

REVERIN IN A TROPICAL HOSPITAL

By H. J. Rathscheck

(Chief Medical Officer, Municipal Hospital, Serang/Banten).

REVERIN — pyyrolidino-methyl tetracycline is crystallized in form of light yellow small needles with a melting point of 162 to 165°C. The local tolerability of tetracycline preparations for parenteral use available up to now was far from being satisfactory; i.v. administration was only possible by a permanent infusion of a large volume and therefore time-consuming. REVERIN, however, offers the possibility of administration as a normal i.v. injection within 1 minute. The local and general tolerability is excellent.

Usually the daily dose for adults is the content of one ampoule, i.e. 275 mg. As shown in the case quoted below this dose may safely be repeated at appropriate intervals in particularly severe infections. The strict observation of the instructions not to inject the preparation in less than 1 minute is of particular importance. After a certain by-effect observed (case V) we have fixed the time for injection to 3-5 minutes. Since that time no adverse reaction whatsoever occurred.

Case I. Male patient, 38 years, physical condition considerably reduced, high temperature.

Clinical and X-ray diagnosis: Pulmonar abscess of the right superior lobe, size of an apple, non-specific. Beginning of the disease 4 weeks ago. Treatment so far: high doses of penicillin-streptomycin, oral tetracyclines. Since no improvement was noticed, admittance to the Central Hospital.

Findings on admission: 13th August 1959 Sputum; Tb. bac. negative. Staphylococci and streptococci in masses. Malaria: Tertian ring. Faeces: ascarides ++ Urine: protein + Hb 40% Leuco 12,800 BSR 80/120 (Westergren) RR 120/80 mm Hg. Spleen: Schueffner III body weight: 40.5 kg. Temperature: varying between 39 and 40°C (102.2-104°F.) per day. Treatment: first 3 days: 275 mg REVERIN i.v. b.i.d. (at 12 hours interval), subsequently 3 days 275 mg. Additionally Strophanthine and roborants were given. Likewise malaria was treated.

Already after 4 ampoules of REVERIN (275 mg) temperature was reduced to 37.8-38.5°C. (100.0 to 101.3°F.). Remarkable improvement of the general condition. Considerable reduction in amount of the sputum which was initially

messy and creamy. Discharged as cured and free from complaints on August 27th, 1959. By means of X-rays a complete healing of the abscess of the lung with formation of scar-tissue could be demonstrated. Total dose of REVERIN: 2,475 mg.

Case II. Female patient, 22 years, reduced general condition, high temperature.

Clinical diagnosis: Cysto-pyelitis after bilateral parametritis post partum. 8 weeks ago treatment for parametritis with penicillin, penicillin-streptomycin, sulphadruugs. Clinically cured after 16 days. 5 days ago starting of disease. Diagnosis above. Admission to our hospital on September 16, 1959.

Findings on admission: Urine: protin ++ Sugar Ø Cylinders Ø leucocytes +++ single erythrocytes: bacteriologically Enh. wei in masses. Malaria Ø Faeces: ascarides + Hb 55% leuco 10,200 BSR 65/90 (Westergren) RR 120/90 mm Hg; body weight 48.2 kg.

Treatment: at the beginning sulphy-drugs in high doses. After 4 days therapy had to be discontinued on account of severe vomiting. Finding not changed. Beginning of REVERIN i.v. since oral administration was impossible by continuous vomiting. During 5 days 275 mg REVERIN each were given. After the 3rd injection the temperature dropped to normal. On the 12th day another rise of temperature to 38.6°C (= 101.5°F.) was observed. Malaria: negative. Urine: negative. Bacteriological control: single Esch. coli only. REVERIN treatment was resumed for another 3 days, 275 mg. i.v. each. On October 6, 1959, after performing a course of treatment against ascarides the patient could be discharged as clinically cured and free of complaints. Total dose of REVERIN: 2,200 mg.

Case III. Male patient, 56 years, general condition and state of nourishment reduced.

Diagnosis: Neoplasm of the ileo-caecal region. After treatment of a simultaneously existing malaria and vermication the patient received cardiaes and sulfadruugs for preparation of surgery. October 13, 1959 operation: extirpation of caecum and colon ascendens; ileo-transverso-stomy at the same stage. On the 6th day after operation beginning of infiltration around the

wound. Penicillin-streptomycin and chloramphenicol were given. On the 10th day p.o. the wound was opened: an abscess from the deeper parts was discharged (*Esch. coli*), temperature rose to 39.5°C. (= 103.1F.). On the 15th day p.o. status idem in spite of antibiotic treatment as mentioned in massive doses and local treatment of the wound. Simultaneously a considerable reduction of the general condition was noticed. Beginning of REVERIN treatment 275 mg. b.i.d. (at 12 hours intervals). Three days thereafter lowering of temperature and considerable reduction of the putrid secretion from the wound. REVERIN was continued for 5 days in the usual daily dose viz. 275 mg. On the 30th day after the operation, only a slight secretion from the subcutaneous layers was noticeable. Temperature normal, increasing appetite, normal defaecation. On November 10, 1959, wound closed, patient discharged free from complaints. Total dose of REVERIN 3.025 mg.

Case IV. Female patient, 23 years, septic picture, loss of consciousness.

Diagnosis: Septicaemia following an abscess produced by an injection. 16 days ago intragluteal injection of 10 ml. calcium. Since 8 days bedridden at home. Treatment penicillin-streptomycin and oral tetracyclines. On December 14, 1959, admission to the hospital in unconscious state. Very severe septic picture. In the right gluteal region plate-sized swelling and compact infiltration appearing like a wood-phlegmon. Incision without result: the tissue is solid like a stone, no discharge of secretion.

Therapy: Since the condition appeared to be very dangerous, REVERIN i.v. was started immediately: on the first day 275 mg. t.i.d., on the second day 275 mg. b.i.d., on the third-sixth day 275 mg. per day. Already on the second day after 3 times 275 mg. REVERIN temperature dropped to 37.5-38.2°C. (= 99.5-100.8F). The stone-like infiltration of the right gluteal region turned into a softening during 4 days of REVERIN treatment and a clear sterile exudate was discharged from the incision. We expected formation of a gangrene but this did not occur. Almost 2 hours after the second REVERIN injection the patient regained consciousness and retained it until discharge on December 29, 1959. She was cured and definitely free from complaints. Recurrences did not occur. Total dose of REVERIN: 2.2475 mg.

Case V. Male patient, 26 years.

Diagnosis: Chronic osteomyelitis of the left foot after snake-bite. Approximately 3 months ago snake-bite into the 2nd toe left with subsequent slow formation of gangrene and self-amputation of the left fore-foot. Besides local treatment, the dresser stationed there had already given 15 penicillin injections and sulfa-drugs without success. Admission to our hospital on July 25.

Findings on admission: Extended open dirty wound spread over the whole left forefoot of metatarsalia with heavy putrid secretion. Metatarsale I, III, and IV are partly prominent of the wound, metatarsale II and V are completely absent. Temperature: 37.6-38.2°C. (= 99.7-100.8F.).

X-ray findings: Osteomyelitis of all tarsal bones and of the rest of metatarsal bones I, III, and IV. Tibia and fibula normal. Since adequate supply of protheses is rather difficult in our region, our goal was to preserve as far as possible the total length of the lower extremity by formation of a Pirogoff-stump.

Therapy: Beginning of REVERIN i.v. on July 30, 1 ampoule 275 mg. per day. The daily injections were given by a dresser who had special instructions from us. This dresser being unable to give the injection on the 3rd day, had asked another one to do this. As it could be revealed later, this one had performed the injection in 30 seconds. Approximately 10 minutes after the injection, the patient went into a medium grade collapse. After adequate treatment he was well again within 2 1/2 hours. Already after the 5th injection the wound showed fresh granulation: secretion was no more putrid. Whereas the dressings had to be changed 4-5 times daily, now a change was necessary every other day. After another series of 5 injections of REVERIN—total duration of treatment 10 days—X-ray control was made on August 9th, 1959. This examination turned out to a surprise: the osteomyelitic foci present in calcaneus and talus without any doubt on the first X-ray picture shot on July 27, 1959, had completely disappeared. A remarkable reduction in size showed the other foci in the other metatarsal bones. Thereafter, surgery was done on August 10, 1959. After the operation a gypsoplastic dressing was applied to the lower limb. On the day of the operation 275 mg. REVERIN b.i.d. were injected i.v., on the two subsequent days 275 mg. each. Besides antimalarials no other medication was given. On August 31, 1959, the gypsoplastic dressing was removed. The wound showed primary

healing. The patient was discharged as cured on September 10, 1959. Total dose of REVERIN: 3.850 mg.

In conclusion we can say that we did not encounter any therapeutic failure in spite of the fact that very severe conditions were treated. The therapeutic result particularly in the case of osteomyelitis after snake-bite was impressive. In the patient with septicaemia following an abscess after an i.m. injection, the effect was immediately present, nearly before our eyes. In all cases temperature was normalized on the 3rd day of treatment at the latest. We have no objection in the cases described to giving doses of 275 mg. REVERIN repeatedly during a day because also here no complications were seen. We should like to emphasize in full agreement with other investigators that the recommended time of one minute for the injection should be adhered to: In order to achieve avoidance of any undesired effect in any case REVERIN should be given during 3-5 minutes. Compared to the tetracycline preparations for i.v. use available so far we consider REVERIN to be a real progress in any case.

SUMMARY

The recently introduced REVERIN therapy is described in 5 cases typical for a hospital in the tropics. Further patients are under observation. The cases quoted, viz. abscess of the lungs, infection with *Esch. coli.* of severest grade, septicaemia, osteomyelitis demonstrate the broad spectrum of effectiveness of REVERIN. Surpassing the recommended daily dose of 275 mg. REVERIN i.v., which proved to be generally sufficient, is possible provided that appropriate intervals (5-6 hours) and the time for injection — in our cases 3-5 minutes, generally not below one minute—are observed. Even when the quoted cases cannot be compared in number to those observed in large hospitals, we are right to conclude that REVERIN means likewise a real progress for the pharmacy of a hospital in the tropics.

Ed. Comment—This article is of topical interest in that it affords us a view of medicine in Indonesia.
