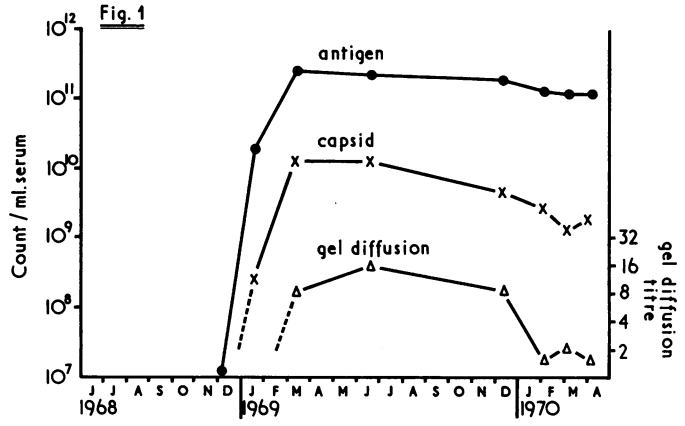

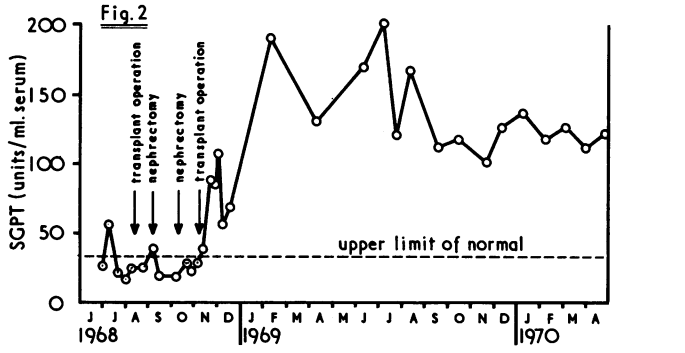

FIG. 1.—Australia antigen and capsid counts with gel diffusion titres.
FIG. 2.—SGPT titres.

capsid is coated with the same material, because a slightly wider spacing on the capsid would be expected from radial arrangement of the units.

The long particles sometimes appeared to be undergoing breakdown, often showing a series of bulges (Fig. 3 C), continued by a line of separate rounded particles suggestive of fragmentation. As no regular structure resembling that of the long forms could be found in the rounded particles, which also have a wide range in size of about a mean of 20 nm. (Barker *et al.*, 1969; Dane *et al.*, 1970), they might well result from fragmentation and structural disorientation of the longer type.

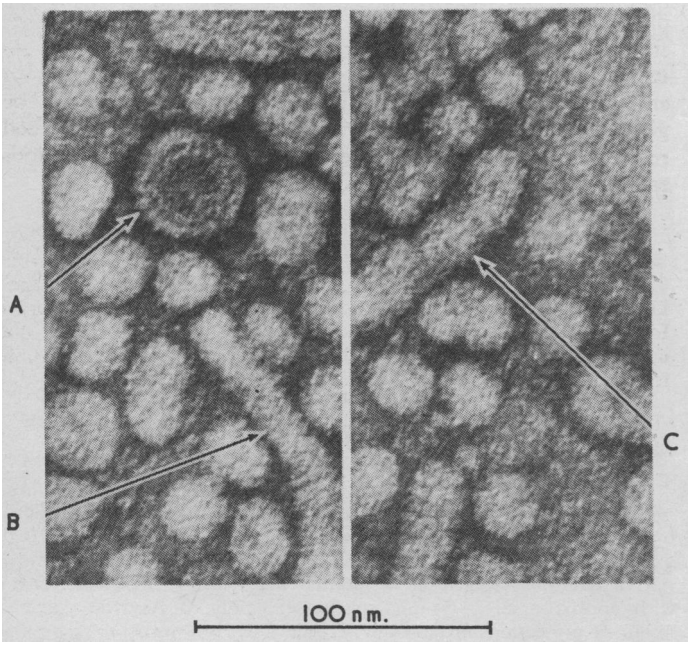

FIG. 3.—Capsid particle (A) shows projections of the coat layer. The periodicity along the long forms is indicated at (B). One of the long forms (C) shows the series of bulges which may precede fragmentation. (Phosphotungstate preparation photographed at instrumental magnification of 112,000).

CONCLUSIONS

The infection described was completely symptomless and it underlines the hazard of the silent carrier who can emerge while on a surgical ward. This patient could have produced disastrous infection of the unit had not his second transplant been successful so that he was discharged without further dialysis and before he was heavily infected.

Eradication of infection from dialysis units is very difficult, and there is a pressing need for sensitive techniques to monitor not only inpatients but prospective patients and blood for transfusion in order to prevent the entry of infection. Chronic carriage of Australia antigen after hepatitis or associated with chronic hepatitis is now well recognized. The influence of immunosuppression in the case described here cannot be assessed, but it would hardly be surprising if silent carriage of this type did not occur in the normal population.

I am grateful to Professor R. Y. Calne and Dr. D. B. Evans for clinical material and information, and to Dr. G. C. Turner for the Australia antigen detector serum.

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Combined Rifampicin and Erythromycin for Bacterial Endocarditis

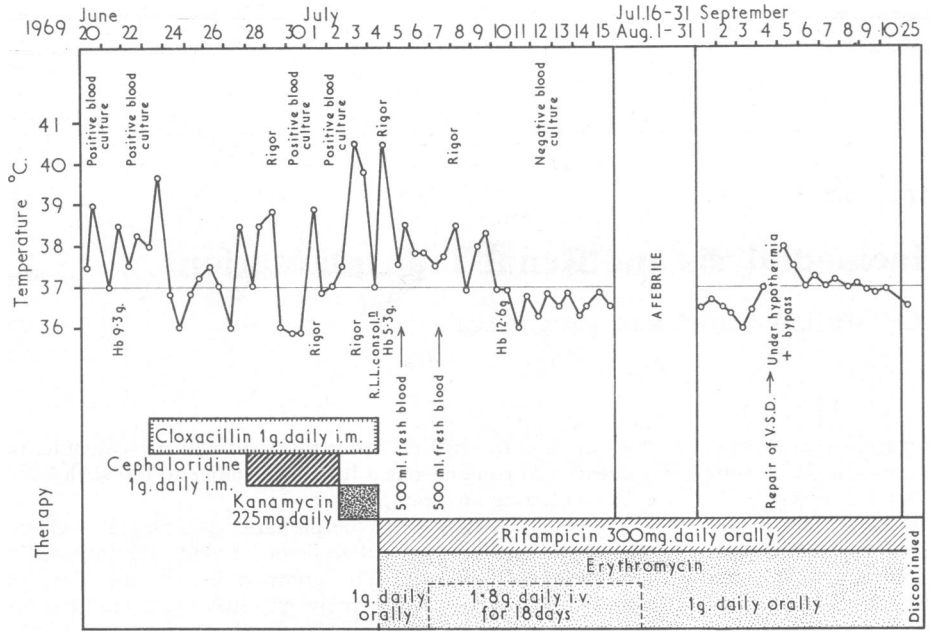
British Medical Journal, 1970, **4**, 410-411

The following case illustrates the necessity for tests of bactericidal action in devising treatment for endocarditis. The combination of antibiotics chosen has never, to our knowledge, been used for this purpose before.

CASE HISTORY

A 3-year-old Saudi Arabian boy was known to have had a small ventricular septal defect from infancy. He developed chicken-pox on 31 May 1969, with persistent pyrexia up to 40°C., and was given a seven-day course of tetracycline for secondary infection of the pustules. He remained febrile and received chloramphenicol for five days without response. On 14 June he was admitted to hospital in Jeddah, where investigations were essentially negative, except for an E.S.R. of 60 mm. Blood cultures were not done. Sulphafurazole and novobiocin were given over the next four days, and the swinging pyrexia continued. On 19 June he was admitted to hospital in London.

On admission there were signs of slight left ventricular enlargement (confirmed radiologically), a pansystolic murmur to the left of the sternum, and a short mid-diastolic murmur in the mitral area. The pulse was regular at 120/min. There was moderately firm smooth enlargement of the spleen and liver. Haemoglobin was 9·3 g./100 ml., W.B.C. 13,000/mm.^{3}, and E.S.R. 88 mm. (Westergren). Blood culture yielded *Staphylococcus aureus*, phage type 52/52A/80, resistant by disc test to penicillin, streptomycin, and tetracycline, but sensitive to cloxacillin, methicillin, cephaloridine, erythromycin, chloramphenicol, kanamycin, gentamicin, lincomycin, and fusidic acid.



Clinical course of endocarditis.

He was treated (see Fig.) with cloxacillin i.m. together for a time with cephaloridine and kanamycin. After an initial fall fever mounted, rigors occurred, two blood cultures were positive, haemoglobin fell to 5·3 g., and signs of right basal consolidation developed.

Tests of Bactericidal Action.—A culture had been sent to the Royal Postgraduate Medical School for further tests. The results of those performed by the method of fluid medium and subculture to detect bactericidal action (Garrod and Waterworth, 1969) are shown in the Table. The only antibiotic totally bactericidal when acting alone was gentamicin, and five combinations with it had the same effect. So also had five combinations with rifamide, though it was ineffective alone. The more promising of these combinations were further tested by the cellophane transfer method, which affords a visual picture of synergic bactericidal effect. The largest area of total bactericidal action was produced by rifamide + erythromycin, and it was therefore suggested that this combination be used in treatment. Rifamide was tested because it was not known that rifampicin, which was actually used, would be available, but the findings with one derivative of rifamycin are applicable to another.

Results of Tests of Bactericidal Action

	Methicillin	Vancomycin	Gentamicin	Novobiocin	Erythromycin	Cephaloridine	Kanamycin	Fucidic Acid	Rifamycin
Methicillin	+	+	(+)	+	+	+	+ +	+	(+)
Vancomycin		+ + +	+	+	+	+	+	+	
Gentamicin			−	(+)	−	−	−		−
Novobiocin				+	+	+	+	+	−
Erythromycin					+	+	+	+	−
Cephaloridine						+ + +	+	+	−
Kanamycin							+ + +	(+)	(+)
Fucidic Acid								+ + +	(+)
Rifamycin									+ + +

Concentrations in broth inoculated with 10^4 organisms per ml.
Methicillin and vancomycin 10 µg./ml.
All other antibiotics 5 µg./ml.
+ + + = Growth in broth culture. Other symbols indicate amount of growth in plate subcultures.
+ + = Number of colonies equivalent to original inoculum (static effect only).
+ = Fewer colonies (partial bactericidal effect).
(+) = Very few colonies.
− = Sterile (total bactericidal effect).

Treatment with Rifampicin and Erythromycin.—On 4 July, when these results were known, treatment was changed to rifampicin 0·3 g. daily and erythromycin estolate 1 g. daily, both given by mouth; the latter was changed to erythromycin lactobionate 1·8 g. daily intravenously for 18 days, when oral medication was resumed. Two transfusions of fresh packed red cells were also given. Though fever abated somewhat at once one further rigor occurred. On 10 July, six days after the treatment was started, the patient became afebrile and remained so, his general condition steadily improving. On 4 September, after nine weeks' treatment with rifampicin and erythromycin, the ventricular septal defect was closed by Mr. Charles Drew. An infracristal defect 0·5 cm. diameter with a small thrombus adherent to its margin was found. The thrombus was removed and found to be sterile. The erythromycin-rifampicin combination was continued for three weeks after the operation.

Comment

Conventional sensitivity tests are no guide to the treatment of this disease. The staphylococcus was sensitive to cloxacillin and to cephaloridine, but the condition worsened while these were being given. Only a totally bactericidal combination can eradicate the infection, and tests in vitro are required to identify it. The new combination chosen in this case has two outstanding advantages: both antibiotics can be given by mouth and staphylococci are more sensitive to rifampicin than to any other antibiotic. Nevertheless, rifampicin should not be given for infections other than tuberculosis without very good reasons, and since otherwise bacterial resistance develops rapidly, it should never be used alone.

We thank Dr. Ursula James, Dr. Aubrey Letham, and Mr. Charles Drew for permission to publish this case. We also thank Dr. C. Pinckney and Dr. Haith Rafik Sadik, of the Dr. Khalid Idress Hospital, Jeddah, for referring the patient and for the information provided. We are indebted to Lepetit Pharmaceuticals for the supply of rifampicin.

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