not the blood. Pfeiffer's bacillus was present in 11 cases, 10 per cent.; pneumococcus, 25 cases, 22 per cent.; a diphtheroid bacillus, 3 cases, 3 per cent.; a Gram-positive diplococcus, 111 cases, 100 per cent.

Latterly, the trypsinised blood agar medium recommended by Dr. J. Matthews¹ has been employed, without any marked increase in the cases yielding *B. influenzae*. A point noted in the present epidemic is that though Pfeiffer's bacillus is comparatively easily obtained during the first three days of the illness, its isolation becomes increasingly difficult with each succeeding day. This fact may in part account for the divergent results of different observers. The increased virulence of the disease does not appear to have been associated with any marked change in the actual organisms present.

A brief resume may be given of the main pathological findings in 12 fatal cases.

1. Gram-positive diplococci and pneumococci obtained from lungs; no organisms from other organs. 2. A small Gram-negative bacillus resembling *B. influenzae* obtained from lungs, with Gram-positive diplococcus; latter isolated from liver and spleen. 3. Gram-positive diplococci from lungs, liver, spleen, and kidneys. 4. Pneumococci and Gram-positive diplococci from lungs; latter organism in pure culture from liver and spleen. 5. Pneumococci and Gram-positive diplococci from lungs; diplococci from liver and spleen. 6. Gram-positive diplococci from lungs, liver, and spleen; *B. influenzae* and pneumococci from lungs. 7. Pneumococci and Gram-positive diplococci from lungs; diplococci from liver. 8. Gram-positive diplococci in pure culture from lungs. 9. Gram-positive diplococci and Gram-positive diphtheroid bacilli from lungs, liver, spleen, and kidneys. 10. Diplococci in pure culture from lungs, liver, and spleen. 11. Gram-positive diplococci in pure culture from lungs, liver, kidneys, and spleen. 12. Gram-positive diplococci in pure culture from lungs, empyema, liver, and spleen.

The only organism constantly present is a Gram-positive diplococcus. In smears from portions of lung showing consolidation it is found in considerable numbers, the microscopic appearances being not unlike those seen in smears from the lungs of pneumonic plague. For the most part the diplococcus is extracellular, but in smears from the lungs of Cases 9 and 12 it was found almost entirely within the polymorphs.

The diplococcus is an oval organism occurring in pairs, the opposed sides slightly flattened. It occurs either singly or in short chains made up of two or three diplococcal elements. It stains readily with ordinary stains such as methylene blue, but shows no beading with Neisser's stain, a point of some interest, as Stitt states that he has often isolated from the throats of healthy individuals a Gram-positive diplococcus which gave a diphtheroid reaction with Neisser's stain.

The diplococcus now isolated does not grow very readily on ordinary agar; on blood agar it produces colonies very similar to those of a streptococcus; it is hæmolytic. Trypsinised blood agar appears unfavourable to its growth. In nutrient bouillon the organism produces a diffuse cloud which eventually falls to the bottom. It has no action on glucose, lævulose, or maltose. When *B. influenzae* and the Gram-positive diplococcus are grown together on blood agar the former grows only very feebly or not at all.

Pathogenic Properties of the Diplococcus.

The pathogenic properties of the diplococcus have been investigated in monkeys and rabbits.

A culture of diplococci in nutrient broth, heated to 37° C., was sprayed over the naso-pharynx of two monkeys (*Cercopithecus*). Neither monkey developed any symptoms.

The sputum from four cases of influenza with broncho-pneumonia was mixed with normal saline, heated to 37° C., and sprayed over the naso-pharynx of two other monkeys. No untoward symptoms.

In rabbits the results were somewhat contradictory. The first experiments were made in July with the Gram-positive diplococcus isolated from the sputum. 0.5 c.cm. of nutrient broth culture were injected intraperitoneally. Slight rise of temperature; no other symptoms. On killing the rabbits three days later diplococci were found in peritoneal cavity; they did not appear to have undergone multiplication. It was concluded that the diplococcus was non-pathogenic to rabbits.

In view of the increased virulence of the disease in October the experiments were repeated with rabbits. 0.5 c.cm. of nutrient broth culture were injected intra-

peritoneally, the diplococci having been isolated in pure culture from the liver of fatal cases. Some 12 to 14 hours after inoculation the rabbit began to show signs of distress; its temperature gradually rose, it suffered from diarrhoea, and gradually became more and more lethargic, finally dying in from 22-28 hours in a state of coma. Post mortem, Gram-positive diplococci were found in the peritoneal cavity, in lungs, liver, spleen, and kidneys, in pure culture. In every case the pleural cavities contained a hæmorrhagic exudate which yielded the diplococcus in large numbers.

By passage through three or four rabbits the virulence of the organism can be still further increased and a fatal result obtained in from 15-20 hours.

These experiments suggest that in the period July to October the virulence of the diplococcus has increased greatly—a fact which may be correlated with the increased severity of the symptoms during the same period.

Conclusions.

1. Pfeiffer's bacillus is undoubtedly present in a certain number of cases, more particularly at the beginning of the illness.

2. A Gram-positive diplococcus is almost constantly present in all cases.

3. The growth of this diplococcus is unfavourable to that of *B. influenzae*.

4. The diplococcus is now highly pathogenic to rabbits, its virulence having been in some way recently augmented.

A CASE OF RAPIDLY FATAL ULCERATIVE ENDOCARDITIS

DUE TO A GRAM-POSITIVE PLEOMORPHIC DIPLOCOCCUS.

By M. J. STEWART, M.B. GLASG., M.R.C.P. LOND.,

PROFESSOR OF PATHOLOGY, UNIVERSITY OF LEEDS;

AND

H. L. FLINT, M.D. LEEDS,

LATE CAPTAIN, R.A.M.C.

THE case here reported is one of acute infective endocarditis of the aortic valve, coming on rapidly in a man the subject of an old aortic lesion, and ending fatally within three days of the first onset of acute symptoms. Its chief interest lies in the fact that the causative organism is a Gram-positive pleomorphic diplococcus, very similar in its morphological and cultural characters to that described by certain authors in connexion with the influenza pandemic.

Clinical Report.

Patient, aged 29, was admitted to hospital as a case of valvular disease of the heart on Nov. 6th, 1918.

Past medical history.—He had had no serious illness, and was perfectly well before going out to France in 1914. No history of rheumatic fever or of chorea. Coal-miner before enlistment; served four years in France with artillery. He had pneumonia in November, 1915; in hospital for six weeks. In February, 1916, he had influenza and bronchitis; in hospital for one month. He was slightly wounded in the left knee in May, 1917; in hospital six weeks. He had influenza again in June, 1918; he was told that his heart was affected.

On admission the patient complained of shortness of breath and pain over the heart on exertion, these symptoms dating from the attack of pneumonia in 1915. The apex-beat was in the fifth space, internal to nipple line; left limit of cardiac dullness just internal to nipple line; no thrill. On auscultation at the base systolic and diastolic murmurs were heard in both aortic and pulmonary areas. At the apex the first sound was loud and preceded by a rumbling presystolic murmur, probably an Austin Flint murmur. The basal systolic and diastolic murmurs were audible at the apex. Well-marked Corrigan's pulse of regular rhythm. Lungs and abdomen normal. Urine: Specific gravity was 1025 and reaction acid; trace of albumin, no sugar. Microscopic examination of the centrifuged sediment showed nothing of note. The electrocardiograph showed a relative hypertrophy of the left ventricle.

The diagnosis of aortic regurgitation was made and the patient retained in hospital until he could be discharged from the Service. In the meantime he walked about with comfort.

¹ THE LANCET, 1918, ii., 104.

History of the acute illness.—On Nov. 16th patient was out in the afternoon with his wife. After a good supper he went to bed feeling quite well. He did not sleep well; slight headache during night. On the morning of the 17th he did not feel well; headache still. Temperature 104.2° F., pulse 132, respirations 24. Previous to this he had been apyretic; ordinary pulse-rate 80 to 90. At 10 A.M. he had a good deal of pain in the back, general aching over the whole body, and pain in the left knee. The throat was found acutely inflamed; tonsils, fauces, and uvula very much injected; some dirty white patches on tonsils and uvula. (A swab taken from the throat showed no diphtheria bacilli, but yielded an abundant coccal growth.) The cardiac signs were unchanged; no other abnormal physical signs. Diagnosis: Influenza. In the afternoon he vomited a small quantity of bile. In the evening the respirations were 48 per minute.

On Nov. 18th patient had not slept during night; had wandered at times. He had taken a lot of fluids but had vomited most of them back. Incontinence of urine and faeces. He had been sweating profusely; no rigors. Temperature 103.6°, pulse 128, respirations 44. The tongue was dry and coated with a brown fur; throat very much inflamed. A few petechiae on upper part of back, on front of chest, and on chin and both arms and legs. The heart was rapid; otherwise no change in physical signs. The spleen could not be felt, but its area of dullness was increased upwards; some tenderness over splenic area, no friction sounds. There was diminution of breath sounds at both bases; no signs of pneumonia, and no cough or spit. The pupils were equal in size; no rigidity of neck; knee-jerks normal. There were no signs of blocking of any of the larger arteries. Nothing abnormal found in left knee.

The diagnosis was changed from influenza to infective endocarditis. (A blood culture taken on the 18th subsequently yielded a pure growth of a pleomorphic, Gram-positive diplococcus.)

On Nov. 19th patient was much worse; many more petechiae had appeared. No sign of pneumonia; no rigors. Temperature 101°, pulse 128, respirations 56. The incontinence of urine and faeces continued. He gradually got worse, and died at 6.20 that evening.

Post-mortem Report.

A post-mortem examination was made on Nov. 20th, 16 hours after death.

External appearances.—A well-developed subject. Many small petechial hæmorrhages on trunk and limbs, especially on neck and face; a number on lips and eyelids.

Internal examination.—*Circulatory system.*—Heart weighed 14 oz.; left ventricle considerably hypertrophied and slightly dilated. The aortic valve was the seat of a typical ulcerative endocarditis. The anterior and left posterior cusps were partially fused along adjacent margins. As the conjoined part was elongated and bulged, the effect was to produce practically one large cusp in place of two. To the margin of this large cusp there adhered a large, red, soft, friable mass of vegetation, easily broken down and separated by the finger. A similar vegetation of larger size was present in middle of ventricular aspect of right posterior aortic cusp, and was associated with an actual perforation of considerable size. The aortic cusps showed also a slight degree of chronic fibrous thickening; valve was incompetent to water test. The other valves and the myocardium were normal. The pericardium presented numerous irregular patches of hæmorrhage in the parietal layer, especially towards base of heart and in visceral layer on posterior aspect. The aorta and coronary arteries were normal.

Respiratory system.—The fauces, pharynx, soft palate, uvula, and epiglottis showed evidence of acute inflammation, with intense vascular engorgement and a small amount of purulent exudation on the surface. Pus could be expressed from tonsillar crypts. The larynx, trachea, and bronchi were acutely inflamed, with much mucopurulent exudation. The lungs were most intensely engorged; basal portions also somewhat oedematous. Considerable degree of purulent bronchitis of larger tubes; no evidence of extension to smaller bronchi or parenchyma of lung. There was old tuberculous scarring at the apices, also a few small calcareous foci in other parts of lung. A number of petechial hæmorrhages in pleura on posterior aspect of both lungs. The bronchial glands were the seat of an old caseous and calcareous tuberculous lesion.

Alimentary tract.—The œsophagus was the seat of numerous punctiform hæmorrhages, chiefly in middle and lower thirds. The gastric mucosa showed much irregular ecchymosis. The whole length of the gut, both small and large, presented a number of pyæmic infarcts of various sizes. These had all undergone suppurative softening in the centre; each was surrounded by a broad zone of peritoneal hæmorrhage.

Other organs.—The liver was much enlarged, weighing 88 oz. It was the seat of typical cloudy swelling. Spleen greatly enlarged, 21 oz.; very soft; a number of large recent infarcts present, some with extensive early suppurative softening in centre. Adrenals very soft, cavitating readily; cortical lipid had almost disappeared. The kidneys (15½ oz.) were enlarged; innumerable small hæmorrhagic and suppurating infarcts throughout. These were best seen on the surface after stripping capsule, but present also in medullary pyramids and throughout cortex. Several infarcts of larger size (¼ to ½ in. in diameter) were also present, with suppurating centres and zone of hæmorrhage round. The brain and membranes showed intense vascular engorgement; a number of diffuse patches of pia-arachnoid hæmorrhage on surface of cerebrum. A number of tiny punctiform hæmorrhages were present in white matter of centrum ovale; also small focal hæmorrhage about ¼ in. in diameter in surface convolutions of left lobe of cerebellum.

The remaining organs appeared normal.

Smears and cultures were taken from the aortic vegetations and from the pyæmic lesions in kidneys, spleen, and intestines. From all these situations the same organism was recovered as had been got from the blood during life. The vegetations in particular contained the coccus in enormous numbers.

Characters of the Diplococcus.

An account of the characters of the organism follows.

Morphology.—The organism is a fairly large, bean-shaped, Gram-positive diplococcus, morphologically not unlike the gonococcus. It exhibits marked pleomorphism, including numerous pairs of very large size. The appearances are similar in direct smears from the aortic vegetations and in agar cultures. In cultures short chains of three, four, and five cocci are common, the members of which often show division at right angles to the length of the chain. The cocci also occasionally form small clusters, but are most often found as discrete pairs. Broth cultures are particularly diplococcal.

Cultural characters.—On agar the organism forms discrete circular colonies, measuring 1 to 1.5 mm. in diameter after 24 hours' incubation at 37° C. They are white by reflected light; yellowish, especially in the centre, by transmitted light. Under the low power of the microscope the colonies present a finely granular appearance throughout, and are brownish at the centre and pale at the margin. The colony emulsifies readily in water on the slide. On defibrinated human blood-agar the coccus forms white colonies of a similar size, each surrounded by a narrow zone of hæmolysis and clearing. In the original (broth) blood culture taken 36 hours before death, well-marked hæmolysis was present after 48 hours' incubation. Nutrient broth cultures show general turbidity. A gelatin stab culture at room temperature shows within a week a narrow tube of liquefaction along the needle track. In a month there is a large funnel of liquefaction reaching to the walls of the test-tube at the upper end. The liquefied portion of medium shows general turbidity, and there is a fairly dense deposit at the apex of the funnel. Litmus milk is rapidly clotted and rendered strongly acid. Later the clot tends to become bleached, but is not liquefied. The organism ferments glucose, lactose, saccharose, mannite, galactose, and maltose, with formation of acid but no gas. Dulcitate and inulin are unaffected.

Pathogenicity.—A mouse was inoculated subcutaneously in the flank with 1 c.cm. of a recent broth culture. It manifested no ill-effects.

Summary.

The case is one of acute infective endocarditis of the aortic valve due to a Gram-positive pleomorphic diplococcus. Clinically it is characterised especially by its extraordinary virulence and rapid course. The patient, who suffered from an old aortic lesion, with regurgitation, dating apparently from an attack of pneumonia three years previously, was apyretic and in reasonably good health up to three days before death. At that time he was suddenly seized with acute illness accompanied by high temperature and rapid

pulse and respirations, acute tonsillitis and pharyngitis, and signs and symptoms generally suggestive of "influenza." Next day a purpuric eruption made its appearance, and blood culture yielded a rapidly prolific growth of an atypical Gram-positive diplococcus. Death took place within 60 hours of the onset of acute symptoms, and at post mortem the Gram-positive diplococcus was recovered from the aortic vegetations and from the various pyæmic lesions.

The chief interest in this case at the present time lies in the bacteriological findings. The causative organism, a Gram-positive pleomorphic diplococcus of well-defined cultural characters, is apparently similar in many respects to certain diplococci which have been isolated from cases of influenza during the present epidemic. Such organisms have been described in cases occurring in England, France, America, and Germany.

Records of Organisms Similar in Certain Respects.

1. The pleomorphic Gram-positive diplococcus described by Little, Garofalo, and Williams¹ (France, 1918), and isolated by them from the nasopharynx, throat, and sputum, in 20 cases of influenza, is clearly different, although morphologically similar. It grows with difficulty on ordinary media, is of small size, and forms small transparent colonies like a streptococcus. It does not ferment any of the ordinary sugars and does not cause hæmolytic in blood-agar plates, although in blood broth the red cells are broken up. In a later and fuller account of this organism, Little² mentions that it forms acid but no gas on glucose, saccharose, lævulose, galactose, and maltose; mannite, dextrin, and glycerin being unaffected. It is highly pathogenic for rabbits, but only one mouse out of six succumbed.

2. The diplococcus described by Keegan³ (America, 1918), and found by him as the preponderating organism in the throat and sputum in 100 influenza cases as well as in 100 controls, is also pleomorphic and Gram-positive. It forms small grey colonies on blood agar, each surrounded by a zone of hæmolytic. Keegan thought that it probably corresponded to the organism described by Little, Garofalo, and Williams.

3. The *Diplococcus mucosus* (Leipzig) of Stephan,⁴ described by him as the agent of a clinically typical "endemic" of influenza occurring at Leipzig in December, 1916, presents characters which very closely resemble those of the organism under discussion. It was Gram-positive (Scheller), non-pathogenic to animals, grew well on ordinary media and at 20° C., and fermented glucose, lævulose, galactose, and maltose.

4. Whittingham and Sims⁵ recovered from the blood of a case of influenza which was subsequently fatal a pleomorphic diplococcus resembling the *Diplococcus mucosus* of Stephan. It was non-pathogenic to young rabbits, showed variable Gram-staining, and grew on ordinary media both at 20° and 37° C. It was markedly pleomorphic, with Gram-negative bacillary forms as well as Gram-positive and Gram-negative cocci. It was only slightly hæmolytic. Acid was produced in glucose, saccharose, maltose, lævulose, and galactose, but not in lactose, mannite, dulcitol, or inulin. Milk was rendered slightly acid and slightly clotted.

5. Kolle⁶ (Frankfort, July, 1918) failed to detect Pfeiffer's bacillus in any of the few cases which he had thoroughly examined. In practically all cases there were found large numbers of a Gram-positive pleomorphic diplococcus, occurring either in pure culture or in symbiosis with pneumococci. It tended to form chains in the water of condensation.

6. Synnott and Clark⁷ (America, 1918) found, in various combinations with *B. influenza*, pneumococcus, and streptococcus, "frequently a Gram-positive pleomorphic coccus" in the sputum and secretions from the bronchi and lungs of influenza cases. No bacteriological details are given.

In none of these cases is there any mention of the action on gelatin.

Present Organism.

The organism in the present case is a fairly large Gram-positive diplococcus, showing striking pleomorphism and growing readily on ordinary media. On agar the colonies are white (yellowish by transmitted light) and measure 1 to 1.5 mm. in diameter after 24 hours' growth at 37°. Gelatin is slowly liquefied. Glucose, lactose, saccharose, mannite, maltose, and galactose are fermented with formation of acid; dulcitol and inulin are unaffected. The colonies on blood agar are surrounded by a narrow zone of hæmolytic. It is non-pathogenic for the mouse.

It does not correspond, so far as we can make out, to any of the recognised pathogenic bacteria, but it must clearly be credited with very definite pathogenic properties under certain circumstances. It bears a close resemblance in many respects to some of the diplococci isolated from the respiratory tract in cases of "influenza," whose pathogenicity is by no means so obvious. In all probability we are dealing with a large and ill-defined group of Gram-positive diplococci, analogous to the *B. coli* group, and, like it, possessed of contingent pathogenic properties. The members of the group, or some of them, have doubtless participated in the general exaltation of virulence which has affected so many other organisms, especially streptococci and pneumococci, during the present influenza epidemic.

We beg to acknowledge our indebtedness to Professor T. Wardrop Griffith for the facilities he accorded us to investigate this case.

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Clinical Notes:

MEDICAL, SURGICAL, OBSTETRICAL, AND THERAPEUTICAL.

RECURRENT CHYLOTHORAX FOLLOWING TRAUMA.

By A. E. MALONE, M.B., B.A. DUB.,

SURGEON LIEUTENANT, R.N.;

AND

J. G. WARDROP, M.B. LOND.,

TEMPORARY SURGEON LIEUTENANT, R.N.

CHYLIFORM fluid in the pleural cavity is comparatively rare, and the following case may be of interest.

Account of the Case.

A French sailor, aged 22, was admitted into hospital suffering from great dyspnoea. He had fallen 10 metres from a mast on to a hatch cover 10 days before, but of his condition during the interval nothing is known. The heart was found displaced to the left, with cardiac impulse in the sixth space, outside the nipple line. Pulse poor, irregular, and rapid (120); respiration, 30; temperature, 98° F. No cough or sputum. Complete dullness over right chest, with total absence of breath sounds, except at root of lung. Examination of left lung, heart, abdominal viscera, &c., failed to give any evidence of disease. No signs of external injury, except for small incised wound of scalp. Urine was normal.

A diagnosis of pleural effusion was made. Paracentesis was done at once; 200 oz. of milk-like fluid, slightly tinged with blood, were withdrawn, resulting in great relief. Resonance returned to the lung and very fair breath sounds were audible. On the third day respiration became embarrassed; signs of reaccumulation of fluid; paracentesis; 80 oz. of similar fluid withdrawn. The patient remained quite comfortable until evening of sixth day; respiratory distress reappeared. A short irritable cough, with a little sputum, was noticed for the first time, but did not seem to worry him much. On the seventh day 148 oz. of fluid were withdrawn. Some of the fluid was plated on agar. No growth. Examination of the fluid and sputum for tubercle bacilli proved negative.

Two days later 195 oz. were removed; improvement temporary. On the 11th day 152 oz. were aspirated. The operation now became necessary every other day. Finally, on the 24th day after admission, he collapsed and died with symptoms of acute cardiac failure.

The temperature was swinging and mostly subnormal, ranging from 96° to 99.2°.

The total amount of fluid withdrawn was 81 pints, the various amounts being:—

Day	...	1	3	7	9	11	13	15	17	18	20	22
Ounces	...	200	80	148	195	152	141	190	106	140	126	150