SHORT REPORTS

Spread of multiresistant strains of *Salmonella typhimurium* phage types 204 and 193 in Britain

Since June 1977 two phage types of *Salmonella typhimurium*, both showing multiple drug resistance, have caused many infections in bovines and humans throughout Britain. The phage types are type 204, with resistance to chloramphenicol, streptomycin, sulphonamides, and tetracyclines (R-type CSSuT), and type 193, with resistance to ampicillin, chloramphenicol, neomycin-kanamycin, streptomycin, sulphonamides, and tetracyclines (R-type ACKSSuT).

The CSSuT-resistant type 204 strain first appeared in calves in June 1977 and has subsequently caused infections in cattle in many areas of Britain.¹ Symptoms were of severe scouring and there was a high mortality rate among infected animals. There have been 56 human isolations of type 204 of R-type CSSuT, mostly from cases of mild enteritis. Some cases were in families in farming communities, but many had no obvious connection with farms. The strain has also been isolated from minced beef prepared for human consumption.

In December 1977 strains of *S. typhimurium* phage type 193 of R-type ACKSSuT affected calves on farms in Herefordshire and Worcestershire. Subsequently, infections occurred in bovines in many areas of England, Wales, and Scotland, and the transport of infected animals facilitated this spread. Human infections first occurred in December 1977, and by the end of June 1978 there had been 44 isolations of multiresistant type 193 strains. As with type 204, some infections occurred in farming families, but most had no direct connection with bovines. So far, there have been no isolations from milk or human foods.

Characterisation of the resistance plasmids in the type 193 strains from both bovine and human sources showed that these strains had an identical plasmid content and represented a single clone. This had been derived from the epidemic phage type 204 strain of R-type CSSuT by the acquisition of an R factor of compatibility group I₁, coding for resistance to ampicillin, kanamycin, and streptomycin (AKS). This plasmid inhibits the lysis of strains of *S. typhimurium* by several typing phages. When the AKS group I₁ plasmid is displaced from the multiresistant strains of phage type 193, the resultant lines belong to phage type 204 of *S. typhimurium*, and have the CSSuT R-type and plasmid content of the epidemic strain.

Earlier studies showed that the CSSuT-resistant type 204 strain was derived from a strain of phage type 204 of R-type SuT, by the acquisition of an R factor of compatibility group H₂, which codes for chloramphenicol, streptomycin, sulphonamide, and tetracycline resistance (CSSuT).¹ Type 204 of R-type SuT became the predominant strain in bovine and human *S. typhimurium* infection in 1976, and remained so until the establishment of the chloramphenicol-resistant epidemic type 204 strain, in late 1977. The possible progenitor of type 204 of R-type SuT was a sulphonamide-resistant strain of phage type 49, which had acquired a non-autotransferring plasmid of an unidentifiable compatibility group coding for tetracycline resistance. This tetracycline plasmid changed the phage type of type 49 to type 204.¹ The overall sequence of events is illustrated in the figure.

The progressive acquisition of drug resistance plasmids by a sulphonamide-resistant type 49 strain may have been produced by the

use of antibacterial drugs in bovine salmonellosis. Firstly, tetracyclines may have acted to produce type 204 of R-type SuT. Subsequently, the use of chloramphenicol, which has been administered for bovine salmonellosis, may have exerted selective pressure to maintain the epidemic CSSuT-resistant type 204 strain in calf herds. Streptomycin and sulphonamides may also have exerted selective pressure, but this is unlikely, since their use in veterinary practice is more limited. Finally, the use of ampicillin or kanamycin in bovines may have contributed to the appearance of the multiresistant phage type 193 strain. Some bovine isolations of the type 193 strain have recently acquired plasmid-encoded resistance to trimethoprim (Tm), which suggests that drugs such as co-trimoxazole are now being used in cattle.

Since 1970 multiresistant salmonellae with enhanced virulence and a tendency to produce septicaemia have caused epidemics in many countries. A multiresistant strain of *S. wien* has spread through paediatric units in countries of Southern Europe and the Middle East,^{2,3} with a high mortality rate among infected infants. Similarly, a multiresistant strain of *S. typhimurium* phage type 208 has caused many severe infections throughout the Middle East.⁴

The emergence and establishment of the multiresistant type 204 and 193 strains in Britain have been facilitated by the use of antibacterial drugs in attempts to control bovine salmonellosis. More prudence in the use of antibiotics in veterinary practice is necessary to prevent the emergence of other, possibly more virulent strains of resistant salmonellae, which may present a serious threat to human health. Should the multiresistant *S. typhimurium* strains described in this paper cause extra-intestinal infections in humans, the clinician's choice of antimicrobial treatment would be extremely limited.

¹ Threlfall, E J, Ward, L R, and Rowe, B, *Veterinary Record*, 1978, in press.

² Le Minor, S, *Médecine et Maladies Infectieuses*, 1972, 2, 441.

³ McConnell, M M, Smith, H R, Leonardopoulos, J, and Anderson, E S, *Journal of Infectious Diseases*, 1978, in press.

⁴ Anderson, E S, et al, *Journal of Hygiene*, 1977, 79, 425.

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Thyroid crisis and tracheal compression in patient with retrosternal goitre

Thyroid crisis is now fortunately rare and usually seen as a complication of a stressful illness.¹ In cases of true retrosternal goitre, which represent only 1% of all goitres,² toxicity is uncommon and when present is normally mild. We describe here a patient with retrosternal goitre who had severe toxicity. The condition was difficult to manage because of inadequate initial treatment.

Case report

A 74-year-old woman was admitted complaining of palpitations, giddiness, and weight loss despite a good appetite. On examination the thyroid gland was enlarged and partially retrosternal. She had a fine tremor and pronounced lid lag. She was in mild congestive cardiac failure with a pulse rate maintained at 80 beats/min by beta-blockade.

Triiodothyronine (T₃) concentration was 7.3 nmol/l (4.8 ng/ml) (normal 1.2-3.0 nmol/l (0.78-2.0 ng/ml)); thyroxine (T₄) > 290 nmol/l (225 ng/ml) (normal 70-90 nmol/l (54-70 ng/ml)). Antibodies to thyroid microsomal antigen were present in high titre. Technetium scan showed an enlarged

Plasmid acquisition and phage type change.

thyroid with increased irregular uptake of 4.7% (normal 0.2-2%). Radiographs of the thoracic inlet showed considerable tracheal compression.

We decided to perform a subtotal thyroidectomy after rendering the patient euthyroid with carbimazole 20 mg three times daily. After 18 days T3 and T4 concentrations had fallen slightly (5.8 nmol/l (3.8 ng/ml) and 224 nmol/l (174 ng/ml), respectively); and at her insistence she went home on continued treatment.

One week later she was found unconscious at home and readmitted in grade 1 coma. She had discarded all tablets on leaving hospital. She was jaundiced, apyrexial, with a pulse rate of 160 beats/min and had signs of bronchopneumonia.

Investigations showed: T3 7.3 nmol/l (4.8 ng/ml), T4 >290 nmol/l (225 ng/ml), and a polymorphonuclear leucocytosis of $20.7 \times 10^9/l$. Blood gas tensions and serum and cerebrospinal fluid biochemical values were normal, except for raised alanine aminotransferase (183 U/l (normal <43 U/l)), bilirubin (73 μ mol/l (4.3 mg/100 ml) (normal <23 μ mol/l (1.3 mg/100 ml)), and γ -glutamyltransferase (54 U/l (normal <3.5 U/l)) concentrations and prothrombin time (15.12 s).

Progressive tracheal compression and displacement 10 days before thyroidectomy.

She was treated with practolol, potassium iodide 500 mg three times a day, carbimazole 30 mg three times a day, hydrocortisone 100 mg four times a day, antibiotics, and physiotherapy. While her conscious level improved her respiratory state deteriorated. She became increasingly dyspnoeic with stridor and could not expectorate or swallow her secretions due to a bulbar palsy. Emergency surgery was therefore undertaken. The goitre with its bilateral retrosternal extensions was mobilised with difficulty and a subtotal thyroidectomy performed. The thyroid was oedematous, engorged in a tight retrosternal compartment, and weighed 108 g. Histological examination showed the goitre to be multinodular with areas of hyperplasia and lymphocytic infiltration.

Her postoperative course was stormy, being complicated on the first day by a severe metabolic alkalosis: pH 7.65, PCO_2 5.2 kPa (39 mm Hg), PO_2 6.9 kPa (52 mm Hg), standardised bicarbonate 39 mmol(mEq)/l, base excess +18, plasma sodium 142 mmol(mEq)/l, plasma potassium 3.5 mmol(mEq)/l, urinary sodium 6 mmol/l, urinary potassium 8 mmol/l. She was treated with a glucose, insulin, and potassium infusion. On the second day she suffered a full-thickness, extensive anterior myocardial infarct, which was uncomplicated. Symptomless hypocalcaemia (calcium 1.76 mmol/l (7.0 mg/100 ml), albumin 29.5 g/l) developed on the fifth day and was treated with oral calcium supplements. She was discharged on the 20th day, and when reviewed as an outpatient at nine months had gained 12.7 kg, looked and felt well, and was taking no drugs.

Comment

We considered that this patient suffered from the "apathetic" thyroid crisis described by Montgomery and Welbourn³ and characterised by "profound prostration, weakness, clouding of consciousness, and eventually coma." As the condition often lacks the hyperreflexia and hyperactivity thought to be typical of thyroid crisis, it is often overlooked and carries a high mortality.

The hypocalcaemia in our patient was attributed to temporary

parathyroid ischaemia, as serum calcium concentrations returned to normal after two months without calcium supplement.

The association between jaundice and severe hyperthyroidism was noted by Newark *et al.*¹

The severe postoperative metabolic alkalosis was thought to be due to total body potassium depletion, which was partly explained by diuretic treatment, longstanding self purgation, and corticosteroid treatment.

Reeve⁵ emphasised the dangers of a longstanding retrosternal goitre accompanied by gradual reduction in the tracheal lumen presenting as an insidious respiratory insufficiency or as acute respiratory distress. To our knowledge there have been no recorded cases of tracheal compression complicating thyrotoxic crisis.

¹ Newark, S R, Himathongkam, T, and Shane, J M, *Journal of the American Medical Association*, 1974, **230**, 592.

² Ehrenhaft, J L, and Buchwalter, J A, *Archives of Surgery*, 1955, **71**, 347.

³ Montgomery, D A D, and Welbourn, R B, *Clinical Endocrinology for Surgeons*. London, Edward Arnold, 1963.

⁴ Eriksson, M, *et al*, *New England Journal of Medicine*, 1977, **296**, 263.

⁵ Reeve, T S, *et al*, *Surgery, Gynaecology and Obstetrics*, 1962, **115**, 223.

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Outpatient suite: a new design

A doctor's time at a clinic is often wasted because many procedures connected with consultations, including the patients' undressing and dressing, take place in one room. In 1970 a new articulation of rooms for dermatological use, designed to improve efficiency, was built at the Wrekin Hospital, Telford.

Design and use

The space (55 m²) is divided into four rooms and four changing cubicles (figure). The consulting room (14 m²) has a desk, chairs, washbasin, and cupboards with a worktop. It is smaller than the standard A-size room (16 m²) recommended by the DHSS in pamphlet HN(76)193 for dermatological clinics. On either side is an examination room (5.5 m²), each with two changing cubicles (2.5 m²). Each examination room has a couch, angle-poise lamp, chair, and trolley. Each cubicle contains a seat, mirror, hooks for clothes, and a dressing gown. The outer door leading into the waiting area can be locked from the inside. One examination room can be blacked-out for examinations under ultraviolet light. Next to the suite is the treatment room (20 m²).

One button in the consulting room operates a buzzer and light over the door into the waiting area to summon a patient. A clerk tells patients their place in the waiting order, and presents their notes in that order to the doctor. After telling his story the patient is taken to a changing cubicle. He locks the outer door, undresses to the required extent, and, when ready, presses a button which lights a panel. While the first patient is undressing the second is called into the consulting room for interview. He then goes to another of

Plan of dermatology outpatient consultation suite, Wrekin Hospital.