muscular relaxation. Since the ratio of the molecular weights of SMC-I and SDC-Cl₂ is about 0.8, the hydrolysis of 0.05 to 0.15 mg. of SDC-Cl₂ will produce the equivalent of 0.04 to 0.12 mg. of SMC-I. This dose of SMC-I has little or no effect on neuromuscular conduction in patients whose ability to hydrolyse and excrete SMC-I is unimpaired. However, in patients with low cholinesterase activity, especially if their kidney function is also diminished, the administration of relatively large doses of SDC-Cl₂ for prolonged periods might lead to the accumulation of SMC in sufficiently high concentrations to potentiate the neuromuscular action of the unhydrolysed SDC-Cl₂. Such a set of circumstances can arise if muscular relaxation is maintained in patients with low plasma cholinesterase activity with SDC-Cl₂ by the "apnoeic technique."

With this technique the administration of SDC-Cl₂ is carried to a point where the patient's voluntary respiratory movements are completely abolished and gas exchange is maintained by manual compression of the breathing-bag of the anaesthesia machine. Since the administration of SDC-Cl₂ in amounts many times higher than the apnoeic dose has no discernible effect on blood pressure, pulse rate, or any other physiological process, there is no sign that would indicate whether just enough SDC-Cl₂ is administered for production of apnoea or whether large doses of SDC-Cl₂ accumulate in the organism. If the latter of the two possibilities occurs in patients with low plasma cholinesterase activity and with decreased urinary excretion, prolonged post-operative respiratory depression will result. Since adequate muscular relaxation can be obtained with SDC by utilizing the difference in sensitivity to this agent between the diaphragm and intercostals, there seldom is a need for the application of the apnoeic technique.

It is unlikely that SMC plays a similar part in the prolonged respiratory depression occasionally observed after the administration of a single large dose of SDC-Cl₂ (Hewer, 1952; Love, 1952; Harper, 1952; and others). The hydrolysis of as large a dose as 100 mg. of SDC-Cl₂ will yield only about the equivalent of 80 mg. of SMC-I, and this dose is not likely to have any neuromuscular blocking effect. The prolonged apnoea under such circumstances is caused either by an exceptionally low plasma cholinesterase activity of the patient or by the combination of acapnia due to too energetic controlled respiration, and reflex breath-holding arising from the stimulating effect of the endotracheal tube on the larynx and trachea in the patient in whom the level of general anaesthesia was allowed to become too light.

Owing to the relatively large doses in which SMC-I has to be administered, the less satisfactory relaxation obtained, and the lack of rapid and easy controllability of its neuromuscular effect, SMC-I does not seem to offer any advantages in comparison with other available muscle relaxants, especially SDC-Cl₂.

Summary

In man SMC-I in doses of 5-7 mg. per kg. produced in three to five minutes muscular relaxation of 8 to 12 minutes' duration.

Muscular relaxation could be maintained by repeated intravenous injections of SMC-I in doses of 3-5 mg. per kg. 8 to 12 minutes apart.

These doses of SMC-I caused little respiratory depression.

The administration of SMC-I markedly potentiated the neuromuscular action of subsequent doses of SDC-Cl₂.

The possible role of the accumulation of SMC in the development of prolonged apnoea after the use of SDC-Cl₂ is discussed.

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BACTERIAL ENDOCARDITIS DUE TO CHROMOBACTERIUM PRODIGIOSUM

REPORT OF A CASE

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Chromobacterium prodigiosum (*Serratia marcescens*) is usually regarded as non-pathogenic for man, and Wilson and Miles (1946) were unable to quote any indubitable report to the contrary. In 1952, however, Patterson, Banister, and Knight described a case of septicaemia due to this organism, and reviewed the literature concerning human infections with members of the *Chromobacterium* group. They quoted 21 records of infection by *Chr. prodigiosum*, including their own, only one of which was a case of endocarditis (Wheat, Zuckerman, and Rantz, 1951).

Case Report

An African man aged 38 was admitted to the Gold Coast Hospital, Accra, on April 30, 1953, after a month's sickness; this began with fever and headaches, accompanied by rigors. After taking mepacrine and "phensic" tablets he was able to continue his work as an omnibus inspector. About a week before admission he had had further headaches with fever and pain in the neck. He attended the out-patient department on April 25, when a blood film proved negative for malarial parasites, but the urine was found to contain albumin. He was given an injection of sulphasolucine, 5 ml., and another of quinine, 10 gr. (0.65 g.), both intramuscularly, as well as 2 ml. of mersalyl. He was subsequently referred to A. J. H. and was admitted for investigation.

On admission he complained of feverishness and pain in the umbilical region. His temperature was 101° F. (38.3° C.). A blood film was again negative for malarial parasites and there was a heavy cloud of albumin in the urine. He was systematically examined on May 1. It was noticed that he had lost weight. He was obviously a sick man, but in no way distressed. No rash was found on his skin and his temperature was 104.2° F. (40.1° C.). His bowels had been open daily and the stools were semi-solid. His tongue was moist and a little furred. Except for the complaint of pain in the umbilical region no abnormality was found in the alimentary system. The chest was clear and the sinuses appeared to be normal; the respiration rate was 30 a minute. The cardiovascular system showed nothing abnormal beyond a pulse of 120 a minute. The patient complained of a frontal headache, which was worse when the fever was high in the evenings, but a clinical examination

of the central nervous system proved negative. There was no lymphadenitis. The urine was passed freely without pain.

A white blood cell count showed a total of 11,200 leucocytes (70% polymorphs, 25% lymphocytes, 2% eosinophils, 2% monocytes, 1% basophils). Coliform bacteria were cultured from the urine, and were at the time reported as *Bact. coli*, a finding which was later doubted. Serological reactions with *Salmonella* antigens were negative. A Weil-Felix test gave the following result: *Proteus* OX₂ 1/160, X_K 1/40 X₁₉ 1/80. Two successive stool cultures on May 6 and 8 proved negative. Blood culture on May 2 was discarded as sterile 21 days later.

On May 6 treatment was begun with alkalis and "sulpha-triad" in full doses. After three days, since there was no response, he was given chloramphenicol, 2 g., as a loading dose and 1 g. every four hours thereafter; after four days, when he had received 25 g., the available supply of chloramphenicol was exhausted, and although there had been a favourable response this was not maintained when the drug was stopped. By this time blood had appeared in the urine. The patient's condition had deteriorated, and he was very weak; he was thought to be too ill for cystoscopy or pyelography, both of which had been considered. Streptomycin was given from May 16 in doses of 1 g. daily, but with no beneficial effect.

On May 20 a further blood culture was taken, by which date the only positive finding had been the growth of coliform bacteria from the urine. On May 11 a re-examination revealed a full appearance of the abdomen; because of general resistance palpation was difficult, but the liver, spleen, and kidneys could not be felt. Rectal examination revealed generalized tenderness only. The lungs remained free from clinical signs, but an apical systolic cardiac murmur was noted; the significance of the latter finding was overlooked. The urine continued to show a heavy albuminuria with red and white blood cells. On May 25 a third blood culture was taken which five days later yielded a pure growth of *Chr. prodigiosum*, which was reported as being probably a contaminant. The patient's condition continued to deteriorate, and he died on June 2 without a diagnosis having been made.

Post-mortem Examination

A post-mortem examination was made 19 hours after death by Dr. F. C. Harris. The main finding was a friable vegetation, buff in colour, attached to the free margin of the posterior cusp of the mitral valve; there was some erosion of the cusp. A haemorrhagic nodule, 0.5 cm. in diameter, was found on section of the liver. There were five recent infarcts in the spleen, which was moderately enlarged, and a large white infarct involving the whole of the upper pole of the right kidney.

On the following day the blood cultured on May 20 was found to have produced a belated pure growth of *Chr. prodigiosum*, after 15 days' incubation in a combined liquid and solid medium put up in the same bottle by a technique modified by Hughes (1953) from that described by Castaneda (1947); the important feature of this technique is that it prevents contamination of the culture between the inoculation of the medium and the isolation of the organism, and it is thus quite certain that the growth of *Chr. prodigiosum* in a second blood culture could not have been due to laboratory contamination. The cut surface of the mitral vegetation removed at necropsy was rubbed on the surface of a blood-agar plate, and this also yielded a pure culture of *Chr. prodigiosum*. Thus *Chr. prodigiosum* was isolated from two ante-mortem blood cultures taken on different dates, and also from the mitral vegetation after death.

Bacteriology

The culture of *Chr. prodigiosum* isolated from this case had the following characteristics: Motile Gram-negative coccus-bacillus without a capsule. Good growth on nutrient agar, sheep's blood agar, MacConkey agar, and "bacto" SS agar. Growth at room temperature (about 25° C.) was

slightly better than at 37° C. No haemolysis on blood agar. On nutrient agar the colonies after 24 hours were from 0.5 to 1 mm. in diameter, smooth, shiny, and low convex with entire edge, and bright red in colour. After 48 hours the confluent growth was orange-red, and the single colonies were between 1 and 2 mm. in diameter, umbonate, surface becoming granular, with pink centre and orange-red periphery. After five days the colonies were from 3 to 4 mm. in diameter with a rough appearance.

The pigment was very slightly soluble in water, moderately soluble in absolute alcohol, and completely removed from a peptone water culture by chloroform. In peptone water and in gelatin a red surface ring was formed, but this did not occur in broth or in glucose phosphate medium. The colonies on MacConkey agar were bright red; this appearance, coupled with a red colour in lactose-peptone water simulating that of acidified Andrade's indicator, probably resulted in an erroneous report of *Bact. coli* in the patient's urine, although if *Chr. prodigiosum* had been recognized at that time it is improbable that the finding would have been regarded as significant.

In peptone water "sugar" media, acid and a moderate amount of gas were formed from dextrose, saccharose, maltose, mannitol, and salicin; there was no fermentation of lactose, dulcitol, arabinose, rhamnose, xylose, and inositol. There was no growth in Koser's citrate. Indole was not formed. H₂S was formed on liver infusion agar, but not in peptone water, when tested for by a lead acetate strip in the top of the tube. Catalase was not formed. The methyl red test was negative. In a five-day glucose phosphate culture the Voges-Proskauer test was negative by O'Meara's method but positive by Barritt's modification of the test. Coagulated serum and gelatin were both liquefied.

In vitro sensitivity tests showed the strain to be completely resistant to penicillin and aureomycin, but sensitive to chloramphenicol and streptomycin. White mice died within 12 hours when injected intraperitoneally with 0.5 ml. of a 24-hour broth culture; these mice showed pleural exudates.

The specific identity of the organism described by us as *Chr. prodigiosum* may be open to doubt. Breed, Murray, and Hitchens (1948) used the formation of gas in carbohydrate media as a criterion for the separation of species within the genus *Serratia*, and on this ground our organism could not be *Chr. prodigiosum*. Wilson and Miles (1946), however, stated that some strains of *Chr. prodigiosum* do form gas. Again, Breed *et al.* used acetyl-methyl-carbinol formation as a means of separating species, but without specifying what method they used for testing for this metabolite; the results with our strain were equivocal by this standard also, and it was not possible to classify it according to the criteria of *Bergey's Manual*. Without aspiring to taxonomic authority we have therefore thought fit to call our organism *Chr. prodigiosum*, a course in which we are fortified by the treatment of this group of organisms by Wilson and Miles.

It is of interest to note that both in our own case and in that described by Patterson *et al.* (1952) there was some clinical response to chloramphenicol, although in both cases the treatment with this drug was interrupted by extraneous circumstances. Patterson *et al.* also found that their strain was highly sensitive to neomycin, and one of these two antibiotics would appear to be the treatment of choice in cases of infection by this organism.

Summary

A case of acute endocarditis is described in which *Chr. prodigiosum* was isolated twice from the blood during life and again from an endocardial vegetation after death. The strain was sensitive *in vitro* to streptomycin and chloramphenicol, and slight improvement followed treatment with the latter drug. The characteristics of the organism are described. Chloramphenicol, or perhaps neomycin, may be the

treatment of choice should further cases of this rare infection by a common saprophyte be brought to light.

Our thanks are due to Dr. F. C. Harris for permission to make use of his necropsy report, and to Dr. L. G. Eddey, Chief Medical Officer, for permission to publish this paper.

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Medical Memorandum

Congenital Tuberculosis after Pleural Effusion in the Mother

A woman aged 23 was admitted to a general hospital with a left pleural effusion on December 1, 1949, when five months pregnant. There was no family history of tuberculosis or known contact. She did not remember having had any illness until July, 1949, when her husband was at home on leave and she had a cold and lost weight. In the early weeks of her pregnancy she gained weight, but began to get pains in the left chest in October. The findings on aspiration of approximately 500 ml. of straw-coloured fluid were: red cells, moderate numbers; lymphocytes, fairly numerous; polymorphs, nil. The blood picture was: haemoglobin, 64%; leucocytes, 8,000 (polymorphs 66%, lymphocytes 30%, monocytes 3%, eosinophils 1%). There was nothing abnormal on urinary examination. On January 7, 1950, after the illness had run a typical course, she was discharged home, apyrexial, to await admission to a sanatorium.

On February 7, when admitted to a chest hospital, she was symptomless. The physical signs were those of a small pleural effusion, the anaemia persisted, and the sedimentation rate was 18 mm. (Westergren). Radiologically an opacity remained in the left lower zone. Treatment was by rest and haematinics whilst the pregnancy proceeded uneventfully to full term.

On April 17 she complained of generalized aches and pains and there was an evening pyrexia to 99.2° F. (37.3° C.). Next day the symptoms were improved, and on the 19th she went into labour and was delivered of a normal female child the same day, after transfer to the maternity hospital. The child was isolated. The placenta was examined and recorded as "complete." During the puerperium she had an evening pyrexia of 101° F. (38.3° C.) and was readmitted to the chest hospital on April 25, when treatment was begun with streptomycin, 1 g. daily, and 18 g. of para-aminosalicylic acid. On April 27 the baby died, aged 8 days.

FINDINGS AT NECROPSY ON THE BABY

The body was well nourished and of normal colour. About 5 ml. of clear yellow fluid was present in both pleural cavities, and a little less than 5 ml. in the peritoneal cavity. Both lungs showed severe congestion and oedema. Weight, right 62 g., left 58 g. Dispersed throughout the lung substance of both sides and beneath the pleural surfaces were miliary tubercles consisting of grey-yellow areas 2-3 mm. in diameter and some the size of a small pinhead. The tubercles were either one size or the other, there being none of intermediate size.

The heart showed no congenital or acquired abnormality. The peritoneal cavity contained about 10 ml. of free fluid. There was matting together of the structures around the spleen and yellowish-white exudates were present in small amount. The spleen weighed 35 g. and measured 7.5 by 4

by 3 cm. It was engorged and contained tubercles similar in size to those in the lungs. A direct smear from the cut surface revealed many tubercle bacilli. The liver weighed 260 g., and contained tubercles throughout, and beneath its peritoneal surface. The most interesting feature of this organ was the presence of a mass of glands in the hilum. These measured 3 by 2.5 by 2 cm. The cut surface was yellow and caseous-looking. The kidneys, bladder, uterus, and alimentary tract appeared to be normal. The brain was not congested and seemed normal in every respect, no evidence of tubercle being present.

PROGRESS OF MOTHER

The woman continued to have an evening pyrexia until June 15, by which date 50 g. of streptomycin had been given. Apart from the pyrexia the post-puerperal period continued normally, but the reappearance of menstruation was delayed until August 12. No abnormal physical signs were present in the chest, and radiography demonstrated only a clearing of the pleural opacity. Clinical improvement with a gain in weight began with the subsidence of the pyrexia, but chemotherapy was continued until August 28, when 120 g. of streptomycin had been given. At this time no clinical or radiological abnormality could be detected. She was discharged home on October 19, apparently a healthy woman, the sedimentation rate being 4 mm. (Westergren) and her weight 128 lb. (58 kg.).

Subsequent progress during 1950 was uneventful and her weight increased to 143 lb. (64.8 kg.). On February 26, 1951, a laparotomy was performed and section of the Fallopian tubes and appendicectomy were carried out. No abnormality of the pelvic organs was detected. Progress was again uneventful until December, 1951, when a fluctuant swelling was detected in the left breast. At incision in February a localized abscess was removed.

Microscopically, non-specific chronic inflammation was reported and culture of the material evacuated remained sterile, but a sinus persists, although the patient remains well three and a half years after the birth of her child.

COMMENT

The primary lesion in the hepatic glands of the infant is consistent with haematogenous infection via the placenta, whilst its size and maturity would suggest that it originated a considerable time before birth, probably coincident with the onset of pleurisy in the mother. The miliary tuberculosis in the lungs, spleen, and liver would seem to be a secondary haematogenous dissemination in which the mother shared infection just before delivery, the usual effects of such dissemination being suppressed by streptomycin.

Any typical primary focus other than the pleural effusion in the mother remains undisclosed, but it has been shown (Kayne *et al.*, 1948) that quite a large proportion of "idiopathic" pleural effusions occur in close time relationship with the primary infection.

This case contrasts with the almost invariable sequel of healthy infants born to mothers suffering from progressive, advanced, or miliary tuberculosis.

I am informed by Mr. L. E. Perkins that in veterinary practice congenital tuberculosis was not so uncommon and was found in association with primary tuberculous infection, usually believed to be in the uterus, rather than in association with established or widely disseminated tuberculosis.

CONCLUSIONS

Treatment by chemotherapy is justified in primary tuberculosis occurring in pregnancy. Routine B.C.G. vaccination at birth of babies born to such tuberculous mothers should be preceded by a Mantoux test.

I am indebted to Dr. J. F. Horley for the necropsy findings.

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