A SECOND CASE OF GONORRHŒAL SEPTICÆMIA AND ULCERATIVE ENDOCARDITIS WITH OBSERVATIONS UPON THE CARDIAC COMPLICATIONS OF GONORRHŒA.*

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PLATE I.

Cardiac complications of gonorrhœa with or without coincident or preceding arthritis, while not of frequent occurrence, are by no means so rare as has, even within recent years, been supposed. The literature shows over a hundred cases in which a diagnosis of gonorrhœal endo-, peri- or myo-carditis has been made, and during the last several years considerable attention has been attracted to the subject by the accumulation of evidence demonstrating the fact that many of these complications are due to actual local infections with the gonococcus.

It was the good fortune of Blumer and one of the writers to observe a case of gonorrhœal ulcerative endocarditis in 1895 and to succeed for the first time in obtaining the gonococcus in pure culture during life from the circulating blood; moreover organisms showing all the characteristics of gonococci were demonstrated in the lesions upon the affected valves, thus furnishing definite proof of the possibility of the existence of a true gonorrhœal septicæmia and endocarditis.

This case, which has already been reported,† it may be well to summarize:

The patient, a woman 34 years of age, entered the Johns Hopkins Hospital, April 25, 1895. Her family and personal history were nega-

* This case was reported at the Twelfth International Medical Congress at Moscow in August, 1897.

† *Arch. de méd. expér. et d'anat. pathol.*, 1895, vii, 701; also, *The Johns Hopkins Hospital Bulletin*, 1896, vii, 57.

tive, excepting that for three months she had had rheumatism off and on in various of her joints. From the beginning of her rheumatism she had complained of weakness and dyspnœa on exertion. A few days before her entry into the hospital she had a severe chill and took to bed. On entrance there were well-marked signs of mitral stenosis. During the period of her sojourn in the hospital there was irregular fever associated with severe chills. The blood showed throughout a well-marked leucocytosis; the urine contained a trace of albumin and the sediment contained occasional casts. The patient grew rapidly feeble and died May 16.

The diagnosis of ulcerative endocarditis having been made during life, cultures were taken from the blood on several occasions. These cultures were made by Dr. Blumer according to the method of Sittman. The blood, taken from the median basilic vein by a sterilized syringe, was mixed with melted agar which was immediately plated. Large quantities of blood were used, so that the medium contained at least one-third blood. The first culture, taken May 4, was negative, but in the cultures of May 7 and 12 the plates showed very minute white colonies representing a pure culture of small biscuit-shaped diplococci which failed to grow on transmission to agar-agar, gelatine, potato, bouillon or litmus-milk. These organisms were decolorized entirely by Gram's method.

The autopsy confirmed the diagnosis made during life, revealing an extensive ulcerative and vegetative endocarditis of the mitral valve. In the thrombi upon the valve were found large numbers of diplococci having all the morphological and tinctorial characteristics of gonococci. At the time of autopsy there were unfortunately no media at hand suitable for the cultivation of gonococci, and implantations, made upon agar-agar and ox's blood serum, from the heart's blood, valves, liver, spleen, lungs and kidneys, were entirely without result; it should be stated that in these post-mortem cultures but a small quantity of the heart's blood was mixed with the agar. Inoculation of a mouse with a piece of thrombus from the valves was without result.

The characteristic appearance and disposition of the cocci, their decolorization according to the method of Gram, their failure to develop upon ordinary media, and finally their growth on two occasions during life upon a medium practically the same as that recommended by Wertheim, leaves, it seems to us, little doubt that this was a true gonococcal infection. Similar organisms were found after death in the vagina and uterus.

Certain reviewers have been inclined to doubt the complete reliability of this observation. Thus, Fraenkel* asserts that "because during life a gonorrhœal affection was not discovered in the patient despite careful search, and cultures of the observed microörganism were not made on human blood serum or Wertheim's serum agar, the observation cannot be considered as entirely free from criticism." We confess that we cannot see the justice of Fraenkel's observations. It is well known to gynæcologists that gonorrhœal affections often exist in women without being recognized by the ordinary methods of examination. As was stated in the previous communication, we had not thought during the life of the patient of the possibility of the case being one of gonorrhœal infection, and the vaginal secretion was not examined. But after death characteristic gonococci, answering to all tinctorial and morphological characteristics, were found both in the vagina and the uterus. Moreover, the medium upon which the successful cultures were twice obtained during life—the mixture of blood fresh from the veins with melted agar—was essentially similar to the human blood-serum agar of Wertheim. Upon this medium the organism grew; upon all ordinary media it failed to reappear.

Shortly after the publication of the foregoing case we observed a second instance of endocarditis and septicæmia of undoubtedly gonorrhœal nature.

J. K., aged 19, a day laborer, unmarried, a native of Germany, was admitted to the Johns Hopkins Hospital on February 5, 1896, complaining of fever and weakness.

Family history.—Father died with dropsy; mother, one brother and two sisters living and well; several brothers and sisters died in infancy.

Personal history.—There is no history of the ordinary diseases of childhood. He has never had any severe infectious diseases; is sure that he has never had rheumatism or scarlet fever, stating that he has always been a healthy man. He drinks beer in moderation.

Present illness.—The patient contracted gonorrhœa for the first time six months ago. Several weeks after the onset he began to suffer from chilly sensations, fever and general weakness. Toward the end of November he began to have violent chills, occurring usually in the morning hours; these were followed by fever and profuse sweating.

* *Hygienische Rundschau*, 1896, vi, 254.

Under treatment the shaking chills disappeared, but the fever continued, becoming, however, more irregular. He has grown progressively weak and pale, and for two weeks before entry there has been œdema of the feet and ankles.

Physical examination.—The patient is very dull and drowsy. He is a large well-nourished man; lips, mucous membranes and skin extremely pale; pulse large, but of low tension, 108; respiration 30; T°, 103.4°. Lungs, clear throughout. *Heart:* Point of maximum impulse in the 4th space just inside the mamillary line. Relative dulness begins in the 3d interspace and is not increased to the right. Absolute cardiac dulness is obliterated by pulmonary resonance. On auscultation the first sound at the apex is booming and prolonged; there is no actual murmur. Passing toward the base a soft systolic murmur becomes audible; most marked in the pulmonic area. The second pulmonic sound is a little sharper than the second aortic. *Liver:* hepatic flatness begins at the 7th rib in the mamillary line, the lower border being palpable, 6.75 cm. below the costal margin. *Spleen* is greatly enlarged, flatness above beginning at the 7th rib, while the lower border is palpable 9.5 cm. below the costal margin. *Abdomen:* full, bulging a little in the flanks, tympanitic in the elevated, flat in the dependent parts; well-marked movable flatness. The left knee-joint contains an excess of fluid, being distinctly swollen and fluctuating. No redness or tenderness. No tenderness or irregularities on any of the long bones. Moderate enlargement of the inguinal glands. Slight œdema of the feet and ankles. There is a thick, purulent urethral discharge showing characteristic gonococci. The *blood* contains no malarial parasites or pigment. There is a moderate poikilocytosis. Red blood corpuscles, 2,292,000; colorless corpuscles, 9,000.

Urine: reddish amber; acid; 1015; no sugar; albumin, 0.1 per cent. Sediment: considerable; whitish; microscopically, numerous pus cells, usually separate, not in clumps; red blood corpuscles; small round cells about the size of leucocytes with single nuclei; numerous hyaline and granular casts with adherent pus and degenerated epithelial cells; epithelial casts; pus casts.

The patient remained in the hospital but nine days, during which time the temperature ranged between 99.6° and 103.3°. The urine was somewhat reduced in quantity, averaging a little under 1000 cc. in the 24 hours. The specific gravity ranged between 1013 and 1015, while the amount of albumin and the character of the sediment continued about as noted above.

11/ii/96. *Examination of the blood:* Red blood corpuscles, 2,283,000; colorless corpuscles, 14,250; hæmoglobin, 45 per cent. Dried specimens prepared according to Ehrlich's method showed slight variations in the size of the corpuscles, moderate poikilocytosis; a few nucleated red corpuscles, no malarial parasites. Differential count of leucocytes: small mononuclear leucocytes, 4.8 per cent; large mononuclear and transitional leucocytes, 2.6 per cent; polymorphonuclear neutrophilic leucocytes, 92.6 per cent; eosinophilic leucocytes, none.

The direct sequence of the symptoms upon the gonorrhœa suggested to us the possibility that we might be dealing with a gonorrhœal pyelo-nephritis and possibly with a general septicæmia, and cultures were taken on two occasions by Dr. Lazear from the circulating blood by the same method adopted in the previous case. These cultures were without result in both instances.

The patient was kept in bed, placed upon a milk diet, diuretics and iron. On February 14 he left the hospital, objecting to the strict régime.

March 9 the patient re-entered the hospital, having grown steadily worse.

10/iii/96. *Physical examination.*—The patient was extremely sallow, pale; tongue dry and fissured; pulse 108; moderate œdema of the dependent parts; slight puffiness of the face. The point of maximum cardiac impulse had moved outward and downward to a point in the 5th space slightly outside of the mamillary line, while a soft systolic murmur, which was not present on the former admission, was now to be heard all over the cardiac area, loudest at the apex. The second sounds at the base of the heart were not loud, but were of normal relative intensity; no accentuation of the second pulmonic sound.

The urethral discharge had almost disappeared.

The anæmia had increased, the *blood count* showing on 10/iii/'96: red blood corpuscles, 1,920,000; colorless corpuscles, 8500; hæmoglobin, 18 per cent.

The *urine* of the same date was of a pale but distinctly smoky color; acid; sugar absent; albumin 0.4 per cent. Sediment, abundant; microscopically, many pus cells scattered throughout the field, not arranged in clumps; many small round cells about the size of leucocytes with single nuclei; many red blood corpuscles, some "shadows," others crenated, others fairly well preserved. Numerous fatty degenerated epithelial cells, somewhat larger than pus cells; some small agglomerations of free yellow fat drops; occasional compound granular cells; casts

extremely abundant; hyaline, finely and coarsely granular with adherent pus and red blood cells; occasional fatty casts and blood casts; many epithelial and pus casts; occasional extremely large, slightly yellowish, typically refractive, waxy casts with broken ends; diazo-reaction absent.

The patient grew rapidly worse; the anæmia increased, the *blood* on the day of death showing: red blood corpuscles, 1,896,000; colorless corpuscles, 18,000; hæmoglobin, 18 per cent.

The *urine*, averaging little over 600 cc. for the 24 hours, was almost suppressed during several days before death. The albumin increased up to nearly 0.5 per cent, while the number of fatty, blood, waxy, epithelial and pus casts increased. On March 23 the paient became extremely dull and drowsy.

23/iii/96. (Professor Osler.) "For the past few days the temperature has been lower, not above 100° since the 19th; no change in the general condition. Pulse about 100; drops a beat occasionally; of low tension.

Heart: apex beat is diffuse during expiration; well seen in the 5th space and a little outside the nipple line. Cardiac impulse is visible in the 4th space inside the nipple. A diastolic shock can be felt at the apex; both sounds are audible; no murmur. Over the entire praecordium there is a to-and-fro superficial pericardial friction murmur, the maximum of which is at the 5th left cartilage; it is well heard at the ensiform cartilage; not heard above the level of the 3d rib; no especial accentuation of the pulmonic second sound."

On the 24th the patient developed a well-marked petechial eruption.

25/iii/96. (Dr. Thayer.) "The patient is lying on his right side; very drowsy and dull. Respirations 15 to the minute, rather deep and noisy; pulse 21 to the quarter; of low tension. Face puffy; pupils not contracted; general anasarca.

Heart: diffuse heaving over the 4th and 5th interspaces just inside the nipple; the point of maximum cardiac impulse is not to be sharply differentiated; flatness does not pass the left sternal margin; begins at about the 4th space. At the apex the first sound is reduplicated and followed by a soft systolic murmur, while in connection with this there is a soft superficial to-and-fro rub. Over the body of the heart the sounds are considerably masked by this friction rub. *The second pulmonic sound is, however, not accentuated.* On the trunk and arms and occasionally on the legs are numerous small petechial spots, the largest scarcely larger than the head of a pin."

On March 21 the patient began to suffer from diarrhœa, the movements

becoming gradually more frequent and fluid. During the afternoon of the 25th the respiration became more stertorous; the patient lapsed into a condition of complete coma and died at 6.30 P. M.

Bacteriological examination during life.—March 22, 1896, cultures were made by Dr. Lazear in the following manner: 2 cc. of blood were drawn from the median basilic vein by a hypodermic syringe previously sterilized by boiling. The skin was, as far as possible, sterilized and every antiseptic precaution was used. The blood was mixed with 4 cc. of melted nutrient agar and the mixture poured into a Petri dish and allowed to harden. It was kept in a thermostat at 35° C. At the end of 24 hours no growth was visible. At the end of 48 hours there began to appear colonies half the size of a pin head, granular in appearance with somewhat irregular borders. These colonies were made up of cocci arranged usually in pairs. The cocci were of biscuit or kidney shape, their flattened sides being adjacent. They stained well with the ordinary basic dyes and decolorized by Gram's method. Transplanted upon human blood-serum agar by a smear upon the surface there developed a fair number of colonies similar to the above, consisting of diplococci having the same morphology and tinctorial characteristics. Transplanted to ordinary agar there was a growth of a few fine colonies of the same diplococci. On gelatine, ox's blood serum and bouillon there was no growth. At the end of ten days the organisms had all died out upon the original plates.

On March 24 and 25, plate cultures were made by the same method, and on each occasion there was an abundant growth, in pure culture, of diplococci identical with those obtained upon the first plates, behaving in the same manner with regard to stains and in their growth upon the various culture media.

On the basis of these positive cultural experiments and the clinical history of the case, the patient was brought before the class on March 25 as an instance of general gonococcal septicæmia with endo- and pericarditis.

Autopsy, March 25, by Professor Flexner.

Anatomical diagnosis.—Gonococcal septicæmia; subacute gonorrhœa; subacute ulcerative and vegetative, tricuspid endocarditis caused by the gonococcus; subacute splenic tumor; chronic passive congestion of the liver; subacute hæmorrhagic and glomerular nephritis; acute sero-purulent pleurisy and pericarditis due to the gonococcus; pulmonary infarct.

The following is a summary of the pathological record:

On opening the abdomen nothing remarkable was to be made out

except the much enlarged spleen, adherent in its upper part to the diaphragm.

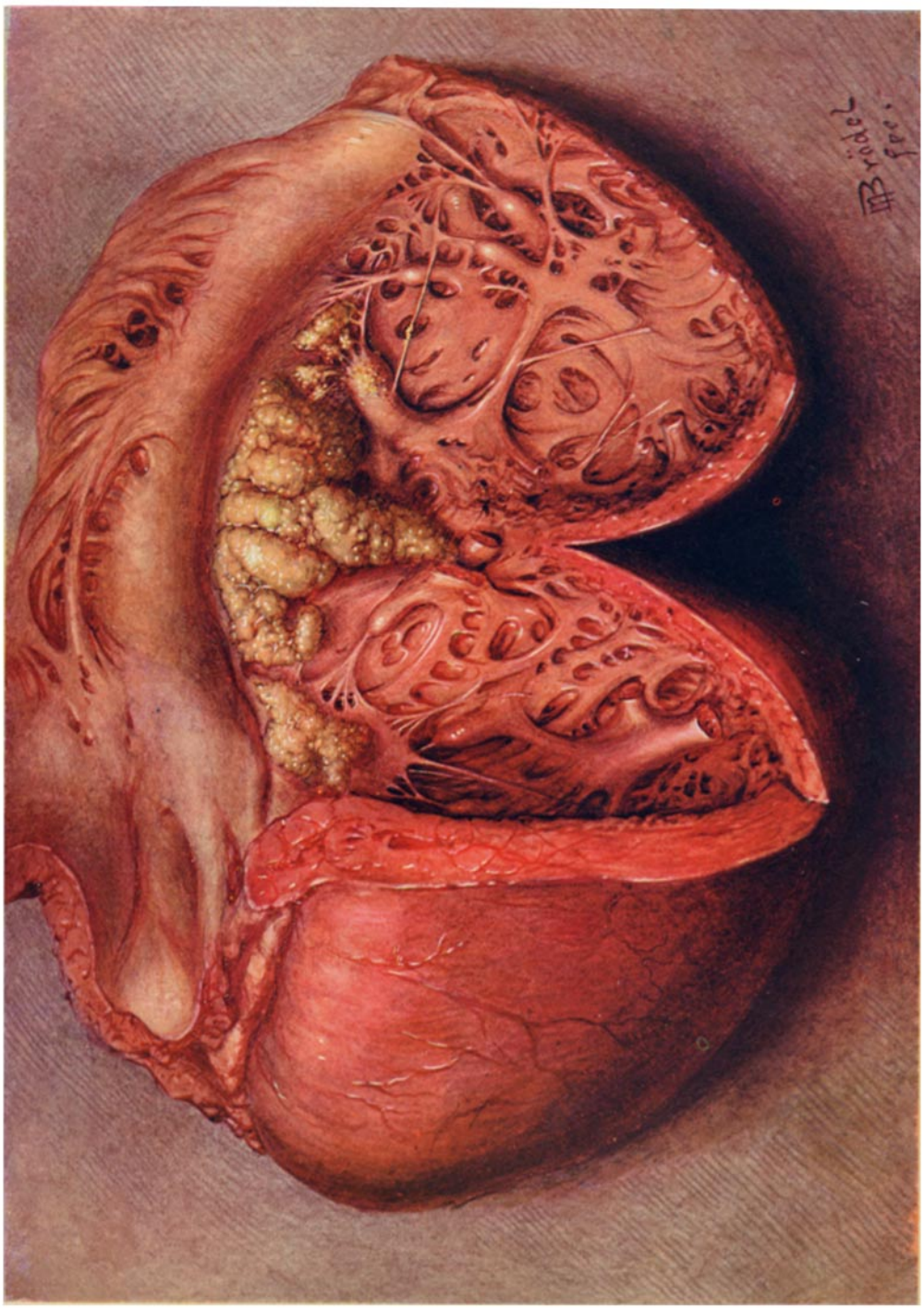
Pleurae and lungs.—The right pleural cavity is free from adhesions and contains about 800 cc. of slightly turbid, yellowish fluid with large flakes of fibrin. On the pulmonary pleura there are small flakes of fibrin and beneath this are many punctiform ecchymoses. The left lung is bound down along its posterior border by firm adhesions. In the left pleural cavity are 550 cc. of fluid containing somewhat less fibrin than on the other side. There are less fibrin and fewer ecchymoses on the visceral pleura than on the right side.

In the middle of the left lower lobe at its inferior border there is a circumscribed, triangular area of infarction $1\frac{1}{2}$x$1\frac{1}{2}$ cm. in extent; opaque, firm, of a brownish-yellow color. The surrounding tissue is congested. On section both lungs are of a light salmon-red color and œdematous. The bronchi are congested. The pulmonary arteries are free and practically normal in appearance. The anterior edges of the lungs are emphysematous.

Pericardium and heart.—The pericardial cavity contains about 300 cc. of turbid yellow fluid with fibrinous flakes. In the dependent portions the fluid is thick and puriform. The surface of the peri- and epicardium is congested, ecchymosed, and covered by a granular deposit. The weight of the heart and pericardium is 680 grammes.

The right ventricle and auricle are dilated and contain fluid blood and partly decolorized clots. The endocardium of the right auricle is delicate, although near the obliterated foramen ovale beneath the endocardium are two or three slightly elevated minute opaque points.

The tricuspid valve is the seat of an extensive thrombus, occupying the entire middle segment, with the exception of its base, and to a less extent the two remaining segments (see Plate I). The thrombus attached to the middle segment is firmly united to the valve at a distance of 5 mm. from its attachment to the auriculo-ventricular ring and projects into the cavity of the ventricle. At the site of attachment of the thrombus the substance of the valve is destroyed. The thrombus presents an irregularly convoluted appearance, and for description may be divided into three distinct portions: The central portion, which is largest, measuring 4.5x2 cm. x4.5 mm. in thickness, has in general a conical shape with its base at the valve and its apex projecting into the ventricle. To the left of this is a second mass 18x22 mm. in extent, almost quadrangular in form but irregular in contour. The remaining mass to the right is about one-half the size of the last. This thrombus



mass is attached at certain points to the endocardium of the right ventricle. Fully one-half of the chordæ tendineæ of the segment of the valve are ruptured and their free ends are covered with grape-like clusters of thrombi. Small miliary vegetations are on the papillary muscle to which these are attached and on a moderator band which extends from the papillary muscle to the mid-portion of the left segment of the valve. The anterior surface of the right segment of the valve is the seat of two thrombus masses projecting into the auricle; they average about 12x10 and 12x6 mm. The pulmonary artery and valves are normal in appearance.

The aortic and mitral valves and the endocardium of the left ventricle are entirely normal. In the lymphatics along the course of the vessels in the epicardium on the right side there are minute discoid nodules similar to those described in the endocardium of the auricle.

The tricuspid orifice measures 16 cm.; length of the right ventricle 12.5 cm.; thickness 5-7 mm. The mitral valve measures 12 cm.; length of the left ventricle 8 cm.; thickness 15 mm. The cardiac muscle is pale and fairly firm.

The *spleen* weighs 840 grammes; dimensions, 21x13x6 cm.; capsule wrinkled; on section the Malpighian bodies very prominent, the trabeculæ visible; the pulp of an opaque grayish-red color, the consistence moderately firm.

The *liver* weighs 2450 grammes, and is the seat of fairly well-marked chronic passive congestion.

Kidneys.—The kidneys weigh together 670 grammes. Dimensions: right, 14x9.5x4; left 15x8x4. They are swollen, the capsule adherent in places; the surface mottled, of an opaque, grayish color with many punctiform hæmorrhages. The cut surface appears swollen and œdematous. The striæ are obscure; the glomeruli visible, but pale. Numerous elongated hemorrhages—9 to 10 mm. long—are visible in the cortex. The pyramids are hyperæmic; the vessels of the mucous membrane of the pelvis are also somewhat congested and a few small hæmorrhages are visible.

The *ureters* are not enlarged; their mucous membrane shows the same condition as that of the renal pelvis.

Bladder.—The vesical mucous membrane is pale, with the exception of the trigonum, where it is moderately congested. About the orifices of the ureters there are a few small hæmorrhages. The neck of the bladder and the prostatic portion of the urethra are somewhat hyperæmic.

Gastro-intestinal tract.—The stomach and intestines show nothing noteworthy.

Pancreas.—A number of small opaque areas of fat necrosis are to be made out in the fatty capsule of the pancreas. Teased preparations show in the necrotic areas groups of fat cells containing finely granular bodies. Treated under the microscope with concentrated sulphuric acid, gas bubbles may be seen to arise and soon fine crystals of calcium sulphate appear.

Bacteriological examination.—Cover-slips from the pleural and pericardial exudates and from the vegetations upon the heart valves showed large numbers of cocci in pairs. They were excessively numerous upon the surface of the tricuspid valve. These cocci were in almost all instances included within polymorphonuclear leucocytes which were numerous. The form of the cocci was, as a rule, typically biscuit-shaped, and at times, though rarely, two pairs lay side by side, suggesting a tetrad arrangement. The cocci stain readily in the usual aniline dyes, but are quickly and uniformly decolorized by Gram's method.

A cover-glass specimen from the spleen showed one pair of cocci; others were not found. Cover-slips from the kidney, renal pelvis and urinary bladder were negative.

In the urethra, among a variety of bacilli, definite intracellular biscuit-shaped diplococci which decolorize by Gram were found.

Cultures.—Cultures were made at the autopsy from the various local exudates, the heart's blood and the organs as follows:

(*a*) Upon Loeffler's blood serum, prepared; (1) from human blood; (2) from bullock's blood; (3) from dog's blood.

(*b*) Upon agar-agar. Only a few tubes of the human serum were on hand and these were used for the local exudates and blood. Upon those from the pericardium, tricuspid valve and heart's blood delicate growths were obtained which consisted in part of confluent minute colonies, in part of small, almost point-like, grayish-white, slightly elevated colonies. Microscopically these colonies were composed of diplococci, readily decolorizing by Gram, and resembling in every way, except perhaps in the feebleness of their growth, the organisms isolated during life. No growths whatever were obtained upon bullock's serum, dog's serum, or plain agar-agar.

Transplantations from the 48-hour old growths from the human blood serum on to ordinary agar, swine-liver agar (Livingood), fœtus agar (Flexner) were negative. As no human serum remained, transplantations entirely failed.

Microscopical examination.—A histological study of the organs was made by Professor Flexner, to whom we are indebted for the following report: The description of the histological changes is confined to those of the kidneys, the liver, the spleen and the cardiac valves, these being the parts chiefly affected. The tissues were hardened in alcohol and Zenker's fluid, and the specimens stained by hæmatoxylin and eosin, Weigert's fibrin stain, and methylene-blue.

Kidney.—Throughout the cortex there is a general increase of connective tissue, uniformly distributed and particularly well marked between the tubules. This tissue is fibrillated, œdematous and not particularly rich in cells. The chief lesions affect the glomeruli and the labyrinthine tubules. The least affected glomeruli completely fill the capsule of Bowman; the number of cells within the glomerular capillaries is increased, this increase being due to an excess of polymorphonuclear leucocytes. The capillary walls are distinct, thicker than normal, hyaline or slightly fibrillated in appearance. The more abnormal glomeruli show, in the first place, thrombosis of groups of capillaries by material presenting characters unmistakably indicative of fibrin. This material within the capillaries appears as a delicate network and may be limited to a single loop of a capillary or occupy a group of loops; it does not completely occlude the vessels. Outside of the capillary walls there is an increase in the number of cells within the glomerular space. These cells are partly of an epithelioid type, being doubtless derived from the capsular and glomerular epithelium, and partly leucocytes. Deposited within and intimately mixed with these cells a fibrinous material, which appears often as a crescentic band, dips down between the lobules of the glomeruli. It is in part distinctly fibrillated, in part dense and hyaline, and everywhere gives a sharp staining reaction for fibrin. Its association with the cells within the capsular space is of the most intimate character. In specimens stained with hæmatoxylin and eosin it takes a vivid red stain. In not a few situations there is evidence of a proliferation of cells clearly derived from the capsular epithelium, and, although less certainly marked, there is in our mind little doubt that a similar increase of cells is taking place within the capillaries themselves.

As has been stated, leucocytes occur abundantly in the capsular spaces; these are derived from the glomerular capillaries and may be seen in the act of migration through the capillaries into the space. Of particular interest is the passage of leucocytes from the capsular space through the capsule of Bowman into the interstitial tissue in which these

cells are increased. The uriniferous tubules contain also large numbers of polymorphonuclear leucocytes; in some places completely occluding the lumen of the tubes, forming definite leucocytic casts. The epithelium, especially of the secreting tubules, is much degenerated, even necrotic, and in some places evidently proliferating, as is evidenced by multinucleated cells in certain of the tubules. The degeneration of the epithelium is partly fatty and granular, but largely of the hyaline variety, to which change can be attributed much cast material and definite casts occupying the tubules. Red blood corpuscles are rarely found within the tubules. The essential lesion is a sub-acute glomerular and intracapillary nephritis. Bacteria were not discovered in this organ.

Spleen.—The connective tissue framework of the spleen is thickened. The new tissue is of a semi-fibrillated character. The blood-vessels of the pulp are diminished in size and apparently also in number. The splenic elements proper are also reduced in number, but there are scattered irregularly throughout the spleen in greatly increased number polymorphonuclear leucocytes, and within the venous sinuses groups of hyaline bodies and single hyaline bodies, globular in shape, varying in size from a red blood corpuscle to one of the largest white cells there present.

The follicles are enlarged and very distinct, many of their cells being swollen and in process of division; they are infiltrated with polymorphonuclear leucocytes, the nuclei of many of which show the greatest irregularity in form. Nuclear fragments are scattered sparsely and irregularly throughout the spleen; for the most part they are not enclosed within other cells.

Liver.—The connective tissue is not increased; the central veins are much dilated and the central portions of the lobules hyperæmic. This congestion varies in different lobules, being in some very marked, with corresponding atrophy of the liver cells. There is an interesting hyaline metamorphosis of some of the liver cells. Those peripherally placed in the congested areas show this change best, and in these the nuclei have become small, contracted and deeply staining. In parts of the liver distant from the congested areas the hepatic cells are swollen, fatty, and free from the hyaline change described, excepting where an occasional cell, more or less loosened from the rows of liver cells and perhaps lying in the capillary, is thus affected. There is a general increase in the number of leucocytes within the blood-vessels.

Heart.—Sections through the tricuspid valve include chiefly the thrombus, which consists of masses of blood platelets, of fibrin and of

included leucocytes. No bacteria appear in sections stained by Gram's or Weigert's method.

The pericardium shows, besides a superficial fibrinous exudate containing leucocytes, a considerable inflammatory infiltration of the subjacent fibrous tissue and a proliferation of the fixed tissue cells. The epithelial covering is in active proliferation. In some of the leucocytes in the pericardial exudate Dr. Lazear was able to demonstrate gonococci.

A further study of the heart valves was made by Dr. Lazear: The tissues were hardened in alcohol and in Zenker's fluid, and embedded in celloidin and paraffin. For the bacteriological study they were stained with Loeffler's and Unna's methylene-blue, Ziehl-Neelsen carbolic fuchsin, Stirling's gentian violet and by Gram's method. For histological study they were stained with hæmatoxylin and eosin and Weigert's fibrin stain.

Tricuspid valve.—The connective-tissue structure of the valve shows areas of necrosis. In places the nuclei are merely swollen. There are also irregular areas extending throughout the valve in which the nuclei have entirely disappeared, leaving a homogeneous material which stains with eosin. Extending into the substance of the valve are numerous spaces filled with leucocytes, among which are a few large phagocytic cells, with large irregularly shaped nuclei and containing red blood corpuscles.

The vegetations are made up of granular masses of platelets surrounded by fibrin and a thick layer of leucocytes. Leucocytes are present also within the masses of platelets, either scattered or occupying spaces.

Upon the surface of the valve and the vegetations is a layer composed of leucocytes and red blood corpuscles with strands of fibrin forming an irregular network through it. The same material occupies the interstices between the vegetations. Many of the leucocytes in this layer and in the more central portions contain micrococci with the typical biscuit shape and other morphological characters of gonococci and completely decolorizing by Gram. Extracellular gonococci are present in the central portion of the thrombi but not in the superficial layers.

At the line of junction of the central platelet mass and the leucocytic layer is a long line of globular bodies varying in size from that of a leucocyte to ten times this size. These bodies are made up of dense masses of gonococci.

There can, it appears to us, be no doubt as to the nature of the organisms obtained in pure culture from the blood during life and

from the affected valves, heart's blood and pericardium after death. This case and that previously reported by Dr. Blumer and one of the authors (Thayer) are the first two recorded instances in which absolute proof of the gonococcal nature of the general infection has been obtained.

The case presents several interesting and unique features. While the diagnosis of ulcerative endocarditis and gonorrhœal septicæmia was made during life, the exact anatomical lesion—the remarkably extensive affection of the tricuspid valve—was not at this time suspected. Much of the thrombus upon the valve may have been of relatively recent formation, but older changes, probably of several months' duration, were clearly present. It is the first instance in which a pure tricuspid lesion has been found in a gonorrhœal endocarditis. It is not uninteresting that while the diagnosis was not made clinically, it was particularly noted that, in association with the systolic murmur, there was no accentuation of the second pulmonic sound, a fact which might well have excited our suspicion.

The changes in the kidney are of especial interest. Clinically the case presented the features of a grave acute nephritis with anæmia, anasarca, ascites and finally uræmic coma. The urine showed, besides the large quantity of albumin, the blood casts and the epithelial cells, so large an amount of pus that a diagnosis of probable pyelitis or pyelo-nephritis was made. Especially interesting is the fact that during life casts consisting entirely of polymorphonuclear leucocytes were repeatedly observed. The absence of gross collections of pus in the kidney or in the pelvis was a surprise at the time of the autopsy. The microscopical examination of the kidney, however, revealed the source of this pus in the unquestioned evidence of the passage of numerous leucocytes directly through the capillaries of the glomeruli into the glomerular spaces and the urinary tubules. The extensive thrombosis of the glomerular capillaries and the accumulations of fibrin in the glomerular spaces form a very remarkable picture. How this special localization of these changes in the kidney and the relative freedom of the liver from those degenerative processes so common in general septicæmia, viz. focal necroses, may be explained is rather

an interesting question. May it perhaps be true that the renal changes were due to the direct deleterious action of the gonococci or their products in the process of elimination through the urine?

That the gonococcus must be recognized as a true pyogenic organism capable of giving rise to the gravest local and general septic complications has been abundantly proven by recent observations. That cystitis, epididymitis, spermatocystitis, prostatitis and periurethral abscesses in man, metritis, vulvo-vaginitis, salpingitis, and peritonitis in woman, may owe their origin solely to the presence of the gonococcus has been clearly demonstrated. And further, suppurative processes in remote parts are now known to be occasionally due to a pure gonorrhœal infection. Horwitz and Lang* found the gonococcus in an ulcer upon the back of the hand, while its presence in joint fluids in cases of gonorrhœal arthritis has been demonstrated by many observers. Within the past 15 months Dr. Young has obtained the gonococcus in pure culture in 7 instances of gonorrhœal arthritis in the Johns Hopkins Hospital, demonstrating that the arthritis in a large proportion of instances represents a true local bacterial infection.

The gonococcus has also been obtained in pure culture from a number of instances of tenosynovitis (Jacobi and Goldmann,† Bloodgood and Young‡), from subcutaneous abscesses (Lang and Paltauf§ and Horwitz‖), from intramuscular abscesses (Bujwid¶), from pleural effusions (Bordoni-Uffreduzzi**), from the circulating blood (Thayer and Blumer,†† Thayer and Lazear‡‡), and recently by Young§§ from a case of general peritonitis following an acute gonorrhœal

* *Wiener klin. Wochenschr.*, 1893, vi, 59.
† *Beiträge z. klin. Chir.*, 1894, xii, 827.
‡ Unpublished observations in the Johns Hopkins Hospital.
§ *Arch. f. Derm. u. Syph.*, 1893, xxv, 330.
‖ *Wien. klin. Woch.*, 1893, vi, 59.
¶ *Centrlb. f. Bakt.*, 1895, xviii, 435.
** *Deutsche med. Woch.*, 1894, xx, 484.
†† Op. cit.
‡‡ *Med. Record*, N. Y., 1897, lii, 497, and present article.
§§ Unpublished observation.

salpingitis. That in some instances, therefore, the gonococcus itself should be the cause of endocarditis, pericarditis, and myocarditis is by no means remarkable. Our own experience during the last several years, together with a study of the literature, indicates that the cardiac complications of gonorrhœa are more frequent than has generally been supposed.

Endocarditis is by far the commonest of the cardiac complications of gonorrhœa. Gurvich* has collected 110 instances in 77 of which the cases are sufficiently well reported to allow of definite conclusions. From the more recent literature it is possible to add some ten or a dozen more cases to those of Gurvich.

In the majority of these cases the cardiac complications have been preceded by an arthritis. In a considerable number of instances, however, joint symptoms have been entirely absent, while in several cases evidences of endo- or pericarditis have appeared before the development of joint manifestations.

Pericarditis is a much less frequent complication. We have been able to collect but 17 positive cases in the literature.

Myocardial changes have been demonstrated in the majority of the cases of acute ulcerative endocarditis of gonorrhœal origin which have come to autopsy, the most satisfactorily studied instance being that of Councilman, where there was no affection of the endocardium.

For a satisfactory study, however, of the cardiac complications of gonorrhœa one must turn to the cases which have been observed anatomically as well as clinically. We have collected 32 instances of gonorrhœa with fatal cardiac complications where there were satisfactory pathological notes. Several of those included in other classifications have been omitted because of insufficient data. Of these 32 cases 31 were instances of ulcerative endocarditis with or without marked pericardial or myocardial affection; one, that of Councilman, was an instance of peri- and myocarditis alone.

Gonorrhoeal endocarditis.—These cases considered from a pathological standpoint may be divided into five classes:

* *Russk. arch. patol., klin. med. i. bakt.*, 1897, iii, 329.

(1) The first class includes six cases, those of Bourdon,* Desnos,† Schedler,‡ Draper,§ Fleury,‖ and His.¶

In these instances, although the history clearly shows the association of the process with gonorrhœa, no note is made with regard to bacteriological examination.

(2) The second class comprises ten cases, those of Martin,** Weckerle,†† Weichselbaum,‡‡ Ely,§§ Wilms,‖‖ Golz,¶¶ Keller,*** Zawadzki and Bregman,††† Babes and Sion,‡‡‡ and lastly an unpublished observation of our own, Case 32 of our series (p. 115). Here there existed mixed or secondary infections. In some instances organisms other than gonococci were obtained in pure culture; in others, strepto- and staphylococci were demonstrated microscopically. In several cases organisms morphologically similar to gonococci were found, while the actual sequence of the infection upon acute gonorrhœa is not to be doubted.

(3) The third class includes four cases, those of Rothmund,§§§ His,‖‖‖ Winterberg¶¶¶ and Fressel.**** Here the infection was probably purely gonococcal. In all of these cases organisms showing the morphological and tinctorial characteristics of gonococci were

* *Gaz. d. Hôp.* Par., 1868, xli, 1.

† *L'Union méd.*, 3s., 1878, xxv, 43; also, *Gaz. d. Hôp.*, 1877, l, 1067.

‡ "Zur Casuistik der Herzaffectionen bei Tripper." Inaug.-Diss., Berlin, 1880.

§ *Medical Bulletin*, Phila., 1882, iv, 81.

‖ *Journ. de méd. de Bordeaux*, 1883-84, xiii, 65.

¶ *Berl. klin. Woch.*, 1892, xxix, 993.

** *Rev. méd. de la Suisse Romande*, 1882, ii, 308, 352.

†† *Münch. med. Woch.*, 1886, xxxiii, 563, 582, 608, 622, 636.

‡‡ *Centralbl. f. Bakt.*, 1887, ii, 209.

§§ *Med. Record*, xxxv, 1889, 287.

‖‖ *Münch. Med. Woch.*, 1893, xl, 745.

¶¶ Ulceröse Endocarditis der Klappen der Pulmonalarterie bei gonorrhoischer Arthritis, Inaug.-Diss., Berlin, 1893.

*** *Deutsch. Arch. f. klin. Med.*, 1896, lvii, 387.

††† *Wien. med. Woch.*, 1896, xlvi, 313, 351.

‡‡‡ *Arch. d. Sc. Méd. de Bucarest*, 1896, i, 505.

§§§ Endocarditis ulcerosa, Inaug.-Diss., Zürich, 1889.

‖‖‖ Op. cit.

¶¶¶ Festschr. z. 25 Jähr. Jub. d. Vereins Deutscher Aerzte zu San Francisco, 1894, 40.

**** Inaug.-Diss., Leipzig, 1894.

demonstrated microscopically. Cultures, however, were not made. Other organisms were not found.

(4) The fourth group comprises six cases, those of Leyden,* Finger, Ghon and Schlagenhaufer,† Hale White,‡ Michaelis,§ Stengel ‖ and Siegheim.¶ Here the proof of the purely gonococcal nature of the process is more nearly complete in that the observers made cultures upon ordinary media from the affected parts and from the circulating blood without obtaining positive results; while at the same time the microscopical demonstration from the affected regions of organisms showing all the morphological and tinctorial characteristics of gonococci would seem to form a fairly conclusive argument in favor of the existence of a pure infection by the gonococcus.

(5) Lastly, there remain five cases, those of Thayer and Blumer,** Dauber and Borst,†† Thayer and Lazear,‡‡ Rendu and Hallé§§ and Lenharz,‖‖ in which the evidence of the purely gonococcal nature of the complication may be considered as definitely proven.

In the first of these cases the gonococcus was obtained in pure culture twice during life and was found microscopically post-mortem in the affected regions.

In the case of Dauber and Borst a pure culture was obtained after death from the heart's blood of organisms concerning the nature of which the reporters were in doubt. Most subsequent observers have, however, recognized them as gonococci.

In the third instance, the writers were able to prove the purely gonorrhœal nature of the affection by obtaining gonococci in pure culture three times during life from the circulating blood, while Dr. Flexner obtained similar results post mortem from the affected valves, heart's blood, and pericardium.

* *Deutsch. med. Woch.*, 1893, xix, 909.
† *Arch. f. Dermat. u. Syph.*, 1895, xxxiii, 141, 323.
‡ *Lancet*, 1896, i, 533.
§ *Zeitschr. f. klin. Med.*, 1896, xxix, 556.
‖ *Univ. Med. Mag.*, Phila., 1897, ix, 426.
¶ *Zeitschr. f. klin. Med.*, 1898, xxxiv, 526.
** Op. cit.
†† *Deutsch. Arch. f. klin. Med.*, 1896, lvi, 231.
‡‡ *Med. Record*, N. Y., 1897, lii, 497 (case reported in this communication).
§§ *Bull. et mém. Soc. méd. d. hôp. de Par.*, 1897, 3. s., xiv, 1325.
‖‖ *Berl. klin. Woch.*, 1897, xxxiv, 1138.

In the case of Rendu and Hallé gonococci were obtained in pure culture from the endometrium during life and demonstrated microscopically in the phlegmon about the elbow. After death they were obtained in pure culture from the thrombus upon the affected valves.

Finally the last link in the chain of evidence has been supplied by Lenharz, who, from a case of characteristic gonorrhœal endocarditis, in which pure cultures were obtained from the thrombi on the aortic valves, introduced a piece of softened thrombus into the human urethra. A characteristic gonorrhœa, with gonococci in the discharge, appeared on the fourth day.

Anatomical lesions.—As to the nature of the anatomical lesion there is little to say. Considering the 15 cases in which the pure gonococcal nature of the infection is probable, one finds that in all instances there were present the usual appearances of ulcerative endocarditis with extensive polypoid ehrombi and more or less actual destruction of the valves, often with aneurism formation and perforation. The localization of the affection, however, presents several points of considerable interest. In ordinary chronic endocarditis it is well known how infrequently the right heart alone is affected; thus, out of 300 autopsies on cases of endocarditis, Sperling found the lesions limited to the right heart in but 3 instances, or 1 per cent. Weckerle out of 846 autopsies on cases showing valvular cardiac lesions in Bollinger's laboratory found that the right heart alone was affected in 3.9 per cent of all cases.

It has, however, been shown that in cases of ulcerative endocarditis the liability of the right side to infection is considerably greater. Thus, while in 802 benign cases from the Munich statistics the right heart alone was affected in 3.24 per cent, in 44 cases of ulcerative endocarditis the percentage of affections limited to the right side was nearly 16 per cent (15.91 per cent). In our 31 cases the lesions were as follows:

Left heart: aortic..... 12; mitral ..... 6; both..... 3 — 21—67.7%

Right heart: pulmonary..... 7; tricuspid ..... 1 — 8—25.8%

Both sides: mitral, aortic, tricuspid..... 1; all four valves ..... 1 — 2—6.4%

This surprisingly high percentage of right-sided cardiac affections in our cases is interesting and difficult to explain. Considering the 15 cases in which the pure gonococcal nature of the infection is probable, we have the following table:

Left heart:	aortic	7	Right side:	tricuspid	1
	mitral	2		pulmonary	2
	both	2			3—20%
		11—73.3%			

Both sides: all four valves.....1-6.6%.

The remarkable high percentage of pure right-sided cardiac affections in these cases, even as compared with the Munich tables, is an interesting point. To attempt to draw definite conclusions from so small a number of instances might well be fallacious, but the fact is none the less worthy of reflection. Indeed, why the right side of the heart should be so much more liable to disease in ulcerative endocarditis is by no means perfectly clear. Another very interesting point is the fact that the aortic valves appear from our tables to be by far the most frequently affected. While this has been the case in those fatal instances which have come to autopsy, yet Gurvich's tables based upon 64 cases in which a diagnosis was made during life show appreciably different figures. His tables show:

Mitral valve	31	Pulmonary	2
Aortic	16	Mitral and tricuspid	2
Mitral and aortic	13		

Age.—The age of the patients in the fatal cases varied between 19 and 51, while taking the larger statistics of Gurvich we find records of one instance at the age of 64 and another at 10. The majority of cases occurred, as might be expected, in early adult life.

Sex.—Of the 31 instances of fatal ulcerative endocarditis due to the gonococcus 23 were in men and 8 in women.

Time of onset.—There appears to be nothing particularly characteristic with regard to the time of onset of these cases with relation to the attack of urethritis, some, as in the case of Prévost, coming on almost immediately after the onset, others some weeks or months later. Some of the cases occurred with the initial attack of gonorrhœa, others in patients who had suffered once or twice before.

Complicating arthritis.—Arthritis preceded the cardiac affection in the majority of instances, though in a considerable number the cardiac complication occurred without or before the development of joint symptoms.

Symptoms.—The symptoms of gonorrhœal endocarditis appear to differ in no essential way from those of endocarditis of other origin. While many instances are reported in which the cardiac manifestations were slight and transient, the proportion of cases of a malignant nature which have so far been recognized is unusually large. It is not improbable, however, that this is due to the fact that the majority of milder cases escape notice. And it is well in this connection to remember how frequently the same is true in rheumatic cardiac affections.

In the fatal cases the symptoms are essentially similar to those in instances depending upon infection with other pyogenic organisms —an irregular intermittent or remittent fever, usually with severe rigors, profuse sweating and rapidly developing anæmia, albuminuria; in fact, the ordinary symptoms of a severe septicæmia. The duration of the attack in the 15 instances in which the pure gonococcal nature of the infection is probable, varied, as far as can be made out, from ten days to two months. The only exception to this rule was in our case, in which the symptoms of septicæmia lasted through a period of six months. From the consideration of these cases and of those others which were followed by recovery, it is rather difficult to see upon what Gurvich bases his conclusion that gonorrhœal cardiac affections pursue a milder course than those depending upon the other pyogenic cocci.

In a number of these instances the renal changes have been particularly severe. In several the patient died with the general appearances of a grave nephritis as in our second case. These changes are possibly to be explained by the special exposure of the kidney through the elimination of the gonococcus or its products which, in these instances of general septicæmia, occurs in all probability through the urine.

Pericarditis.—Pericarditis is a far less frequent occurrence than

endocarditis in gonorrhœal infection. In 7 of the 32 fatal instances there is a note of a pericardial complication. The cases of Weckerle and Golz were mixed infections. In Councilman's case the pericardial cavity was enormously distended, containing 800 cc. of a hæmorrhagic exudate in which there were large masses of clot. Both surfaces of the pericardium were covered with thick membranous masses containing hæmorrhages. A few gonococci were found in the pericardium. In Winterberg's case it is noted that 20 ccm. of sero-purulent fluid were found in the pericardial sac. In our second case the pericardial cavity contained about 300 ccm. of turbid yellow fluid containing flakes of fibrin. In the dependent portions the fluid was thick and puriform. The surface of the peri- and epicardium was congested and contained small ecchymoses; it was covered by a granular deposit. Gonococci were obtained in pure cultures from the fibrin upon the surface of the pericardium. In Rendu's case it is noted that the pericardium contained 500 cc. of translucent fluid and that there were " pericardial lesions," nothing further. Cultures from the fluid were negative.

Thus, it may be seen that anatomically nothing striking is to be made out from a consideration of these observations. The definite proof of the existence of a pure gonorrhœal pericarditis is furnished by the positive result of our cultures in Case II.

Myocarditis.—Grave myocardial changes, necroses with hæmorrhage, leucocytic infiltration, embolic abscesses have been described in a number of instances in association with fatal endocarditis. In Councilman's case the areas of necrosis and suppuration were large and gonococci were found microscopically in the foci.

CONCLUSIONS.

(1) An acute gonorrhœal urethritis may be the starting point for a grave general septicæmia with all its possible complications.

(2) These infections may be mixed or secondary, due to the entrance into the circulation of organisms other than the gonococcus, or they may be purely gonococcal in nature.

(3) Endocarditis is an occasional complication of gonorrhœa.

(4) This endocarditis may be transient, disappearing with but few apparent results, or it may leave the patient with a chronic valvular lesion, or it may pursue a rapidly fatal course with the symptoms of acute ulcerative endocarditis.

(5) The endocarditis associated with gonorrhœa is commonly due to the direct action of the gonococcus, but may be the result of a secondary or mixed infection.

(6) Pericarditis may also occur as a complication of gonorrhœa, but it is less frequent than endocarditis. It may, as in the case of the latter, be the result either of a pure gonococcal or of a mixed infection.

(7) Grave myocardial changes, necroses, purulent infiltration, embolic abscesses are common in the severe gonococcal septicæmias.

(8) In instances of gonococcal septicæmia the diagnosis may, in some cases, be made during life by cultures taken from the circulating blood according to proper methods.

REPORTER.	SEX.	AGE.	HISTORY.	AUTOPSY.	REMARKS.
(1) Bourdon. *Gaz. d. Hôp.*, 1868, xli, 1.	M	24	Gonorrhœa; one month later, arthritis; delirium; irregular chills; evidences of endocarditis. Hæmorrhagic areas in skin, becoming gangrenous; bed sores. Death 13 months after infection.	Verrucous endocarditis of mitral and tricuspid valves with thrombi. Kidneys pale and fatty.	
(2) Desnos. *L'Union Méd.* 3 s., 1878, xxv, 43. Also *Gaz. d. Hôp.*, 1877, L, 1867.	M	?	Gonorrhœa; bronchitis; arthritis; dyspnœa; palpitation; cardiac murmur; irregular fever. Death less than a month after onset of arthritis. The heart was normal on first examination. No history of any previous predisposing malady.	Vegetative endocarditis of aortic and mitral valves.	In the discussion of the case Fournier acknowledged its gonorrhœal origin.
(3) Schedler. "Zur Casuistik der Herzaffectionen nach Tripper." Inaug. diss. Berlin, 1880.	M	22	Gonorrhœa; epididymitis; arthritis and moderate fever, shortly after onset. 7 months later, irregular chills; evidences of aortic endocarditis with insufficiency. Death 5 weeks after onset of acute symptoms.	Ulcerative endocarditis of aortic valve.	Patient had had smallpox and a fever some time previously, which justifies one in asking whether the endocarditis may not have preexisted. At the autopsy the changes pointed to a recent affection. The reporter as well as Prof. Leyden have no doubt as to its gonorrhœal origin.
(4) Draper. *Medical Bulletin*, Philadelphia, 1882, iv, 81.	M	19	Chronic gonorrhœa for a year; arthritis; irregular fever, with chills; embolism in leg. Death 4 months after onset of arthritis.	Ulcerative endocarditis of mitral valve. Infarctions in spleen and kidneys.	

REPORTER.	SEX.	AGE.	HISTORY.	AUTOPSY.	REMARKS.
(5) Martin. *Rev. Méd. de la Suisse Romande,* 1882, ii, 308, 352.	M	24	Previous history good. Lost appetite and began to feel ill 3–4 weeks before entrance into hospital. Chills; irregular fever; evidences of pyæmia; multiple arthritis; hæmaturia; right pleuro-pneumonia; suppurative conjunctivitis; parotitis. Death a month after beginning of symptoms.	Gonorrhœa; suppurative prostatitis; cystitis; suppurative inflammation of vesiculæ seminales; multiple myocardial abscesses. Ulcerative and vegetative endocarditis of mitral valve. In the thrombi on valves were numerous cocci, some of which were exactly similar morphologically to Neisser's gonococci. The kidneys showed fatty degeneration with septic emboli.	The case would appear to be of gonorrhœal origin, whether or not a secondary infection occurred.
(6) Fleury. *Journ. de Méd. de Bordeaux,* 1883-'84, xiii, 65.	M	27	Gonorrhœa; 3 months later disappearance of discharge; arthritis; thoracic pains; pericarditis. Death 3 weeks after arthritis. No signs of cardiac disease on examination before this infection.	Vegetative and ulcerative endocarditis of aortic valves with perforation. A certain amount of blood-stained fluid in the pericardium; a patch of false membrane just below the root of the aorta.	
(7) Weckerle. *Münch. med. Woch.,* 1886, xxxiii, 563, 582, 608, 622, 636.	F	24	Gonorrhœa; inguinal adenitis; arthritis; 1 to 2 months after arthritis, signs of ulcerative endocarditis of pulmonary valve; chills; irregular fever; dry pleurisy. Death a month after onset. The urine, normal at first, showed a large quantity of albumin; sediment; red and white corpuscles: renal epithelium and casts.	Sero-fibrinous pericarditis. Extensive ulcerative endocarditis of pulmonary valves. Numerous cocci in the thrombi on the valves, sometimes in chains, sometimes in groups. These organisms stain according to Gram. No particular search was made for gonococci. Kidneys large—subacute parenchymatous nephritis.	The author does not believe the endocarditis to have been gonococcal. The only portal of entry appears to have been furnished by the gonorrhœa.

REPORTER.	SEX.	AGE.	HISTORY.	AUTOPSY.	REMARKS.
(8) Weichselbaum *Centralbl. f. Bakt.*, 1887, ii, 209. Also, Ziegler's *Beiträge*, 1889, iv, 125.	M	21	Gonorrhœa for 3 weeks; high fever. Death on day of entry. Gonococci in urethral secretion.	Acute splenic tumor. Ulcerative aortic endocarditis. Gonococci in urethra. Only streptococci, morphologically and by culture, on the valves.	W. believes that the gonorrhœa formed the portal of entry for the streptococcus.
(9) Rothmund. "Endocarditis Ulcerosa." Dissertation, Zürich. 1889.	M	51	Gonorrhœa; 8 or 9 weeks later epididymitis; poly-arthritis; heart sounds clear; moderate fever. 3 weeks later loud systolic murmur over mitral and tricuspid areas. 10 days later, high pitched diastolic murmur over aortic and pulmonary regions; delirium; jaundice. Death 5 weeks after arthritis.	Urethritis; cystitis; right knee joint and left ankle contain sero-hæmorrhagic fluid. Extensive ulcerative endocarditis of aortic valves. In the blood of the right heart and in the affected joints were found cocci having the form and grouping of gonococci.	
(10) Ely. *Med. Record*, 1889, xxxv, 287.	M	28	No history. Ill 3 days. Fever; delirium; vomiting. 2 days after entry partial left hemiplegia and death.	Gonorrhœa; old pericardial adhesions; fresh vegetative and ulcerative endocarditis of mitral valve. In thrombi on valve there were cocci and bacilli. In all embolic abscesses in liver, kidneys and in heart valves as well as in urethra, similar cocci staining by Gram and arranged in clusters and chains, are seen. In urethral pus, gonococci decolorizing by Gram are also seen.	The author believes the case to be one of secondary infection with pyogenic cocci.

REPORTER.	SEX.	AGE	HISTORY.	AUTOPSY.	REMARKS.
(11) His. *Berl. klin. Woch.*, 1892, xxix, 993.	M	19	Gonorrhœa; first attack, disappearing apparently in 3 weeks. 2 weeks later syncopal attack, followed by chills; hæmorrhagic eruption; remittent fever; loud systolic murmur; signs of ulcerative andocarditis. Blood cultures from ear negative.	General anæmia; ecchymoses of skin and serous membranes; ulcerative aortic endocarditis; softened thrombus at cardiac apex. Acute interstitial myocarditis; septic emboli in spleen, kidneys and lungs. In the thrombi on the affected valve cocci resembling gonococci were found; these decolorized when treated according to Gram. Unfortunately, the specimen had been previously put in Müller's fluid.	
(12) His. *Op. cit.*	M	19	Gonorrhœa; arthritis; a few days later irregular fever and chills, sometimes two a day. 4 months after onset of gonorrhœa there were signs of ulcerative endocarditis; aortic stenosis. Death 5½ months after onset of gonorrhœa.	Acute aortic endocarditis; partial aneurism at root of aorta with papillary thrombi; enlarged spleen with fresh infarcts; subacute parenchymatous nephritis; slight hydrothorax; hydropericardium. No bacteriological examination.	Case observed by Wagner in 1879. Autopsy by Huber.
(13) Leyden. *Deutsch. med. Woch.*, 1893, xix, 909.	M	22	Chronic gonorrhœa; epididymitis; arthritis of right knee; signs of ulcerative endocarditis with aortic insufficiency; irregular fever; chills. Death 6 to 7 weeks after onset of arthritis. Cultures from vein on ordinary media, negative.	Acute myocarditis; ulcerative endocarditis of aortic and vegetative endocarditis of mitral valves. Typical gonococci decolorizing by Gram in the thrombi on valves. Cultures on ordinary media negative.	Doubtless a pure gonorrhœal endocarditis.

REPORTER.	SEX.	AGE.	HISTORY.	AUTOPSY.	REMARKS.
(14) Wilms. *Münch. med. Woch.*, 1893, xl, 745.	M	26	Gonorrhœa 6 months ago and again later; 3 weeks after second attack, chill, arthritis in knee; a week later signs of aortic insufficiency; high fever. Death 6 weeks after the second infection.	Ulcerative endocarditis of aortic valve extending through into right auricle; suppurative myocarditis. Numerous cocci in thrombus, some separate, some arranged like gonococci and intracellular. They decolorize almost immediately by Gram. In leucocytes in the sub-mucous tissue of urethra there were scanty diplococci, some resembling gonococci.	The author does not believe the organisms were *gonococci* though the description is more than suggestive.
(15) Golz. "Ulceröse Endocarditis der Klappen der Pulmonalarterie bei gonorrhoischer Arthritis." Inaug. Diss. Berlin, 1893.	M	21	Gonorrhœa; right-sided bubo; 6 days later arthritis in right shoulder and left foot. Gonococci found in urethra. 2 weeks later chills; heart sounds clear; chills and fever continued, and 2 weeks later systolic murmur became audible; diastolic murmur in pulmonary area. 3 weeks later pericarditis and pleurisy with hæmorrhagic exudate; pulmonary embolism. Death 3½ months after infection and a little less than 3 months after apparent onset of endocarditis.	Fibrinous pericarditis; in *pericardium ½ litre of fairly* clear fluid. Ulcerative endocarditis of pulmonary valve and of wall of *right auricle.* No cultures. The specimen had been left for a considerable time in alcohol before a bacteriological examination was made. Small cocci at times in groups and sometimes in chains were found. No characteristic gonococci.	The organisms described by the author appear to have been staphylococci and *streptococci.*

REPORTER.	SEX.	AGE.	HISTORY.	AUTOPSY.	REMARKS.
(16) Councilman. *Am. Jour. Med. Sci.*, 1893, cvi, 540.	M	?	Gonorrhœa; 10 days later arthritis in various joints. Five weeks after infection pericarditis. Death suddenly 3 days later.	Pericardium contained 800 cc. of hæmorrhagic exudate in which there were large masses of clot. Both surfaces of pericardium covered with thick membranous masses, containing hæmorrhages. Suppurative myocarditis. Gonococci, characteristic morphologically, in suppurative foci in heart muscle, pericardium, urethra and joints; they decolorized by Gram. No cultures.	
(17) Fressel. Inaug. Diss. Leipsic, 1894.	F	26	History imperfect. Severe symptoms came on a few days before death. Extreme weakness; emaciation; orthopnœa; arthritis of left ankle.	Ulcerative and polypoid endocarditis of mitral and aortic valves. Kidneys practically normal. Cystitis; urethritis; vaginitis. The thrombi on valves showed organisms having microscopically the characteristics of the gonococcus; some occupying cells; they decolorized by Gram's method. No cultures.	
(18) Winterberg. Festschrift z. 25 Jähr. Jub. des Vereins Deutscher Aerzte zu San Francisco, 1894, 40.	M	25	Gonorrhœa; 6 weeks later right epididymitis; double bubo; arthritis of both elbows; dyspnœa; systolic and diastolic murmurs especially in aortic area. Death after onset.	Pleural effusion on both sides; 20 cc. sero-purulent fluid in pericardium; myocardial abscesses. Ulcerative endocarditis of aortic and pulmonary valves which were almost entirely destroyed. Endocarditis of mitral and tricuspid valves of a lesser extent. Amyloid kidneys. No cultures. Cover glass specimens from valves showed organisms answering morphologically and tinctorially to gonococci, decolorizing by the method of Gram.	

REPORTER.	SEX.	AGE.	HISTORY.	AUTOPSY.	REMARKS.
(19) Thayer and Blumer. *Arch. de Méd. Expér.*, 1895, vii, 701, and Johns Hopkins Hospital Bull., 1896, vii, 57.	F	34	Vague history of rheumatism 3 months ago; has been short of breath 3 or 4 years. About 3 months after "rheumatism," irregular fever and chills; signs of ulcerative endocarditis; mitral stenosis. Death 3 weeks after onset of fever. Cultures from median basilic vein 9 and 4 days before death showed pure growths of diplococci resembling in every way gonococci and decolorizing by Gram's method. The medium contained at least one-third blood (the syringe full of blood mixed with agar agar and plated). Transplanted to ordinary media there was no growth.	Ulcerative endocarditis of mitral valve. In the thrombi on valves and in vagina and uterus characteristic intracellular gonococci, decolorizing when treated according to Gram's method. Cultures made on agar agar and bullock's blood serum from all sources were negative.	This is the first case in which gonococci were obtained in pure culture from the blood during life.
(20) Finger, Ghon and Schlagenhaufer. *Arch. f. Dermat. u. Syph.*, 1895, xxxiii, 141, 323.	M	19	Chronic gonorrhœa for a year. Fresh attack in March, 1895. 6 months later arthritis in right knee; fever. Heart sounds clear; gonococci in urethral discharge; chills; 10 days later diastolic murmur over aorta, Death 9 days later.	Myocarditis; ulcerative aortic endocarditis with perforation. Arthritis of right knee joint. Chronic urethritis; prostatic abscess; infarct of spleen; cloudy swelling of kidneys. Characteristic gonococci in urethra and in thrombi on valves, decolorizing by Gram. Cultures on ox's serum peptone agar were negative excepting from urethra, from which an unidentified coccus was obtained.	The authors believe the case to be purely gonorrhœal, the gonococci having lost their vitality, possibly owing to high temperature before (and after, W. S. T.,) death, and hence failing to grow.

REPORTER.	SEX.	AGE.	HISTORY.	AUTOPSY.	REMARKS.
(21) Zawadzki and Bregman. *Wien. med. Woch.*, 1896, xlvi. 313, 351.	F	17	A month ago purulent vaginitis with staphylococcus and micrococcus tetragenus; chills and fever; 6 weeks after infection, arthritis in hip not yielding to salicylates; 11 days later, serous pleurisy on right side, showing on culture, streptococcus pyogenes; staphylococcus albus; micrococcus tetragenus. 15 weeks after onset right hemiplegia and death.	Verrucous mitral endocarditis; embolism of right arteria fossæ Sylvii. In the excrescences on valves among other organisms were numerous characteristic gonococci. These were in part in groups in the intermediate tissue, in part in the cells and in their neighborhood. They had the character and shape of gonococci and were decolorized when treated according to Gram. They were more numerous on the free border of the valves as were the other cocci.	A mixed infection. Some question as to whether the organisms found were gonococci.
(22) Dauber and Borst. *Deutsch. Arch. f. kl. Med.*, 1896, lvi, 231.	M	20	Gonorrhœa; tenosynovitis of left hand; inguinal buboes; periurethral abscesses. 2 weeks after onset, chill; irregular fever; heart's sounds clear. Pain in cervical vertebræ. 3 months after infection evidences of aortic insufficiency; septic nephritis. Gonococci gradually disappeared from urethral discharge, other bacteria appearing. Cultures from blood, negative. Death.	Ulcerative and vegetative endocarditis of aortic valve; suppurative myocarditis; acute nephritis; septic emboli and infarctions of kidney. In thrombi organisms showing all the characteristics of gonococci, decolorizing by Gram; also once in colorless corpuscle in heart's blood. Cultures negative excepting one on human blood serum agar on which there developed after 36 hours separate point-like, yellowish brown translucent colonies. On feeble magnification these appeared round, had a sharp clean-cut border, showed no outgrowths from their peripheries or daughter colonies so characteristic of gonococci. Micro-organisms obtained from the culture were almost entirely diplococci, in part biscuit shaped, in part, round.	While the authors doubt that these were gonococci, most will probably accept the case as positive. Vide Michaelis, *Op. cit.* and Thayer and Blumer. *Johns Hopkins Hospital Bulletin*, 1896, vii, 57.

REPORTER.	SEX.	AGE.	HISTORY.	AUTOPSY.	REMARKS.
(23) Michaelis. *Zeitschr. f. kl. Med.*, 1896, xxix, 556.	M	25	Gonorrhœa; 3 weeks later, arthritis; slight fever; no albuminuria; 4 days later, systolic murmur over aorta; diastolic sound not clear. Sudden death 10 days later. Gonococci in urethral discharge.	Vegetative and ulcerative aortic endocarditis with perforation. Pericardial and pleural cavities showed abundant serous fluid with a few fibrinous flakes. Purulent cystitis. Characteristic gonococci in thrombi on valves, i. e. shape; intracellular arrangement; decolorization by Gram's method; failure to grow on attempts to cultivate on ordinary media.	In all probability a pure gonococcal endocarditis.
(24) Keller. *Deutsch. Arch. f. kl. Med.*, 1896, lvii, 387.	M	25	Gonorrhœa; arthritis 4 weeks after; later pains in chest; chills; irregular intermittent fever; evidences of pulmonary endocarditis; pericarditis. Death 4 months after infection and 3 months after arthritis. Diagnosis: pulmonary stenosis and insufficiency.	Increase in pericardial fluid which was made cloudy by the presence of fine flocculi. Vegetative endocarditis of pulmonary valves and pulmonary artery; myocarditis. Streptococci in cultures from pericardial fluid. In polypi on pulmonary valve streptococci were found; streptococci in kidneys.	The author believes that this was a mixed infection through the urethra.
(25) Hale White. *Lancet*, 1896, i, 533.	M	19	Gonorrhœa; 3 weeks later, chills; irregular intermittent fever; anæmia; systolic and diastolic murmurs in pulmonary area; 5 weeks after infection, acute nephritis; œdema. Two weeks later, death.	Ulcerative and vegetative endocarditis of the pulmonary valve and artery. Acute nephritis; characteristic gonococci in vegetations on valves. These decolorized when treated by Gram's method. Cultures taken on agar, glycerine agar, broth and blood serum were without result. No cultures were made on serum agar. (These latter particulars were obtained in a personal communication from Dr. Pakes.)	The author remarks on the frequency of nephritis in ulcerative endocarditis, and believes it to be a not uncommon cause of death.

REPORTER.	SEX.	AGE.	HISTORY.	AUTOPSY.	REMARKS.
(26) Babes and Sion. *Arch. d. Sc. Méd. de Bucharest*, 1896, i, 505.	M	?	August 5, gonorrhœa; 20 days later cystitis; epididymitis; purpura; fever; chills; vomiting; splenic tumor. On September 2, aortic systolic murmur; albuminuria; diarrhœa. Death October 14. In blood during life Opresco saw cocci resembling gonococci and decolorizing by Gram; they were within leucocytes.	Gangrene of skin over lower abdomen and genitalia; hæmorrhagic infarct of kidney; ulcerative aortic endocarditis. In the thrombi on valves organisms similar to gonococci were found, decolorizing by Gram. On ordinary media saprophytes alone grew. No growths on beef blood serum agar. In spleen and kidney strepto- and staphylococci.	They believe the case to have been gonorary streptococcus and rhœal with a second staphylococcus infection. They seem to think that, the pus cocci having entered and caused a general septicæmia, the gonococci profiting by the diminished resistance of the organism entered later and attacked the valves.
(27) Stengel. *Univ. Med. Mag.*, Phila., 1897, ix, 426.	F	20	Had had valvular heart disease, since rheumatism, at age of 7; gonorrhœa for a year (?); 6 days before entry into hospital diarrhœa; headache, vomiting, tympanites; evidences of mitral stenosis; acute nephritis. Continued fever. Death after 32 days.	Chronic endocarditis of mitral valve. Fresh ulcerative and vegetative endocarditis of mitral valve and part of auricle, particularly marked on an anomalous adventitious leaflet. Muco-purulent exudate in uterus and vagina. Cultures: Streptococcus from lungs and staphylococcus from right auricle and spleen; endocardial vegetations negative. Characteristic gonococci were found in two thrombi on valves, mainly intracellular, decolorizing by Gram. No gonococci found in exudate in uterus or vagina. Deeper tissues not examined.	

REPORTER.	SEX.	AGE.	HISTORY.	AUTOPSY.	REMARKS.
(28) Thayer and Lazear. Subject of present communication, read before XII International Congress in Moscow, 1897. *Med. Record*, 1897, lii, 497.	M	19	Gonorrhœa 6 months before entry into hospital; several weeks later chill; 5 to 6 months later œdema of legs; subacute nephritis; grave anæmia; systolic murmur; pericarditis. Death 7½ months after infection, about 6 months after onset of chills. Gonococci obtained three times during life from circulating blood. Diagnosis: gonorrhœal septicæmia, endo- and pericarditis.	Ulcerative and vegetative endocarditis of tricuspid valve. Sero-purulent pleurisy and pericarditis; subacute hæmorrhagic and glomerular nephritis. Gonococci obtained microscopically and in pure culture on Loeffler's blood serum agar from heart's blood, pericardium and affected valves. All other cultures negative.	This is the first case in which gonococci were obtained in pure culture before and after death from the blood, thus permitting a positive ante-mortem diagnosis of gonorrhœal septicæmia.
(29) Rendu and Hallé. *Bull et. mém. Soc. méd. de hôp. de Par.* 1897, 3 s., xiv, 1325.	F	30	Gonorrhœal metritis; about 2 weeks later fever; night sweats; evidences of septicæmia. Gonococcus isolated from uterine mucus. Phlegmon near elbow joint; intermittent fever; endo- and pericarditis about 5 weeks after onset of fever. Death 10 days later. In phlegmonous œdema at elbow gonococci "à l'état de pureté" were found. Blood cultures negative.	Vegetative endocarditis of aortic valve and of ascending aorta. Sero-fibrinous pericarditis. Cultures from pleural and pericardial fluids negative. The bacteriological and histological examination of the aortic vegetations showed the exclusive presence of gonococci.	Were the gonococci obtained in pure culture?
(30) Siegheim. *Ztschr. f. kl. Med.* 1898, xxxiv, 526.	F	20	Chills and fever and systolic murmur in tricuspid area in June; later, systolic murmur in mitral, and diastolic in aortic area; dyspnœa; irregular intermittent fever; chills. Death July 11. Cultures from blood on Kiefer's agar agar and peptone bouillon were negative.	Ulcerative endocarditis of aortic valve; myocarditis; nephritis; purulent endometritis and cystitis. Cultures on Kiefer's agar from heart's blood and vegetations negative. Microscopical examination of smear preparations from thrombi revealed organisms showing all the morphological and tinctorial characteristics of gonococci.	

REPORTER.	SEX.	AGE.	HISTORY.	AUTOPSY.	REMARKS.
(31) Lenharz. *Berl. kl. Woch.*, 1897, xxxiv, 1138.	F	19	Abundant vaginal discharge; symptoms of *ulcerative* endocarditis of pulmonary valve. Death.	Vegetative endocarditis of pulmonary valves. Characteristic gonococci in softened thrombi. These were obtained in pure culture. A piece of softened thrombus was introduced into the human urethra resulting in the development, after four days, of gonorrhœa with typical organisms.	This case would appear to remove all doubt as to the possibility of the existence of a true gonorrhœal endocarditis.
(32) Unpublished observation from the wards of Prof. Osler, Johns Hopkins Hospital. (Case observed by one of the authors—Thayer).	M	38	Measles as a child; no other acute infectious diseases. Entered hospital 20/vii/94. Has gonorrhœa with characteristic gonococci in discharge. For 3 weeks irregularly intermittent fever with chills. *Physical examination:* negative; heart sounds clear; apex impulse in 5th interspace, just inside mammillary line. Leucocytes 17,000 per cu. mm.; *urine* shows trace of albumin; no casts found. Irregular fever with severe rigors; left hospital *unimproved on* 2 / viii / 94. Urethral discharge and rigors stopped two weeks later; fever however continued. A few days after leaving hospital, stabbing pains in præcordial region, somewhat relieved by pressure over heart; dyspnœa. In latter part of October puffiness of eyelids, frequency of	(By Dr. Flexner.) Chronic and acute endocarditis (vegetative and ulcerative) of the pulmonary valves; deficiency of one segment; vegetation extending 3 cm. into the pulmonary artery; globular thrombi in left ventricle; acute pneumonia; chronic diffuse nephritis. Coverslips from the thrombi on the affected valve show encapsulated diplococci; others biscuit shaped, resembling gonococci. On treatment by Gram's method some apparently decolorized, others did not. Characteristic *gonococci* in urethra. Cultures on ascitic fluid agar and Loeffler's blood serum from thrombi on affected valve, mitral valve, heart's blood, pleura, lung, kidney, spleen, liver and bladder all showed pneumococci.	The clinical history suggests strongly that the original process was associated with the gonorrhœa, while the pneumococcus infection was a late secondary event. The following note was made by Dr. Flexner: "Note.— Had the gonococcus been present it is probable that it would have been so obscured by the universal presence of the the Diploc. pneumoniæ that it could not have been detected."

REPORTER.	SEX.	AGE.	HISTORY.	AUTOPSY.	REMARKS.
			micturition, purpuric eruption on legs. Re-entered hospital 7/xi.—Physical examination: puffiness of face; pulse of high tension. Heart: apex impulse in 5th space 2 cm. outside nipple; slight to-and-fro murmur over pulmonary orifice, so superficial that it was believed to be pericardial; purpuric eruption on legs and thighs. *Urine:* trace of albumin; sediment: hyaline, granular, pus casts and renal epithelial cells. *Blood:* 13/xi; red corpuscles, 3,920,000; colorless, 31,200; hæmoglobin, 46%. 14/xi; diastolic murmur, heard by Prof. Osler in pulmonary area. Irregular fever disappeared on the 18th and T° was subnormal afterwards, excepting on the 21st, 22nd and 23rd. The dyspnœa increased, pneumonia developed, and on 26 / xi the patient died. The day before death the leucocytes were 78,000 per cu. mm. Cultures from the blood, made by Dr. Blumer on 17/xi, were negative.		