I

GONOCOCCAL ENDOCARDITIS

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ENDOCARDITIS was observed by Ricord as a complication of gonorrhœal urethritis as far back as 1847. Lacasagne (1872) stated that a gonococcal infection might involve the pericardium, myocardium, or endocardium. He (1892) obtained cultures of gonococci from thrombi of the endocardial valves in a fatal case; and Thayer and Blumer (1895) grew gonococci from the blood during life. Horder (1906) described a case with positive blood cultures (the first in this country) and gave an account of the pathological findings.

Gonococcal endocarditis is a rare complication of gonorrhœal urethritis. Thus in 1922 Thayer could collect only 60 cases from the previous literature, and added 12 of his own. Hoffman and Taggart (1932), "in a comprehensive survey of the literature since 1922," could find only 9 more cases, including one of their own. Stone (1934) in "a review of the available literature" found a total of 77 proven cases and a further 45 in which the diagnosis was not certain. In the past twenty-five years (1912-36 inclusive) at the London Hospital out of a total number of in-patients of 405,481, there have been only 6 cases of gonococcal endocarditis. These are:—

Case 1.—Admitted to the London Hospital on January 5th, 1920, under the care of one of us (R. A. R.) and died January 24th, 1920.

Female, aged 41. Registered number 40057/20. This patient came to hospital complaining that for three weeks she had had pain in the epigastrium and præcordium, radiating to the back, and shortness of breath on exertion.

Apart from scarlet fever as a child, there were no previous illnesses. She had five children, who were living, and no miscarriages. Her husband gave a history of

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gonorrhœa three years previously, and had suffered from gleet intermittently ever since.

On admission : T. 102 ; P. 100 ; R. 32. The patient was well nourished, but pallid. Her tongue was furred and the teeth in fair condition. The apex beat was in the 5th intercostal space, $\frac{1}{4}$ inch internal to the nipple line ; a systolic murmur and a reduplicated second sound were present at the apex, and at both the aortic and pulmonary areas systolic and diastolic murmurs were heard. The lungs were clear. The abdominal movements were

Case 1.

good, and there was no tenderness or rigidity, and no enlargement of the liver or spleen.

Blood cultures (G. T. Western) grew a Gram-negative diplococcus having the cultural characteristics of the gonococcus. Blood count showed a leucocytosis of 22,800 with polymorphonuclear cells 85 per cent. Films and cultures from the cervix uteri and urethra were negative during life and after death. The Wassermann reaction was negative.

Six days after admission a pericardial friction rub was audible over the præcordium, but this disappeared after a further five days.

For fourteen days after admission the temperature ranged from 103-97, sometimes being highest in the

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morning, and at other times in the evening. During the fifteenth day after admission, her daily chart recorded no pyrexia, but her four-hourly chart showed pyrexia at noon and at midnight; and for thirty-two hours before death the patient was afebrile.

SUMMARY OF NECROPSY

P.M. No. 43. Necropsy, January 26th, 1920.

Heart failure; bacteraemia; aortic incompetence; subacute fibrino-purulent gonococcal endocarditis; subacute urethritis.

Foramen ovale closed. Heart weight, 12 oz. Petechiae in pericardium over root of pulmonary artery and in endocardium of right auricle. Severe parenchymatous degeneration, chiefly fatty, of myocardium. Dilatation and slight hypertrophy of left ventricle. Large ulcer, bounded by yellow, slightly calcified, tough, fleshy, fibrinous vegetations, in right half of right posterior cusp of aortic valve. Ulceration in corresponding sinus of Valsalva exposing musculature of right auricle. Smaller ulcer, bounded by similar vegetations, in left half of anterior cusp of aortic valve. Nodules of purulent infiltration in interventricular septum, beneath anterior aortic cusp. Pink, fleshy vegetation projecting for 1 cm. from the right superior angle of the ventricular surface of the aortic cusp of the mitral valve. Small yellow vegetations on pars membranacea septi. Slight atheroma of aorta and carotid arteries. Slightly raised, dry infarct in upper pole of chronic septic spleen (5 oz.). Subacute, hæmorrhagic, lipoid, nephritis acris (20½ oz.); petechiae in renal pelves. Very little lipoid in cortex of suprarenal bodies. Central congestion, small areas of confluent "back-pressure" atrophy, and considerable cloudy swelling of liver (4 lb.). Numerous "mixed" stones in gall-bladder. Hæmorrhages and great albuminous oedema in lungs. Fibrous tag upon apex of upper lobe of left lung. Bilateral hydrothorax (2 oz. right; 2 oz. left). Embolic hæmorrhages in submucosa of lower jejunum and lower ileum; petechiae in serosa of small intestine. Hæmorrhage (1.3 cm. diameter) in leptomeninges over left parietal lobe. Congestion and oedema of brain (2 lb. 9½ oz.). Fibrous adhesions about fimbria of right Fallopian tube. Slight subacute inflammation of submucosa of urethra. Slight colloid hypertrophy of thyroid. Ascites (5 oz.). Red marrow in upper three-fifths of femur, and throughout sternum. Height 4 ft. 11 in. Weight 114 lb.

Dr. G. T. Western reported that films from vegetations on aortic valves contained typical gonococci.

Case 2.—Female, aged 20. Registered number 44613/21. Admitted as a gynæcological in-patient on November 6th, 1921.

Six days before admission to hospital there was a sudden onset of sharp pain in the abdomen which doubled her up, and settled in the L.I.F. She had also vomited on the day of onset, and the following day. The pain had continued with slight intermission. Menstruation

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finished two days before admission, and there had never been any leucorrhœa.

The patient was admitted into a gynæcological ward,

Case 2.

Case 2 (continued).

but transferred to a surgical ward as acute appendicitis. T. 98·5 ; P. 106 ; R. 24. She remained under observation for ten days on the surgical side before operation, with an

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evening temperature of 100° to 101° F. On November 18th her abdomen was opened, and a right tubo-ovarian abscess and a left pyosalpinx found. The outer surface of the appendix was inflamed and appendicectomy performed. A tube was placed in Douglas' pouch. Vaginal douches were subsequently given.

Five days after operation the temperature fell to normal and for the next two weeks remained so except for occasional nocturnal pyrexia up to 101° F. After transference to Convalescent Home, the temperature rose every evening to 102° F. The patient therefore was sent back to hospital, and was seen by one of us (R. A. R.) in consultation and admitted under our care. On examination she was seen to be pallid and anæmic, with a clean tongue. The apex beat was in the 5th space, $\frac{1}{2}$ inch internal to the nipple line, and there was a loud blowing systolic murmur at the apex conducted to the axilla, and accentuation of the pulmonary second sound. In spite of the absence of cervical discharge, and an inadvertent omission to examine the pus from the pelvic abscess at the time of operation, a diagnosis of ulcerative endocarditis of gonococcal origin was made. During the next four weeks pyrexia ranged between 99° and 106° F., and frequent vomiting occurred. Blood count showed a leucocytosis of 25,000 and 95 per cent. polymorphonuclear cells. *Blood cultures grew gonococci on two occasions, but no gonococci were found in films from the cervix or urethra.*

The patient died on February 10th, three months after the first onset of symptoms.

SUMMARY OF NECROPSY

P.M. No. 70. Necropsy, February 11th, 1922.

Bacteriæmia; subacute fibrino-purulent gonococcal endocarditis; chronic purulent salpingitis; operation: appendicectomy.

Hydro-pericardium (4 oz.). Foramen ovale closed. Heart weight, 10 oz. Diffuse fatty degeneration of myocardium, with slight "tiger-ing" beneath endocardium of papillary muscles of left ventricle. Three soft, greenish-grey vegetations (largest 2 cm. in diameter), slightly organised at their bases, on the contact surface of the mitral valve; perforation (1 cm. diameter) in posterior cusp of mitral valve; ulceration of a few chordæ tendineæ of mitral valve. Very slight atheroma in aorta and carotid arteries. Enlarged, soft, red spleen (7½ oz.) with visible Malpighian bodies; recent hæmorrhagic infarct (2 cm. diameter), and old, scarring, infarct in spleen. Acute nephritis acris (10 oz.); recent anæmic infarct (1.5 × 0.7 cm.) in right kidney. Almost complete absence of lipid from cortex of

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suprarenal bodies. Severe parenchymatous degeneration, and central congestion, of liver (4 lb. $0\frac{1}{4}$ oz.). Great œdema of lungs; deficient aeration in posterior parts of both lungs, greatest in right lung; purulent bronchitis in bases of both lungs. Bilateral pleural effusion (4 oz. right; 6 oz. left). Patchy chronic purulent infiltration, with groups of fat-granule cells, in mucosa of right and left Fallopian tubes; fimbriated extremity of right Fallopian tube occluded and adherent to right ovary. Delicate fibrous tags scattered over uterine appendages and peritoneum of pouch of Douglas. Injection of mucosa of normally sized uterus. Cheesy concretions in crypts of left faucial tonsil. Mucous catarrh of stomach and intestines. Œdema of feet and legs; slight œdema of back. Very pale, moderately wasted woman. Height 5 ft. 0 in.; weight 90 lb. 12 oz. Examination of head not permitted.

Dr. G. T. Western examined the vegetations from the heart valves and found typical gonococci both in films and cultures.

Case 3.—Female, aged 24. Registered number 41684/14. Admitted to the London Hospital under the care of Dr. W. J. Hadley on June 8th, 1914, and died June 28th, 1914.

Five weeks before admission she was taken ill with "influenza," and symptoms still persisted. Sweating, increasing weakness and recurrent rigors were features of the illness. Anorexia, nausea, occasional vomiting and dryness of the mouth were other symptoms. Menstruation was quite regular, 5/28, and had occurred one week before admission.

Four years ago the patient gave birth to a still-born child, and the father admitted to having had gonorrhœa. The past history was otherwise negative, except for rheumatism at the age of eight, when she was in bed for two weeks.

On examination, on June 8th, 1914, the patient appeared to be pale, wasted and exhausted. T. 103.8; P. 124; R. 24. The tongue was furred and dry, and the teeth carious. The apex beat was in the 5th space, $\frac{1}{2}$ inch internal to the nipple line, and a presystolic thrill and systolic murmur, with an accentuated first sound, were present at the mitral area. The lungs were clear. The abdominal movements were good, with an absence of tenderness and rigidity, and the liver and spleen were not palpable. The uterus was freely movable, not enlarged or tender, and nothing abnormal was detected in the fornices. No cervical discharge was then present.

On June 12th blood cultures grew gonococci (G. T. Western). On June 19th a cervical discharge was noted and bacteriological examination showed gonococci (P. Fildes).

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Pyrexia and vomiting continued, and the patient died on June 28th.

SUMMARY OF NECROPSY

P.M. No. 445. Necropsy, June 30th, 1914.

Bacteraemia; acute fibrino-purulent gonococcal endocarditis; purulent vaginitis and endometritis.

Foramen ovale patent to probe. Heart weight, 8 oz. Slight hypertrophy and dilatation of left auricle; slight dilatation of left ventricle, right ventricle and right auricle. Severe parenchymatous degeneration of myocardium; sub-endocardial and sub-pericardial petechiæ. Soft, polypoid, fibrinous, vegetations (1.5×2 cm.) on contact surface of slightly thickened cusps of mitral valve. A few vegetations on slightly thickened chordæ tendineæ of mitral valve. Small fibrinous vegetations on contact margins of slightly thickened cusps of aortic valve. Very slight atheroma of aorta. Multiple anæmic infarcts, some softened, in large red "septic" spleen (10 oz.); fibrinous perisplenitis. Acute hæmorrhagic nephritis, with focal embolic glomerular necroses; cortical cysts in kidneys ($10\frac{1}{2}$ oz.); anæmic infarct in right kidney. Parenchymatous degeneration and severe oedema of liver (4 lb. 9 oz.). Gross oedema of tough, brown lungs; calcareous nodule below apex of upper lobe of left lung; collapse of lower half of lower lobe of left lung. Bilateral pleural effusion (4 oz. left). Submucous petechiæ in pharynx, oesophagus, colon and urinary bladder. Mucous catarrh of stomach. Commencing organisation of thrombi in vaginal veins. Foci of superficial ulceration and purulent infiltration in cervical canal and vaginal portion of cervix. Foci of slight, superficial, purulent infiltration of endometrium. No microscopic abnormality in Fallopian tubes. Thick yellow pus (1 oz.) in pouch of Douglas. Dilatation of hæmorrhoidal veins.

An extremely wasted, pallid, poorly developed woman. Height, 5 ft. $0\frac{1}{2}$ in.; weight, 77 lb. 11 oz. Examination of head not permitted.

In paraffin sections Gram-negative diplococci were found in the vegetations upon the mitral valve, and in an embolus at the apex of an infarct in the spleen.

Case 4.—Male, aged 42. Registered number 30054/12. Admitted to the London Hospital under the care of Dr. Percy Kidd on January 5th, 1912, and died January 8th, 1912.

The patient was admitted with a history of having been ill for two months. His symptoms were increasing weakness, shivering attacks, loss of weight and appetite. On November 21st, 1911, he contracted acute gonorrhœal urethritis, but the discharge was said to have ceased after seven days, and the patient was quite well until December 6th, when general malaise and other symptoms started. His previous history was negative, and his general condition and strength previous to this illness were very good.

On examination the patient appeared to be in a collapsed typhoidal state with cyanosis and cold, clammy extremities. T. 101; P. 136; R. 40. A purpuric rash was present on the lower limbs, chiefly below the knees. The apex beat was present in the 5th space, $\frac{1}{2}$ inch internal to the nipple line, and the only abnormality detected on auscultation was a systolic murmur at the mitral area. Although the breathing was laboured, no abnormal physical signs were present in the lungs. The abdominal movements were good, but there was slight tenderness over the liver. *Blood cultures on January 8th (P. Fildes) grew gonococci.*

The patient died three days after admission.

It is interesting to note that a friend of this patient had coitus with the same woman on the same day, and did not acquire any infection.

SUMMARY OF NECROPSY

P.M. No. 35. Necropsy, January 10th, 1912.

Bacteriæmia; acute fibrino-purulent gonococcal endocarditis.

Hydropericardium. Foramen ovale closed. Heart weight, 15 $\frac{3}{4}$ oz. Severe parenchymatous degeneration and subendocardial fatty "tigering" of myocardium. Considerable dilatation of left ventricle; slight dilatation of other chambers of heart. Large polypoid vegetations on extensively ulcerated aortic valve; ulceration and aneurysm of sinus of Valsalva. Small fibrinous vegetations upon wall of left ventricle. Very slight atheroma of aorta and carotid arteries. Recent anæmic and hæmorrhagic infarct in enlarged grey "septic" spleen (1 lb. 0 $\frac{1}{2}$ oz.). Severe parenchymatous degeneration of kidneys (14 oz.), with very slight focal inflammation. Central engorgement and atrophy of lobules of liver (5 lb. 2 $\frac{1}{2}$ oz.). Great œdema and congestion of lungs. Bilateral pleural effusion. Slight ascites. No microscopic abnormality in bulbous urethra; no macroscopic abnormality in urethra, prostate, epididymis or testicles.

A stout, well-developed man. Height, 5 ft. 8 in.; weight, 129 lb.

Gram-negative cocci, resembling gonococci morphologically, in large number within discrete neutrophil leucocytes and in masses amidst leucocytic debris, were found in paraffin sections of the aortic valve. Professor Bulloch made a film from substance expressed from the cut surface of a vegetation before fixation, and identified numerous gonococci and a few other organisms.

Case 5.—Male, aged 28. Registered number 16103/14. Admitted under the care of Mr. Robert Milne.

This patient was admitted to hospital with a peri-urethral abscess, balanitis, and acute urinary retention.

A No. 8 catheter was passed with ease. The abscess was opened under general anæsthetic, and the patient

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died on the operating table. The operation was undertaken, as an emergency, a few hours after admission. The temperature was only 98° F. and the pulse 102. Complete diagnosis was determined at autopsy. It seems reasonable to assume that the routine pre-anæsthetic examination of the heart showed no gross abnormality.

SUMMARY OF NECROPSY

P.M. No. 763. Necropsy, December 21st, 1914.

Death during anæsthesia. Bacteriæmia ; subacute fibrino-purulent gonococcal, on chronic rheumatic, endocarditis ; gonococcal abscess of prostate. Operations : prepuce slit, infra-urethral abscess incised.

Foramen ovale closed. Heart weight, 12½ oz. Sub-pericardial petechiæ. Slight dilatation of left ventricle. Row of small, soft fibrinous vegetations on contact margins of thickened, retracted and vascularised cusps of mitral valve. Slight mitral stenosis. Slight thickening of cusps of aortic valve. Very slight atheroma of aorta, and coronary and carotid arteries. Chronic septic spleen, with visible swollen, blurred Malpighian bodies (11½ oz.). Severe parenchymatous degeneration and diffuse congestion of kidneys (20 oz.) and liver (4 lb. 14 oz.). Congestion of lungs ; collapse of posterior parts of lower lobes of both lungs. Organising fibrinous pleurisy, right ; a few fibrous adhesions over apex of right lung, between lobes of left lung and at base of left lung. Abscess cavities (up to 1.5 cm. diameter), containing thick greenish pus, in lateral lobes of prostate. Abscess cavity (1.5 cm. diameter) beneath and completely separate from penile urethra, 1.7 cm. behind meatus. No stricture of urethra. Chronic inflammation, thickening, and œdema of prepuce and of glans round meatus. Simple atrophy of testicles. Branchial cyst (2 × 1 cm.) on posterior surface of trachea.

Well-developed, muscular man. Height, 5 ft. 8 in. ; weight 125 lb. 11 oz.

The portion of mitral valve embedded in paraffin did not include one of the vegetations, but was infiltrated with neutrophil leucocytes, one of which contained numerous Gram-negative diplococci. In films from an abscess in the prostate numerous leucocytes contained groups of Gram-negative cocci which resembled gonococci morphologically.

Case 6.—Female, aged 29. Admitted to the London Hospital under the care of Professor A. W. M. Ellis, on November 17th, 1932, and died the same day.

The history given was that for nine weeks there had been swelling of the legs, and, for three weeks, dimness of vision, pains in the legs and back, attacks of vomiting and general weakness.

One week before admission there was a sudden onset of shortness of breath and swelling of the abdomen.

On admission she was very ill, and orthopnœac ; her face was pale and puffy. There was gross œdema of the

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mucous membranes, the ankles and sacro-lumbar region. T. 97; P. 120; R. 60. The apex beat was in the 5th space, $\frac{1}{2}$ inch internal to nipple line. A systolic murmur was audible at the apex. Blood pressure was 135 m.m. systolic, and 75 m.m. diastolic. The breathing was very distressed and wheezy. Percussion note was impaired over both lower lobes. Crepitations were audible over both lower lobes. The liver was enlarged and tender, and there was a great deal of ascites. The dyspnoea increased and the patient died one hour after admission.

SUMMARY OF NECROPSY

P.M. No. 494. Necropsy, November 18th, 1932.

Heart failure; gonococcal sero-fibrinous organising pericarditis and ulcerative endocarditis; subacute bacteraemia. Very active normoblastic erythropoiesis in marrow and organs.

Layer (up to 0.1 cm. thick) of fibrin all over pericardium; clear serous pericardial effusion (11 oz.). No milk spots beneath fibrin. Mushroom-like polypoid, dry, shrivelled-looking, opaque, fibrinous vegetation ($2 \times 1.5 \times 0.6$ cm.) covering the greater part of the right posterior aortic cusp on its ventricular aspect; two perforations (each about 0.8×0.3 cm.) through the base of the cusp on each side of the vegetation. Smaller vegetations and layer of fibrin upon superficially ulcerated surface of sinus of Valsalva. Abscesses in adipose tissue behind sinus of Valsalva and in subjacent wall of right auricle. A few patches of hæmorrhage in endocardium of left wall of right auricle. Similar vegetation, somewhat smaller than on right posterior cusp, covering the right two-thirds of the left posterior aortic cusp; perforation of the cusp; layer of fibrin and small vegetations upon sinus of Valsalva; deep ulcer in the sinus of Valsalva extending for about 1.5 cm. into the subjacent myocardium, passing close to the left coronary artery, and leading to a group of abscesses (2×1.5 cm.) beneath the pericardium; thick greenish-yellow pus in some abscesses. No abnormality in remnants of posterior aortic cusps. Anterior aortic cusp thin and transparent. Infiltration of anterior cusp of mitral valve at its attachment, and slightly raised ridge of muco-fibrous thickening on its contact margin. Conspicuous white patch (12×1 cm.) of fibrotic thickening of mural endocardium of posterior wall of right auricle, just involving the auricular aspect of the posterior cusp of the tricuspid valve at its attachment. Severe parenchymatous degeneration of myocardium. Very slight atheroma of aorta and common carotid arteries. Miliary, cheesy masses of epithelial *débris* in crypts of congested oedematous tonsils. Œdema of pharynx. Slight hæmorrhage in mucosa of upper trachea. Congestion of thyroid. Great general oedema and congestion of lungs, with numerous slightly swollen red areas of almost solid oedema; areas of collapse in lower, posterior and mesial parts of both lower lobes. Fibro-caseous, tuberculous nodule (0.25 cm. diameter) under pleura of diaphragmatic surface of left lung. No pleural adhesions. No tuberculosis of bronchial glands. Severe vesicular degeneration and considerable brown pig-

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mentation of liver ; slight general central congestion and areas of conspicuous central congestion and slight atrophy ; myeloid reaction in sinusoids of liver. Macroscopic iron-reaction in liver. Congestion, œdema and severe albuminous degeneration of kidneys. Considerably enlarged ($12.5 \times 5 \times 3.5$ cm.) chronic septic spleen, with myeloid transformation ; Malpighian bodies and trabeculæ distinct, pulp wet, cellular looking, and pink and red. Zone (0.6 cm. wide) of red, finely granular erosion surrounding the external os of small uterus. Congestion of urethra and mucosa of urinary bladder. Numerous follicular cysts (0.3 cm. diameter), but no corpora lutea in large œdematous congested ovaries. Mucous catarrh of stomach ; a few petechiæ in body. Scar (1.7×0.5 cm.) of healed ulcer in posterior wall of duodenum, 1 cm. beyond the pyloric sphincter, and scar (1×0.2 cm.) on corresponding anterior wall. Congestion of duodenum and intestines ; reticular patches of slight hæmorrhage in mucosa of small intestine and cæcum. Little lipoid in pale yellow cortex of suprarenal bodies, above a deep, very dark pigmented zone ; abundant medulla. Red marrow (sinks in water) in part of head, and throughout neck and upper half of shaft of femur ; a few patches of red marrow beneath cortex of lower half of shaft. Hip and knee joints normal. Pituitary normal. Absence of a few teeth, one patch of caries in remainder. Breasts firm and fibrous. Œdema great in feet and legs, considerable in thighs, slight in connective tissues elsewhere. No clubbing of fingers. Well-nourished woman, with numerous freckles on face and short moustache.

Weights : body, 120 lb. (length, 4 ft. 6 in.) ; brain, 2 lb. $3\frac{1}{4}$ oz. ; liver, 3 lb. $9\frac{3}{4}$ oz. ; heart, $11\frac{1}{2}$ oz. ; kidneys, $11\frac{1}{4}$ oz. ; spleen, 10 oz. ; suprarenal bodies, 15.3 grm. ; pancreas, 93.5 grm. ; pituitary body, 0.8 grm. ; thyroid gland, 15.2 grm. ; thymus, 10.4 grm. ; ovaries (together), 25.55 grm.

Microscopic Examination

Right and Left Posterior Cusps of Aortic Valve.—The sections show the extension of the inflammation and the formation of abscesses that have been described in the summary. Only a small fragment of the base of the right posterior cusp and a slightly larger portion of the left is included in the vegetations. The massive vegetations consist of a net of swollen strands of fibrin, which in places becomes homogeneous ; the fibrin is not stained by Weigert-Gram. Within the vegetations and upon their surfaces are a few groups of neutrophil leucocytes and red corpuscles. Close beneath the surface is an almost unbroken zone of clumps of Gram-negative cocci, which is conspicuous even in sections stained with hæmatoxylin and eosin. Deeper to this is a much deeper zone of variable depth of powdering of the vegetation with numerous small isotropic granules of calcium. The granules are stained blue by hæmatoxylin and black by silver nitrate. The tissues behind the sinuses of Valsalva are infiltrated and injected ; hæmorrhage is frequent both within and outside the abscesses. Where the infiltration affects adipose tissue large foam-cells are very numerous. Among the leucocytes upon the surface of the vegetations and in the abscesses are many loaded with Gram-negative diplococci. Upon the surface of the vegetations are a few scattered Gram-positive cocci and bacilli.

The Anterior Cusp of the Mitral Valve.—The base for a short distance is infiltrated with neutrophil leucocytes, a few lymphocytes, plasma

cells and eosinophil leucocytes, and numerous small and large monocytes. On the posterior surface at the contact margin and on the anterior surface just above the uppermost chordæ tendineæ are superficial thickenings. They consist of long narrow spindle and occasionally stellate fibrocytes in a mucoid matrix, in which delicate elastic fibrils are present and collagen fibrils are delicate or absent. In the anterior thickening the spindle cells radiate towards the surface. In the deeper parts of the thickenings are a few round, polygonal and short spindle, epithelioid histiocytes or fibroblasts.

The thickenings are probably reactions to mechanical strain and stress. There is no trace of the swelling and fibrinoid necrosis of collagen fibres that are characteristic of rheumatism.

Right Auricle with Pericardium.—The visceral pericardium is covered with a thin layer of fibrin. In clefts in the fibrin are groups of neutrophil leucocytes, small monocytes and large epithelioid monocytes; there are also a very few spindle fibrocytes and a very few capillaries. Very large, often multinuclear, monocytes are especially numerous at the base of the fibrinous layer. Only one neutrophil leucocyte loaded with Gram-negative diplococci was found. There are occasional Gram-positive large cocci, short stout bacilli and more slender bacilli upon the surface of the fibrin. The subpericardial adipose tissue is injected and is infiltrated with many small and large monocytes and neutrophil leucocytes, a considerable number of eosinophil leucocytes and a few plasma cells; lymphocytes are usually sparse. The interstitial tissue of the subjacent muscle is considerably rarefied by oedema. In it are occasional epithelioid cells, singly or in small groups. Deep in the muscle is one large group of round, polygonal and short-spindle epithelioid cells. This group differs from a typical rheumatic nodule in that the interstitial tissue is in no way altered. The muscle fibres contain lipoidaffin pigment. They show distinct striation, and there is no appreciable degeneration in the paraffin sections.

Cervix and Vagina.—The section includes 2.4 cm. of one side of the cervical canal, the corresponding vaginal portion of the cervix and 1.5 cm. of the vaginal wall. The pars vaginalis for a short distance from the vaginal canal is devoid of epithelium and contains cervical glands. This erosion is infiltrated with lymphocytes, plasma cells and an occasional neutrophil leucocyte. Upon its surface are a few Gram-positive bacilli and large diplococci. Neither here nor in the rest of the section is there an inflammatory reaction suggesting gonococcal infection.

Spleen.—Most of the Malpighian bodies contain hyaline spheres and ribbons, which frequently occupy extensive areas. The pulp is engorged. The venous sinuses contain many large mono- and multi-nuclear cells with abundant cytoplasm, which often contain erythrocytes and normoblasts and occasionally neutrophil leucocytes. Neutrophil leucocytes are numerous, and the abundance of normoblasts is a striking feature. Plasma cells and eosinophil leucocytes are fairly common. There are some groups of early and late primary erythroblasts, the largest seen consisting of eleven cells. A very few neutrophil myelocytes and a hæmocyto blast were also found. The reticular strands of the pulp are less cellular. In addition to erythrocytes, plasma cells are the predominating cells. Eosinophil leucocytes are fairly numerous. There are also a few normoblasts, primary erythro-

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blasts and eosinophil myelocytes. The spleen, therefore, shows a subacute inflammation, and a striking myeloid transformation, which is almost entirely erythroblastic and normoblastic, and almost confined to the venous sinuses.

Liver.—Fat is not present in Herxheimer preparations. The hepatic cells are finely vesicular, and those in the inner two-thirds of the lobules contain much lipoidaffin pigment. There is very little evidence of nuclear degeneration; occasional nuclei are very large; one karyokinetic figure was seen. The portal systems show a slight infiltration with lymphocytes, and occasional plasma cells and eosinophil leucocytes. The sinusoids contain very numerous large mono- and multi-nuclear cells, which are evidently desquamated Kupffer cells. They are frequently phagocytic, containing red corpuscles usually, normoblasts sometimes and leucocytes occasionally. Within the sinusoids there are also many normoblasts and neutrophil leucocytes, several eosinophil leucocytes and late primary erythroblasts, and a few plasma cells, hæmocyto blasts and neutrophil and eosinophil myelocytes. The sinusoids thus resemble closely the venous sinuses of the spleen. The Prussian-blue reaction in tissue fixed in formaldehyde only showed diffuse staining of the Kupffer cells.

Kidney.—Fat is not present in Herxheimer sections. There is severe albuminous degeneration of the epithelium of the first convoluted tubules and ascending limbs of the loops of Henle, and severe dropsical degeneration of the epithelium of the discharging tubules. In some of the first convoluted tubules and ascending tubules of Henle there is a little hyaline coagulum. A few small collecting tubules contain hyaline casts. The glomeruli show no pathological change. There is a little infiltration of the connective tissue round the arcuate arteries with plasma cells, lymphocytes and eosinophil leucocytes. The vasa recta are engorged. Among the erythrocytes in the capillaries are several normoblasts and a few hæmocyto blasts and primary erythroblasts.

Marrow.—In a portion of marrow removed from the upper end of the shaft of a femur, adipose tissue preponderates slightly over hæmopoietic. The hæmopoiesis is almost entirely erythroblastic, and is normoblastic. Hæmocyto blasts are relatively rare and form groups of two to four cells. Primary erythroblasts form groups of nine to twelve cells as a rule. In some groups early erythroblasts predominate, in others late erythroblasts; groups of late erythroblasts are commoner. Associated with these groups are very numerous normoblasts. Myelocytes are relatively scanty; among them eosinophil examples are conspicuous. Megakaryocytes are numerous.

In the marrow, therefore, as in the spleen and liver there is a very active normoblastic erythropoiesis and very little leucopoiesis. A "marked anæmia" was noted clinically, but as the patient was moribund on admission no examination was made of the blood.

Bacteriological Examination

Pus from an abscess deep to the sinus of Valsalva and a portion of vegetation were sent to Professor Bulloch's department.

Gonococci were found in films from both. Cultures of the pus gave gonococci, and of the vegetation gave gonococci, staphylococcus albus and coliform bacilli.

Case 7.

Case 7.

Case 7.—The following case (7) is not one of gonococcal endocarditis, but is included to illustrate the possibility of gonococcal bacteraemia without endocarditis, and with recovery :—

Boy, aged 10. Registered number 31944/26. Admitted to the London Hospital as an in-patient under the care of one of us (R. A. R.) on June 19th, 1926.

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Case 7.

Case 7.

Gonococcal bacteraemia, without endocarditis, and with recovery. The elder brother, a married man, contracted gonorrhoeal urethritis. He then had coitus with a young girl of twelve years on the old supposition that such coitus would cure him of his gonorrhoea. This girl then "seduced" the patient, who at no time gave a history or evidence of urethritis. His illness started with fever,

Case 7.

Case 7.

vomiting, and generalised pains. T. 104 ; P. 130 ; R. 40 on admission to hospital. The skin was dry, and covered with a purpuric rash, small hæmorrhagic macules with erythematous areolæ, and some larger ecchymoses. The patient was seen by Dr. J. H. Sequeira, who thought the rash was due to secondary syphilis. The tongue was covered with a white fur, and the throat clear. The

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conjunctivæ were injected and the eyes watery. The heart sounds were normal, and there were no adventitious sounds. The lungs, abdomen and central nervous system were normal. A cloud of albumen was present in the urine, and the centrifuged deposit showed red cells, with many leucocytes and epithelial cells. A leucocytosis, 20,240, was present, with 77 per cent. polymorphonuclear

cells and a secondary anæmia, 4,675,000 erythrocytes, and hæmoglobin 66 per cent. The Wassermann reaction was positive in the blood, and negative in the cerebrospinal fluid. The latter was clear, without cobweb, and contained one small lymphocyte per cubic millimetre.

A blood culture (P. Fildes) on July 25th, five weeks after the onset, gave the following result: "*Gram-negative coccus appears to belong to the meningococcus gonococcus group, and, although differing from a typical example, is possibly an abnormal form of gonococcus.*" Treatment consisted of four doses of 0.3 gram N.A.B., and three weeks later a blood culture was sterile. As the pyrexia persisted, five injections of autogenous vaccine were given, as well as three intravenous injections of quinine. The patient became afebrile after fifteen weeks and was discharged in good health on November 18th, 1926.

Comment on Case 7.—This case is of great interest not only as illustrating gonococcal bacteriæmia without infective endocarditis, but also because of the clinical similarity with another comparatively rare cause of obscure pyrexia, namely, meningococcal septicæmia. In both conditions intermittent and remittent pyrexia may continue for weeks or months, and complete recovery may ultimately occur. The growth of the organism from the blood stream may be difficult, but repeated blood cultures usually give a positive result.

During the last ten years five cases of subacute meningococcal septicæmia have been admitted to the London Hospital, and their clinical features have been described and published by Lawson Stote and Stewart-Wallace.

It is interesting to note that the gonococcus and meningococcus are both Gram-negative diplococci, which have several similar morphological and cultural characteristics.

Case 8.—For the notes of this case we are indebted to Sir Robert Stanton Woods. It illustrates the condition of gonococcal pyæmia, with multiple abscesses, from which pure cultures of gonococci were obtained.

Male, aged 53, first seen in November, 1925. At the age of 17, he had an attack of gonococcal urethritis. About the middle of October, 1925, extra-marital coitus occurred and was followed by a very slight non-purulent

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urethral discharge. On November 5th he had pain in the rectum. On November 6th the temperature was 102° F., and for some weeks afterwards he had a remittent and intermittent pyrexia. When examined on November 16th, the patient did not appear very acutely ill, but he had an acute arthritis of the left shoulder and a small superficial abscess above the right elbow. There was no obvious urethral discharge and nothing abnormal was detected in the prostate, on rectal examination. On November 17th, the abscess was aspirated, and, from the thick pus obtained, *a diplococcus was isolated and later identified as the gonococcus (Dr. G. T. Western)*. A few days afterwards, a small abscess appeared on the right leg below the knee, and cultures from this also grew gonococci. November 23rd—temperature began to fall, pulse was 100 and respiration 22; crepitations were audible at the bases of the lungs. A generalised rash, mainly vesicular, in places pustular, appeared. Heart remained clear, and tongue was now clean and moist. On November 25th blood cultures were negative. Gonococcal vaccines were administered. Convalescence proceeded steadily, and in January, 1926, the patient was up and about. Movement of the left shoulder was still extremely limited. When seen again in April, 1926, he had made a complete recovery.

SYMPTOMATOLOGY

The symptomatology of gonococcal endocarditis is not pathognomonic of this condition, but is that of a septicæmia, with swinging temperature, weakness, wasting, chills and rigors, sweating, anorexia, vomiting and progressive exhaustion. A purpuric rash was a feature in two patients in this series. Although, in all cases, the autopsy showed valvular vegetations characteristic of infective or ulcerative endocarditis, abnormal heart sounds were not always a conspicuous feature. Thus in Cases 2, 4 and 6 there was only a systolic murmur at the apex, and in Case 5 there was presumably no evidence of a cardiac contra-indication to a general anæsthetic. In Case 1, in addition to a systolic murmur in the mitral area, both systolic and diastolic murmurs were heard at the base of the heart, and a pericardial friction sound appeared for some days during the course of the illness.

In all four females (Cases 1, 2, 3 and 6) there was no

history of a gonococcal infection, and no evidence at the time of admission of a cervical discharge. In Cases 1 and 2 cervical and urethral smears and cultures were negative, but in Case 3 a cervical discharge appeared while in hospital, and was shown to contain gonococci. One patient (Case 6) died within an hour of admission, and at autopsy there was no evidence (naked eye or bacteriological) of urethral or cervical gonococcal infection.

In both men (Cases 4 and 5) there was a history of gonococcal infection, with urethral discharge. In Case 4, this had lasted for only seven days, and general symptoms did not appear until six weeks later. In Case 5, a local peri-urethral abscess was the presenting feature and the underlying septicæmia was unsuspected.

Blood counts showed a leucocytosis of some 20,000 to 30,000 with an increase in the percentage of polymorphonuclear cells, 85 to 95 per cent. Blood cultures grew gonococci in the four cases (1, 2, 3, 4) in which they were attempted. Stone (1934) in a survey of the literature found that of 71 proven cases of gonococcal endocarditis, in which blood cultures were made, only 34 gave positive results. In Perry's patient (1930) several blood cultures were negative, but one taken directly after a chill was positive. Although Stone (1934) stated that 93 per cent. of cases of malignant gonococcal endocarditis emerged from cases complicated by arthritis, the latter did not occur in any patients of the present series.

DIAGNOSIS

Persistent pyrexia and malaise in any patient suffering from, or recently recovered from, a local gonococcal infection, should raise the question of gonococcal septicæmia, with or without malignant endocarditis. Sweating, chills and rigors are significant symptoms. The appearance of cardiac murmurs, especially diastolic murmurs, under observation, suggests ulcerative endocarditis, but, in some cases, the only abnormality on auscultation may be a mitral systolic murmur. Peripheral emboli, petechiæ, and blood in the urine are indicative of malignant endocarditis. Blood counts show a leucocytosis with a relative increase of the polymorphonuclear cells. Definite proof of the gonococcal septicæmia depends upon positive blood cultures.

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An absence of a past, or present, gonococcal urethritis or cervicitis, in women, by no means rules out the diagnosis, even when cervical and urethral smears are negative. In men, there is nearly always a history of a urethral discharge, but this may be transient and may have ceased some weeks before the onset of the general symptoms.

COURSE AND PROGRESS

In the present series the duration of the disease from the onset of general symptoms was 6 weeks, 3 months, 2 months, 9 weeks, undetermined, and 9 weeks.

Stone (1934) found from a study of the literature, that the endocarditis usually developed while the patient was still under the care of the physician for the local gonorrhœal infection, or some common gonorrhœal complication such as prostatitis, salpingitis or arthritis. Thayer (1922), however, found that little evidence could be obtained as to the relation of the onset of the symptoms to the stage of the initial local infection. In the present series this is certainly true of the women patients. In his series, the average duration of the disease from the beginning of the general symptoms was $9\frac{1}{2}$ weeks.

Gonococcal endocarditis is nearly always fatal, as would be expected from our knowledge of ulcerative or infective endocarditis associated with other micro-organisms. Recovery has, however, been recorded. Thus Thayer (1922), reviewing 72 cases, found recovery in 5, but Hoffman and Taggart (1932) found only one further case of recovery in the next ten years. In considering alleged recovery, one must remember that gonococcal septicæmia with positive blood cultures is not necessarily associated with an ulcerative endocarditis. Case 7 is recorded in this paper as an illustration of this. Tabbutt (1926) recorded 2 cases of gonococcal septicæmia with positive blood cultures without endocarditis, but both these cases were fatal, and autopsies were performed. We are inclined to the view that should recovery occur, the condition has been that of gonococcal septicæmia without ulcerative endocarditis. Perry (1930), however, recorded a case in which systolic and diastolic murmurs appeared at the pulmonary areas during the course of the disease, with severe general symptoms, but recovery eventually occurred.

TREATMENT

It is not surprising that a large number of treatments have been indicated for the disease. They include repeated blood transfusions, gonococcal vaccines and sera, and intravenous silver, mercurochrome and arsenic. Perry's (1930) patient recovered after repeated transfusions of citrated blood, but Hoffman and Taggart (1932) used the same technique without any benefit resulting. Perry's patient also received gonococcal vaccine on a few occasions, but apparently with temporary harmful results.

PROPHYLAXIS

Since the condition tends to be fatal when once established, it is important to consider the prophylactic aspects. As to whether a local urethritis remains localised, or becomes a more generalised infection, with relative harmless complications, such as gonococcal arthritis, or fatal complications, such as ulcerative endocarditis, probably depends upon the virulence of the micro-organism and the general condition, or power of resistance, of the patient. The former is beyond our control, but the latter factor should not be lost sight of. Gonococcal urethritis should not be regarded merely as a localised infection, but as a potential septicæmic process. Attention to the general health, and resistance of the patient, might prevent much morbidity and some fatalities.

SUMMARY

(1) Six cases of gonococcal ulcerative endocarditis with autopsy reports are recorded.

(2) Case 7 is included to illustrate gonococcal bacteraemia in the absence of ulcerative endocarditis; and Case 8, gonococcal pyæmia in the absence of ulcerative endocarditis. The inclusion of these cases permits a classification of generalised gonococcal infection into three groups:—(a) bacteraemia, (b) pyæmia, and (c) ulcerative endocarditis.

(3) The absence of a cervical discharge and even negative bacteriological findings of cervical and urethral smears does not exclude the diagnosis in the female.

(4) The time relationship of the general symptoms to the onset of urethritis is usually indeterminate in the

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female, but a matter of weeks and sometimes months in the male.

(5) The symptomatology is that of a septicæmia, and abnormal heart sounds may or may not be a prominent feature.

(6) The duration of the disease is weeks or months.

(7) The condition is nearly always fatal.

(8) The general condition and resistance of the patient is probably an important factor in the prophylaxis of the condition, and should not be ignored.

(9) It will be noted that in this series the complement fixation test was not applied, as at that time the test had not attained the reliability which may now be claimed for it.

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