respiratory failure is a rare manifestation of idiopathic rhabdomyolysis, it appears to occur more often in the toxic myoglobinuria that follows poisoning from sea-snake bite (Mardsen and Reid, 1961).

Our patient presented a clinical picture similar to bulbo-spinal poliomyelitis, but the previous history gave the clue to the correct diagnosis, which was confirmed when myoglobinuria appeared.

The patient's serious condition did not permit transportation to our special treatment unit in a distant building. Hence tracheostomy, bronchoscopy, and open-chest cardiac massage were performed under conditions of difficult access to the patient in the medical ward. The malfunctioning nebulizer of the respirator led to inadequate humidification and prevented the use of therapeutic aerosols to reduce the viscosity of the tracheobronchial secretions. As a result, inspissation and crusting of the secretions occurred necessitating repeated vigorous suction, which traumatized the tracheal epithelium, producing bleeding, infection, and further crusting, which demanded still more energetic suction.

Repeated bronchoscopy would undoubtedly have been most valuable in maintaining a patent airway, but, as the additional hypoxia attendant on bronchoscopy led to cardiac arrest on two occasions, the procedure was abandoned. We have since adopted Rogers and Erhardt's (1961) method in which the bronchoscope is passed behind a previously introduced small endotracheal tube supplying oxygen. This technique, with general anaesthesia and relaxants, permits continuous intermittent positive-pressure respiration. In retrospect, this method might have permitted repeated bronchoscopy and removal of the ball-valve carinal plug which produced the alternating atelectasis and ultimately led to our patient's death.

The episodes of cardiac arrest were caused by severe hypoxia of the heart muscle. In the first episode the heart responded to "pneumomassage" (intermittent positive-pressure respiration) (Bencini and Parola, 1956). The second arrest was treated by pneumomassage plus external cardiac massage, but open-chest cardiac massage was necessary the third time.

The patient's renal complication and other aspects of the aetiology, diagnosis, and pathology of this disease will be presented elsewhere. The renal failure probably added to the pulmonary difficulties by contributing fluid reten-

tion and electrolyte imbalance. The patient appeared to be on the way to recovery from lower nephron nephrosis, but inability to maintain patency of the airways and severe recurrent anoxia led to her death.

Summary

An extremely rare case of idiopathic rhabdomyolysis (myoglobinuria) presenting as an acute respiratory problem is described. Involvement of the diaphragm and intercostal and pharyngeal muscles resulted in a clinical picture simulating bulbo-spinal poliomyelitis. Treatment included sodium bicarbonate to alkalize the urine, tracheostomy, and intermittent positive-pressure respiration. A pseudo-membrane which formed at the carina produced alternating obstruction of the right and left main bronchi with recurring episodes of severe hypoxia which ultimately led to the death of the patient. The condition was further complicated by renal shut-down and repeated cardiac standstill. The latter responded initially to pneumomassage and external cardiac massage. However, after the third episode of cardiac arrest it was necessary to open the chest and massage the heart directly.

At post-mortem examination the typical changes of atrophy, disappearance of muscle fibres, and fragmentation of the sarcolemma were found in the diaphragm and the intercostal and other muscles.

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Preliminary Communications

Pyrimethamine and Sulphadiazine in Treatment of Malaria

The antibacterial action of diaminopyrimidine derivatives is potentiated by sulphonamides, probably because of the sequential blocking of stages in the metabolic synthesis of nucleotides. Sulphonamides interfere with the utilization of *p*-aminobenzoate by the organism, and diaminopyrimidines act as folic-acid antagonists, probably as a result of inhibition of folic-acid reductase (Hitchings, 1962). Potentiation also occurs in experimental infections of *Toxoplasma* (Eyles and Coleman, 1953), *Eimeria* (Lux, 1954), and *Plasmodium* (Rollo, 1955). Pyrimethamine and sulphadiazine are now used together for the treatment of human toxoplasmosis, and the closely related diaminopyrimidine

compound, diaveridine, is used with sulphaquinoxaline for coccidiosis in poultry.

The potentiating effect of sulphadiazine on the activity of pyrimethamine in human *P. falciparum* malaria was shown by Hurly (1959) in the Gambia, and Basu, Mondal, and Chakrabarti (1962) have shown that a combination of pyrimethamine and dapsone is more effective than either drug alone against *P. vivax* in India. Hurly suggested that the combination of drugs might possibly overcome the resistance to pyrimethamine which is sometimes observed in certain strains of the human malaria parasite.

CASE HISTORY

An African girl (age, 11 years; weight, 54 lb.—24.5 kg.) of the Mandingo tribe, reputedly receiving pyrimethamine as a malarial prophylactic at a dosage of 25 mg. a week, was observed on February 8, 1963, to be infected with *P. falciparum* (trophozoite blood density 12,025/c.mm.). As it was not possible to establish beyond doubt that the prophylactic pyrimethamine had been successfully administered, and since

the child was not seriously ill, it was decided to assess the possibility that the infecting parasite was resistant to the drug by treating with pyrimethamine under close supervision.

On February 8, 50 mg. of pyrimethamine was administered and ingestion assured. No vomiting ensued nor was there diarrhoea. Four days later parasitaemia was still present (trophozoite density 715/c.mm.), and the treatment, with the same precautions, was repeated (see Chart). On February 16, as asexual parasites were still present in the blood (density 5,135/c.mm.), a third dose of 50 mg. of pyrimethamine was

Malaria parasite density in a Gambian child. P=50 mg. pyrimethamine. PS=12.5 mg. pyrimethamine given together with 1 g. sulphadiazine. On March 28 the blood contained 150 gametocytes/c.mm.; there were no asexual parasites.

administered. Subsequently daily blood examination confirmed the persistence of parasitaemia; on February 25 the trophozoite density was 3,965/c.mm. At this point it was decided that further treatment with pyrimethamine alone was unlikely to prove successful and that the potentiating effect of sulphadiazine should be investigated.

On February 25, 12.5 mg. of pyrimethamine and 1 g. of sulphadiazine were successfully administered, and 24 hours later the treatment was repeated. On February 28 no asexual parasites could be found after prolonged search of a thick blood film. Daily thereafter, until March 8, blood films remained negative and no asexual malarial parasitaemia could be found. At re-examination on March 28 asexual parasitaemia was still absent.

COMMENT

It appears that in this patient the potentiative effect of sulphadiazine effectively overcame the apparent resistance of the parasite to pyrimethamine; the dose of sulphadiazine given was almost certainly inadequate, by itself, to produce the effect observed unless the strain of parasite had become unusually sensitive to the drug.

One possible explanation of the potentiating action of sulphadiazine is that it might affect the rate of absorption of pyrimethamine, allowing larger amounts to enter the blood-stream and higher blood concentrations to be attained. Unpublished experiments (L. G. Goodwin, I. M. Rollo, and G. M. Trim) made 10 years ago on European volunteers show that this is unlikely, although it is possible that in Africans the presence of bacterial or helminthic intestinal parasites might affect the absorption of drugs. No data are available for this important aspect of therapeutics in the tropics.

A further possible explanation of the effect of the combination of drugs on the patient described above

is that the mysterious phenomenon described by Clyde (1960), in Tanganyika, may also occur in West Africa. Clyde states: "In some cases asexual parasites have persisted after a dose of 100 mg. [of pyrimethamine] only to disappear three weeks later (a lapse of time sufficient to allow excretion of the first dose) upon treatment with as little as 25 mg. Sometimes there are fluctuations in trophozoite density apparently related to treatment, but often there are not."

At present no explanation can be offered for the success of a small dose of pyrimethamine after the therapeutic failure of a much larger one. However, three weeks may not be a "lapse of time sufficient to allow excretion of the first dose," for pyrimethamine is firmly bound in the body and, as shown by Smith and Ihrig (1959), may be detected in the urine for at least 30 days after a large dose.

It is clear that further controlled experiments in tropical regions are required to confirm or refute the apparent effectiveness of a combination of pyrimethamine and sulphadiazine on plasmodial infections resistant to pyrimethamine alone.

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One of the largest hospitals to be built in the Commonwealth, the 1,338-bed Queen Elizabeth Hospital, has been opened in the British Crown Colony of Hong Kong. The hospital was built at a cost of nearly £4½m. and has a school of nursing, specialists' clinic, and a radiological institute for the treatment of cancer. It gives the colony, with its population of over 3½ million people, a total of 9,501 hospital beds. At the specialist clinic, a gift from the Royal Hong Kong Jockey Club, specialists can see patients referred to them by the general clinics in Kowloon and can continue supervision of those discharged from the relevant clinical unit in the hospital. In its four stories the clinic houses 27 examination rooms and facilities for specialists in medicine, surgery, orthopaedic surgery, paediatrics, and obstetrics and gynaecology. There are three minor operating theatres, a laboratory, and an almoner's office. Although the hospital block itself appears as a single unit it has been designed as two separate 13-story wings joined on the first three lower floors by administrative areas. The surgical wing on the east side consists of 31 wards each accommodating 20 to 31 patients, and 18 operating theatres, and the medical wing on the west side has 21 wards, including 10 children's wards and an operating suite. Specialist departments on the ground and first floors are for radiology, including radiotherapy, physiotherapy, and pathology, and there is a blood bank and a casualty department. The Jockey Club Radiological Institute—another donation—contains the most modern equipment for high-voltage radiotherapy in a separate wing of the hospital. It includes a betatron, two British-made linear accelerators, and a radiocobalt telecurie therapy unit.