diverticula of the caecum. Eleven of Bennett-Jones's 22 cases were below the age of 32, whereas of Edwards's 15 cases of diverticulosis elsewhere in the colon the average age was 55 years, the extremes being 38 and 75 years.

Treatment.—All that is necessary is to perform a local resection of the diverticulum and adjacent portion of the caecum. A catheter inserted into the caecum through the stump of the appendix, which is usually removed at the same time, is a simple precaution to relieve any tension on the suture line and allow the giving of fluids if necessary.

Case Report

A muscular but not at all obese bricklayer aged 48 was admitted to Lewisham Hospital on March 21, 1939. Two days before admission he began to have pains across the abdomen which settled in the R.I.F. He vomited once the day before admission. There was a history of a right inguinal hernia for three years. Two years ago he had vomiting and general abdominal pain for one week. During the last 18 months he had suffered from vague abdominal pain without any regular relation to meals. He was never completely free from this pain for more than a week. His weight had kept constant.

On admission he resembled a case of acute appendicitis, there being rigidity in the R.I.F., with deep tenderness over McBurney's point. Temperature 98.4° F.; pulse 88; respirations 22. Under general anaesthesia a gridiron incision was made. The appendix was long, contained three faecaliths, but was not inflamed or obstructed. A diverticulum of the infero-lateral aspect of the caecum admitted the tip of the index finger. It was inflamed and very thin at one part. Some calcified glands were seen in the ileo-caecal region. A wedge-shaped portion of caecum including the diverticulum was resected and the caecum sutured in two layers. The appendix was removed and a catheter tied into the caecum through the invaginated stump of the appendix. A corrugated rubber drain was inserted down to the site of resection.

The patient made an uninterrupted recovery. There was a very little faeces-stained discharge from the catheter. The corrugated drain was removed on the fourth day and the catheter on the tenth day. The wound was dry a few days later, and he was discharged home three weeks after admission.

A plain radiograph of his abdomen confirmed the presence of calcified glands in the right lower quadrant of the abdomen. A barium meal showed no diverticula elsewhere in the colon. The barium meal was repeated in March, 1940: again the whole colon appeared normal. He had no symptoms.

I am indebted to Prof. W. G. Barnard, then Director of the London County Council Histological Laboratory, for the excellent photomicrographs. He reported on the sections as follows:

"Purulent diverticulitis of caecum. The diverticulum is typical of the more common diverticula of colon. It is a hernial protrusion of mucosa and submucosa through the muscularis, and because of

FIG. 1.—Section through solitary diverticulum of caecum. The abrupt termination of the caecal muscular coats (M) on each side of the diverticulum is clearly shown.

this is called a false diverticulum, to distinguish it from a true diverticulum, which would have the addition of the muscular coats in its wall. In Fig. 1 the abrupt termination of the caecal muscular coats on each side of the diverticulum is clearly shown, as are the mucosa and submucosa composing the wall of the diverticulum. At

one side of the diverticulum the mucosa is missing, and here there is a purulent infiltration which has spread to the pericaecal fatty tissue (Fig. 2)."

FIG. 2.—High magnification of the area outlined in ink in Fig. 1, showing purulent inflammation.

Summary

A case of purulent inflammation in a solitary diverticulum of the caecum is reported. The aetiology of the condition is discussed and local excision is recommended as the best treatment.

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PENICILLIN AND FIBRINOLYSIS

BY

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Staph. pyogenes can produce an enzyme fibrinolysin or fibrinase which may dissolve the clot produced by its own coagulase activity (Gonzenbach and Uemura, 1916; Gengou, 1933; Reimer, 1936). Some strains are more active in fibrinolysis than others. This fibrinolysis is well seen on inoculating 0.2-ml. quantities of human citrated plasma (diluted 1:4) in 2 in. by 3/8 in. test-tubes with a large loopful of a 24-hour broth culture of a strongly fibrinolytic strain of *Staph. pyogenes*. After 3 hours' incubation the contents of the tubes

TABLE I.—Comparative Activity of Fibrinolytic and Afibrinolytic Strains of *Staph. pyogenes*

	Clot Present After 3 hrs.	Clot Present After 6 hrs.	Clot Present After 9 hrs.	Colour to Neutral Red Initially	Colour to Neutral Red After 9 hrs.
0.2 ml. plasma 1:4 inoculated with 1 loopful of a 24-hr. broth culture of a coagulase-positive fibrinolytic strain of <i>Staph. pyogenes</i>	++ ++	— —	— —	Yellow "	Pink "
0.2 ml. plasma 1:4 inoculated with 1 loopful of a 24-hr. broth culture of a coagulase-positive afibrinolytic strain of <i>Staph. pyogenes</i>	++ ++	++ ++	++ ++	" "	" "

NOTES ON TABLE I.—(1) Double results refer to duplicate experiments. (2) 0.02 ml. of 0.04% neutral red added to each tube. (3) ++ indicates coherent clot occupying major portion of contents of tube. + indicates some clot. — indicates absence of clot.

have solidified to a gel, but after further incubation for 3 to 6 hours the clot redissolves completely. These facts are illustrated in Table I, which compares the fibrinolytic activity of two strains—one strongly fibrinolytic, the other afibrinolytic.

It will be seen from Table I that the first strain of *Staph. pyogenes* has caused the complete solution of the clot formed by its own coagulase activity within 6 hours of putting up the experiment. The second strain has failed to dissolve the clot even after 9 hours' incubation. Both strains, however, were equally effective in the production of acid. It has recently been suggested by Wilson Smith and Hale (1944), in a valuable study on the mechanism of coagulase activity, that fibrinolysis by *Staph. pyogenes* is associated with dissolution of the clot in the presence of acid formed by the growth of the organism. It is true that acid is formed simultaneously with the solution of fibrin, but fibrinolysis does not merely consist in the solution of fibrin at a low pH, since acid is formed just as readily by strains which cannot readily dissolve fibrin. Fibrinolysis and fermentation are independent phenomena.

Fibrinolysis is readily shown by suitable strains of *Staph. pyogenes* which produce both intense coagulation and rapid subsequent clot solution. Many such strains have been isolated from cases of pyoderma kindly sent to me by Major J. H. Twiston Davies, R.A.M.C. The only available subculture of the Oxford staphylococcus, however (possibly owing to loss of activity by repeated subculture), produced an inconstant and attenuated fibrin web under these conditions, and was therefore not suitable for the study of fibrinolysis.

Penicillin inhibits haemolysis by haemolytic streptococci (Wilson, 1943; Rammelkamp, 1942; Fleming, 1943, 1944). It appeared of interest to ascertain whether penicillin also interferes with fibrinolysis by *Staph. pyogenes*. Since this work was started an account of the inhibition of fibrinolysis by haemolytic streptococci has come from America (Neter and Will, 1944). That penicillin also inhibits fibrinolysis by *Staph. pyogenes* will be clear from the results which follow.

Varying quantities of penicillin dissolved in 0.05 ml. of distilled water are added to 0.05-ml. quantities of human citrated plasma in sterile 2 in. by 3/8 in. test-tubes; 0.10 ml. of saline is added to each tube to give a final volume of 0.20 ml. Then each tube is inoculated with one loopful (2 mm. diameter) of a 24-hour broth culture of a penicillin-sensitive coagulase-positive strain of *Staph. pyogenes*, known from previous experiments to be active in dissolving fibrin. After 3 hours' incubation a clot is seen to have formed in each tube, both in the presence and in the absence of penicillin. But after a further 9 hours' incubation (or even earlier) all the clot is dissolved in the control tubes without penicillin. With concentrations of 0.1 unit of penicillin per ml. and above, the clot remains unchanged, fibrinolysis having been completely inhibited. With less than 0.1 unit per ml., although fibrinolysis is sometimes delayed at the start, disintegration of the clot is generally complete after 9 or 12 hours' total incubation. The results of a typical experiment are recorded in Table II.

TABLE II.—Action of Penicillin on Penicillin-sensitive Strains of *Staph. pyogenes*

Final Concentration of Penicillin in Oxford Units per ml.	Presence or Absence of Clot After Varying Periods of Incubation Following Inoculation with <i>Staph. pyogenes</i> (Penicillin-sensitive and Fibrinase-positive)				Growth After 21 hrs.
	3 hrs.	9 hrs.	12 hrs.	21 hrs.	
0.00	++	—	—	—	+
0.025	++	—	—	—	+
0.05	++	—	—	—	+
0.1	++	++	++	++	—
0.25	++	++	++	++	—

NOTES ON TABLE II.—(1) Double results refer to duplicate experiments. (2) All tubes contained 0.10 ml. saline and 0.05 ml. human citrated plasma. Final volume made up with distilled water containing varying amounts of penicillin to 0.20 ml. (3) ++ indicates presence of large coherent clot occupying a large part of contents of tube. + indicates presence of some clot. — indicates absence of clot.

Penicillin inhibits fibrinolysis by penicillin-sensitive *Staph. pyogenes* readily also in the presence of serum. This action can be used for the detection and estimation of penicillin in serum. The serum sample for estimation is progressively diluted with penicillin-free serum obtained from the same

patient before treatment. Human citrated plasma is added, and each tube is inoculated with fibrinolytic *Staph. pyogenes* as in the above experiments. The titre down to which fibrinolysis is inhibited is determined and compared with controls, using the same penicillin-free serum with added known quantities of penicillin. These control experiments determine the end-point of fibrinolysis with the particular serum employed. It is important to use penicillin-free serum obtained from the same patient before treatment, both as diluent for the serum sample to be tested and in the controls with known amounts of penicillin; otherwise errors due to the presence of antifibrinolytic agents (see Tillet and Garner, 1933; Stuart-Harris, 1935) may arise. This procedure also controls any effect due to decomposition of penicillin in presence of serum (see Bigger, 1944). Some sera are, however, so resistant to fibrinolysis that their penicillin content cannot be measured by this method. Fleming's (1944) recently described method is thus preferable.

Results employing this effect of penicillin on fibrinolysis have, however, found the penicillin concentration in the serum to be of the order of 3 units per ml. 15 to 30 minutes after intramuscular injection of 1,000,000 units, and to be 0.4 to 0.8 units per ml. after 1 hour.

In contrast to the action of penicillin on the fibrinolysis by penicillin-sensitive *Staph. pyogenes*, with insensitive strains no such action is observed. Table III demonstrates the failure of penicillin to inhibit fibrinolysis by an insensitive strain.

TABLE III.—Action of Penicillin on Penicillin-insensitive Strains

Final Concentration of Penicillin in Oxford Units per ml.	Presence or Absence of Clot After Varying Periods of Incubation with Penicillin-insensitive Fibrinase-positive <i>Staph. pyogenes</i>		Growth After 21 hrs.
	3 hrs.	9 hrs.	
0.00	++	—	+
0.05	++	—	+
0.10	++	—	+
0.20	++	—	+
0.50	++	—	+
1.00	++	—	+

NOTES ON TABLE III.—(1) All tubes contained 0.10 ml. human plasma previously diluted with an equal volume of saline and 0.10 ml. water, containing varying quantities of penicillin, to give a final volume of 0.20 ml. (2) Symbols have same connotation as in Table I.

The results in Table III show that concentrations of penicillin which inhibit growth and fibrinolysis with sensitive strains of *Staph. pyogenes* fail to do so when insensitive strains are employed. The action of penicillin in inhibiting fibrinolysis is therefore connected with the inhibition of growth and metabolism, rather than with actual inhibition of the enzymic process of fibrin solution.

Under the conditions studied penicillin did not interfere with coagulase activity, presumably because sufficient preformed coagulase was present in the inoculum to cause rapid deposition of fibrin. The formation of acid, however, which accompanies growth and fibrinolysis is inhibited by penicillin with penicillin-sensitive strains. This is illustrated in Table IV.

TABLE IV

Final Concentration of Penicillin in Oxford Units per ml.	Presence or Absence of Clot After Varying Periods of Incubation with Fibrinolytic Strain of <i>Staph. pyogenes</i>		Colour of Contents of Tubes Before and After Incubation (0.02 ml. of 0.04% Neutral Red was Added to Each Tube)	
	3 hrs.	9 hrs.	Initially	9 hrs.
0.00	++	—	Yellow	Pink
0.025	++	—	"	"
0.05	++	—	"	"
0.10	++	—	"	Orange
0.25	++	++	"	Yellow
0.50	++	++	"	"

NOTES ON TABLE IV.—(1) All tubes contained 0.10 ml. human citrated plasma previously diluted with an equal volume of saline and 0.10 ml. water containing varying quantities of penicillin. To each was added 0.02 ml. of 0.04% neutral red. Final volume, 0.22 ml. (2) Symbols have same connotation as in Table I.

It is seen from the results shown in Table IV that the pH changes which normally accompany growth are abolished by penicillin at the same time as the interruption of fibrinolysis.

With a penicillin-insensitive strain, on the other hand, the production of acid is not susceptible to inhibition by penicillin. This is shown in Table V.

TABLE V

Final Concentration of Penicillin in Oxford Units per ml.	Presence or Absence of Clot After Varying Periods of Incubation with Penicillin-insensitive <i>Afibrinolytic</i> Strain of <i>Staph. pyogenes</i>		Colour of Contents of Tubes Before and After Incubation (0.02 ml. of 0.04% Neutral Red was Added to Each Tube)	
	3 hrs.	9 hrs.	Initially	9 hrs.
0.00	++	++	Yellow	Pink
0.025	++	++	"	"
0.05	++	++	"	"
0.10	++	++	"	"
0.25	++	++	"	"
0.50	++	++	"	"

NOTES ON TABLE V.—(1) Quantities of reagents employed were the same as in Table IV. (2) Symbols have same connotation as in Table IV.

It is seen from the above results (Table V) that even 0.5 unit of penicillin per ml. has not interfered with the production of acid by insensitive *Staph. pyogenes*, which is in marked contrast to the results in Table IV when a sensitive strain was employed. The results in Table V also demonstrate the separate nature of the phenomena of fibrinolysis and acid production. The strain used was *afibrinolytic*, and in spite of good acid production (at all penicillin concentrations used) solution of fibrin did not occur.

Fibrinolysis by *Str. pyogenes* (Group A) is also inhibited by penicillin (as was shown by Neter and Will, 1944). Using the technique described above, this action was found with one strain down to 0.025 unit of penicillin per ml., and with another to 0.0125 unit per ml. As *Str. pyogenes* does not form coagulase, 0.02 ml. of 1% calcium chloride was added to each tube to give the preliminary fibrin clot.

This inhibitory action of penicillin on fibrinolysis by both *Staph. pyogenes* and *Str. pyogenes* may be responsible for some of the therapeutic effects of penicillin, since prevention of the dissolution of fibrin barriers would counteract the spread of infection.

Summary

Penicillin inhibits fibrinolysis by penicillin-sensitive fibrinolytic strains of *Staph. pyogenes*.

The clot produced in human plasma by coagulase activity redissolves on further incubation, but fails to redissolve in the presence of penicillin at concentrations as low as those necessary to inhibit growth.

This effect is shown with penicillin-sensitive but not with penicillin-insensitive strains of *Staph. pyogenes*, and is presumably connected with the inhibition of growth.

I am very grateful to Major-Gen. L. T. Poole for his kind interest in this work, also to Major J. H. Twiston Davies, Lieut.-Col. C. H. Stuart-Harris, and Major S. T. Cowan for valuable advice. I wish to thank Sgt. J. R. McDonald and Sgt. J. Smith for their able assistance.

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The *Soviet Medical Chronicle* for March, 1945, prepared by the Anglo-Soviet Medical Council in London from material supplied by the U.S.S.R. Society for Cultural Relations, Moscow, reports the reopening of the Pirogov Museum in the village of Sheremetka, not far from the city of Vinnitsa in the Ukraine. This museum is dedicated to Nikolai Pirogov, the famous surgeon (1810-81), known as the father of Russian medicine. During their occupation the Germans turned it into a stable and destroyed many valuable exhibits. When they retreated from the village the Germans planted mines both in the house in which Pirogov had lived and worked, and in his tomb. At the risk of their lives the villagers removed the mines and saved the museum. Later on the staff of the local hospital helped to repair the building, which is now open to visitors again.

Medical Memoranda

Identical Disease in Identical Twins

Kallmann and Reisner (1943), in an enlightening study recently reviewed in this *Journal* (1944, **2**, 504), confirmed the conclusions arrived at by various other authors that "hereditary factors play a decisive part in both the origin and the clinical course of tuberculous disease." An extensive literature—mostly German—on this subject is to be found in the original paper.

As a contribution to the pathology of twins the following cases may be of some interest.

The twins in question are 7-year-old daughters of a tuberculous mother under my treatment. These little girls, so far as I am able to judge, are identical—monozygotic—twins. In the course of routine contact examination of the children I learnt that they were complaining of cramp-like abdominal pains. The plain abdominal radiographs of the twins show calcified mesenteric glands,

so alike in size, site, and configuration that one feels entitled to call them identical. As the two radiographs were taken on different days some allowance should be made for a slight difference in positioning, with slightly different projection of the glands in relation to the spine. There is no doubt that in both cases exactly the same group of glands is affected.

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Diffuse Peritonitis from Gangrene of Hernial Sac

Gangrene of a hernial sac, though rare, is well known. It may or may not be associated with gangrene of the sac contents, the latter usually occurring in an elderly patient with a long-standing hernia. However, the following case, if not unique, appears to be of such rarity as to be worth recording.

A man aged 59 was admitted to the City General Hospital, Sheffield, on Nov. 15, 1944, for retention of urine. The relevant history was that six months previously he developed bilateral inguinal herniae, for which he was given a truss. This did not control either side adequately, and 10 days before admission the left hernia became irreducible, painful, and tender. This local tenderness was followed by colic pain, nausea, and later vomiting, also with absolute constipation for four days and retention of urine 12 hours before admission, for which he had been catheterized.

On examination his general condition was poor, he was dehydrated, and his tongue was red and dry. The abdomen was distended, tender all over, but intestinal sounds were present. In the left inguinal canal there was a tender swelling, which was irreducible, non-expansile on coughing, and covered by red oedematous skin. Seven oz. of urine was withdrawn by catheter. The provisional