence—its failure to find gonococci—is only final when the urethral discharge is free and has not been influenced by any local treatment. Otherwise the suspected pus must be submitted to the test of culture.

Finally, emphasis must be placed on the use of 95% alcohol for decolourizing, and the avoidance of water in every stage of the operation until after decolourization.

Gonococcus Culture.—Since the cultivation of the gonococcus requires laboratory facilities and considerable technical skill, it should not be undertaken by any but an expert bacteriologist. The detailed studies of Dr. Henry Heiman explain the methods to be employed.[1]

The necessity of employing this test before pronouncing a patient finally cleansed of his gonococci is insisted upon in another place.

[1] Med. Record, 1895, xlvii, 746; *ibid.*, 1896, l, 887; *ibid.*, 1898, liii, 80.

GONORRHEAL URETHRITIS

Morbid Anatomy.—The most accurate data we possess in reference to the invasion of the urethral tissues by the gonococcus are those published by Finger, Gohn, and Schlagenhaufer.[1] These authors inoculated the urethræ of criminals condemned to death, and were able, by means of immediate post-mortem examination, to investigate the various stages of invasion of the tissues by the specific microbe. Thirty-eight hours after inoculation the gonococci had only just begun to effect an entrance between the epithelial cells. The lacunæ of Morgagni were crowded with the cocci, diapedesis had begun, and intracellular gonococci were found among the few leukocytes on the surface of the epithelium. At the end of three days[2] the inflammatory process was well under way. The surface of the mucous membrane was covered with pus, the epithelium infiltrated by bacteria from one side and by leukocytes from the other. The inflammation showed four striking characteristics, viz.: 1. The pavement epithelium of the fossa navicularis, although swollen with leukocytes, resisted the invasion of the gonococci almost absolutely. 2. The cylindrical epithelium of the penile urethra was generally invaded. 3. This invasion was most marked about the crypts and glands, which were packed with pus and gonococci; and 4. The subepithelial connective tissue, though showing every evidence of inflammation, contained few gonococci, except in the neighbourhood of the crypts and glands and in all places not covered by epithelium.

These conclusions—viz., that squamous epithelium is especially resistant to gonococcal invasion, and that the urethral inflammation is habitually confined to the epithelium and is sharpest about the crypts and glands—are generally accepted.

The importance of *gono-toxin*, the virus of the gonococcus, in producing the inflammatory reaction has not been definitely determined. Our knowledge of the subject is summed up by Christmas.[3]

Symptoms.—True gonorrhea requires no idiosyncrasy, no ale nor champagne, no excess, no weakened condition of the urethra for its development, but simply the contact of the gonococcus with the mucous membrane of the urethra, a contact usually effected through intercourse with a woman having a gonorrheal discharge. Here, after a period of perfect rest, lasting habitually from three to five

[1] Arch. f. Derm. u. Syph., 1894, xxviii, 277.

[2] Since the average period of incubation is rather longer than this, the rapid onset in these experimental cases may be attributed to the massive infection.

[3] Ann. de l'Institut Pasteur, 1900, xiv, 331.

days, the urethral disturbance commences and runs the given course of virulent specific gonorrhea.

Incubation of Gonorrhea.—The incubation or hatching time—the period that elapses between suspicious contact and the first appearance of discharge—varies from one to fourteen days. The earlier authors recognised longer incubation periods. But I confess to some suspicion of inaccuracy in reference to those cases on the subjoined list that give a story of more than ten days' incubation. Experimental inoculation produces a discharge on the second, third, fourth, or fifth day; but it has been my experience that the shorter incubations are clinically due to the association of sexual strain or of simple urethritis with the gonococcus. Several of the cases noted below have begun with a light discharge on the second day which did not assume a purulent and specific character until two or three days later. Such a condition may be expected to occur most often in the damaged urethra of the *roué;* hence the relatively large number of short invasions among recurrences as compared with first attacks. In fact, an uncomplicated gonorrheal infection of the virgin urethra has an incubation period of from three to ten days.

Length of Incubation[1]

Day.	First Attack.	Recurrence.
1	0	2 cases.
2	2 cases.	12 "
3	2 "	15 "
4	3 "	13 "
5	11 "	10 "
6	6 "	4 "
7	4 "	10 "
8	1 case.	2 "
9	1 "	1 case.
10	1 "	4 cases.
11	1 "	1 case.
12	1 "	0
13	1 "	0
14	0	2 cases.
Total	34	76

Average incubation of 34 primary attacks, 6 days.

Average incubation of 76 secondary attacks, 4.88 days.

Of the primary attacks, 20% appeared before the fifth day; 61% on the fifth, sixth, and seventh.

Of the secondary attacks, 55% appeared before the fifth day; 31% on the fifth, sixth, and seventh.

[1] I have included in this list only those cases in which the incubation period was unmistakable and the disease absolutely characteristic—microscopically, clinically, or both.