

# Rifampicin therapy in Gram-negative bacteraemia in infancy

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**Rifampicin therapy in Gram-negative bacteraemia in infancy.** Rifampicin was given to 3 severely ill infants suffering from septicaemia due to klebsiella, *Shigella flexneri*, and *Esch. coli*, after numerous other antibiotics had proved ineffective. Rifampicin proved to be rapidly effective. No untoward side effects were observed.

Rifampicin is a semi-synthetic, orally active bactericidal antibiotic, related to the rifamycin antibiotics that are fermentation products of *Streptomyces mediterranei*. Though mainly used in tuberculosis, it has also been fairly extensively used in other bacterial infections in adults. Little information has been published about its use in children.

We report here its successful use in 3 severely ill infants, each of whom had failed to respond to a number of other antibiotics.

## Case reports

**Case 1.** An 8-month-old female was admitted with diarrhoea, vomiting, and fever of 7 days' duration. Oral streptomycin treatment had been ineffective and she was therefore referred to hospital. She was a moderately dehydrated infant; weight 6.5 kg, and temperature 39 °C. Hb 13.7 g/100 ml, white blood cell (WBC) count 12,300/mm<sup>3</sup> of which 1% were band forms and 45% segmented neutrophils. Urine analysis normal; stool smear and culture normal; blood cultures on the 1st and 2nd hospital days were sterile; chest x-ray normal.

She was put on intravenous fluids, and chloramphenicol 300 mg daily was started.

On the 3rd hospital day the leucocytosis increased to 25,700/mm<sup>3</sup> of which 43% were band forms and 43% segmented neutrophils. On that day kanamycin 100 mg daily was added.

On the 7th hospital day purpura appeared on her palms and soles. Laboratory tests supported a diagnosis of disseminated intravascular coagulation, which was treated with heparin with clearance of the purpura.

Blood culture taken on the 7th day yielded a profuse growth of klebsiella resistant to penicillin G, erythromycin, tetracycline, chloramphenicol, sulphonamides, ampicillin, kanamycin, carbenicillin, cephalo-

ridine, lincomycin, and vancomycin, but sensitive to colistin, gentamicin, and rifampicin. Accordingly, kanamycin was replaced by gentamicin 20 mg daily and colistin 400,000 units daily as seen in Fig. 1. Nevertheless, high fever continued unremittingly, and on the 27th hospital day signs of osteomyelitis of left femur and septic arthritis of right knee appeared, and were later confirmed by x-ray.

On the 28th hospital day, all antibiotics were stopped and replaced by rifampicin 100 mg twice daily orally. 3 days later the temperature dropped to normal for the first time since admission and remained so for 7 days. On the 10th day of rifampicin treatment, however, her temperature rose again but dropped to normal after aspiration of a purulent exudate from the right knee joint, and subsequently the infant remained afebrile.

Rifampicin treatment was continued for about 2½ months. The infant was then discharged in good condition with normal joints and normal x-rays of the lower limbs.

**Case 2.** A 6-month-old female was admitted with diarrhoea, vomiting, and fever of 3 days' duration. She was moderately dehydrated, weight 6.75 kg, temperature 39 °C, and pulse rate 140/min. Hb 12.2 g/100 ml and WBC count 17,000/mm<sup>3</sup> of which 33% were band forms and 28% segmented neutrophils. Urine analysis normal; stool smear showed much mucus and many WBCs; stool cultures taken on the 3rd, 9th, 16th, 17th, and 18th hospital days and blood cultures taken on the 2nd, 3rd, and 4th hospital days yielded a growth of *Shigella flexneri*. All the strains isolated from the stool and blood showed identical sensitivity patterns, being resistant to tetracycline, chloramphenicol, streptomycin, sulphonamides, and ampicillin, but sensitive to nitrofurantoin, kanamycin, colistin, cephaloridine, gentamicin, and rifampicin.

In view of the septic fever and the leucocytosis with marked shift to the left, a probable diagnosis of septicaemia was made. Intravenous fluid was administered and kanamycin 100 mg daily was started.

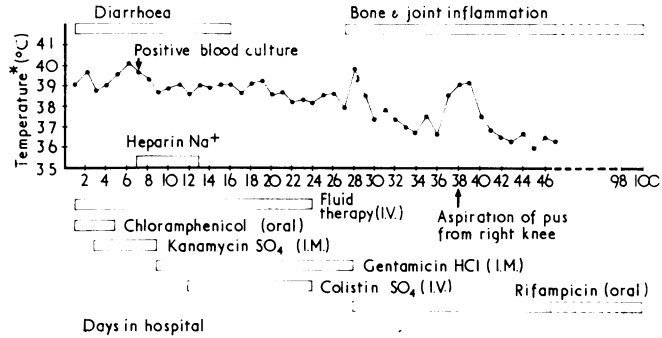


FIG. 1.—Case 1. *Klebsiella septicaemia*, course of disease and therapy. \*Maximal daily temperature plotted in Fig. 1 to 3.

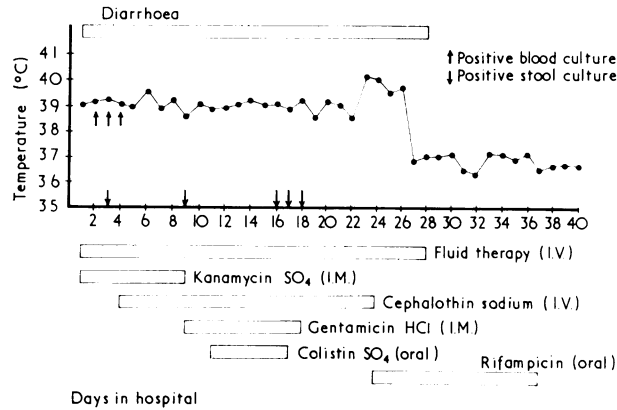


FIG. 2.—Case 2. *Shigella flexneri septicaemia*, course of disease and therapy.

This was followed by cephaloridine 300 mg daily, gentamicin 20 mg daily, and colistin 1 million units daily (Fig. 2). These treatments failed to improve her diarrhoea or to affect the septic fever.

On the 24th hospital day, all other antibiotics having been stopped, rifampicin was started, 75 mg twice daily orally. As seen in Fig. 2, the fever fell to normal on the 4th day and the diarrhoea ceased on the 6th day of treatment. Rifampicin was given for 14 days and the patient was discharged clinically well.

**Case 3.** A 14-month-old male was admitted with diarrhoea, vomiting, and fever of 2 days' duration. He was a well-developed, moderately dehydrated child; weight 8.65 kg, temperature 38 °C. Hb 10.1 g/100 ml and WBC count 10,300/mm<sup>3</sup> of which 9% were band forms and 20% segmented neutrophils. Urine analysis normal. Stool examination showed much mucus and many WBCs. Stool cultures were negative.

He was started on intravenous fluids and furazolidone 80 mg daily, and this was replaced by colistin 1 million units daily (Fig. 3).

A blood culture taken on the 6th hospital day yielded

*Esch. coli* sensitive to nitrofurantoin, carbenicillin, cephaloridine, gentamicin, rifampicin, and trimethoprim-sulphamethoxazole. When sensitivity tests were

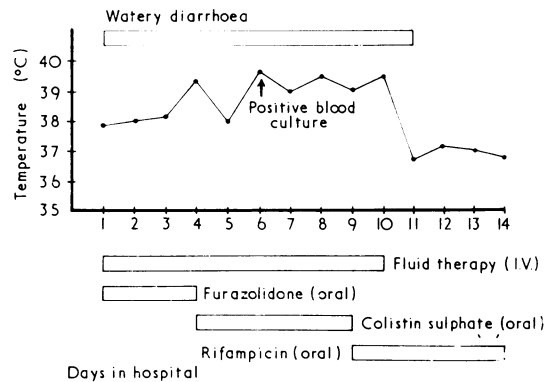


FIG. 3.—Case 3. *Esch. coli septicaemia*, course of disease and therapy.

available, rifampicin 100 mg orally twice daily was substituted; within 3 days the fever cleared and the diarrhoea ceased 1 day later. Rifampicin was given for 5 days, and the patient was discharged well on the 14th hospital day.

### Discussion

A review of recent published reports disclosed only five papers reporting rifampicin therapy in nontuberculous infections in childhood (Rosaschino, 1968; Durand, 1969; Scarzella, 1969; Valente and Luvara, 1969; Bessudo, Duarte, and Bucio, 1972).

Our patients were infants who suffered from serious infections caused by Gram-negative bacilli. In large series of bacteraemia due to Gram-negative bacilli, high mortality rates were reported (McCabe and Jackson, 1962; Johnston and Sell, 1964; Freid and Vosti, 1968; Du Pont and Spink, 1969).

The dramatic results of treatment in our cases leave no doubt of the effectiveness of rifampicin. The drug was used after other potent antibiotics failed to achieve clinical improvement in Cases 1 and 2, though some of these antibiotics which preceded rifampicin therapy were those to which the microorganisms were shown to be sensitive *in vitro*.

The daily dosage generally recommended is 10 mg/kg in ordinary infections, and 20 mg/kg in more severe infections (Scarzella, 1969). We used somewhat higher doses in Case 1 on account of the clinical resistance of this case to other potent broad-range antibiotics.

The drug was absorbed well despite diarrhoea in Cases 2 and 3. The high temperatures subsided from the 3rd to 5th day of treatment (Fig. 1-3) in all 3 cases, though different Gram-negative bacilli were involved. Diarrhoea ceased in Cases 2 and 3 on the

6th and 4th day, respectively, of rifampicin treatment. No adverse side effects were observed despite prolonged administration of rifampicin in Case 1.

The drug has the advantage of ease of administration, since it is given orally in twice-daily doses, and according to Durand (1969) a single daily dose may suffice.

We are indebted to Ciba Ltd., Basle, Switzerland, for supplying rifampicin (Rimactane).

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