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An antibiotic policy for bacterial infections after thoracic and other injuries

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Atherton, S. T., Wright, D. M., White, D. J., and Jones, E. S. (1977). *Thorax*, **32**, 596–600. **An antibiotic policy for bacterial infections after thoracic and other injuries.** Twenty-four patients suffering from thoracic and other injuries were admitted to an intensive care unit over a three-year period. The first four patients died from infection by Gram-negative bacilli with associated features of bacterial toxaemia although it was anticipated that most, if not all, of the patients would have recovered with intensive care. Antibiotics had been started when a patient showed signs of bacterial toxaemia but were ineffective. Retrospective analysis showed that, in each patient, a rapid rise in rectal temperature, white cell count, and blood sugar preceded the clinical features of bacterial toxaemia by one or two days. These observations were incorporated into an antibiotic policy for patients with similar injuries.

The criteria for starting two or three wide spectrum antibiotics were as follows: (1) Gram-negative bacilli in the tracheal aspirate together with radiological evidence of consolidation or absorption collapse; (ii) two of the following three signs—a rectal temperature of 38·5°C or more, a white blood cell count of $11{\cdot}0\times10^9$/l or above, a blood glucose of 11·2 mmol/l or above; (iii) laparotomy. This policy was tested out over two years on 20 patients with thoracic and other injuries. Sixteen of the patients fulfilled the criteria for antibiotic therapy. Two of the six deaths were due to bacterial infection with toxaemia, a result which suggests that the policy was beneficial.

Bacterial infection or toxaemia is an important cause of death in patients with crushed chests or severe multiple injuries, especially when ventilator treatment is necessary. In such patients it is often difficult to decide when relatively harmless bacterial colonisation of the respiratory tract develops into infection or toxaemia. The death rate and morbidity from bacterial infection or toxaemia is high despite intensive therapy with antibiotics effective against the causative organisms. In the past, antibiotic policies for such patients have varied from unit to unit or from patient to patient in the same unit. Thus an antibiotic may be given to all such patients in the hope of preventing bacterial infection; alternatively, therapy is started only when pulmonary infection, bacteraemia or toxaemia are evident. We have carried out an uncontrolled trial of a new antibiotic policy which depends on giving broad spectrum antibiotics when certain criteria are fulfilled. The criteria are based on nonspecific clinical, laboratory, or radiological signs and are taken as evidence of bacterial infection or toxaemia; the observations can be made simply and quickly.

Methods

The patients were treated in a general intensive care unit established in 1964 (*Lancet*, 1964). When indicated, crushing injuries of the chest were treated by means of prolonged intermittent positive pressure ventilation (IPPV) through a tracheostomy; details were given in a previous paper (Ambiavagar *et al.*, 1966). Each patient was nursed in a single room and hospital infection was minimised by standard techniques.

Bacterial monitoring consisted of daily cultures from wounds, the urine, tracheal aspirate, nose, throat, and blood and then identifying all the

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bacteria isolated. The results were then charted. Bacterial colonisation of the eyes, wounds or the respiratory tract was diagnosed when potential pathogens were cultured from these sites without evidence of inflammation or toxaemia. Infection was inferred when there were signs of inflammation or systemic signs of toxaemia or bacteraemia. Bacterial pneumonia (consolidation) following thoracic or other injuries is difficult to recognise radiologically. We have used the criteria previously determined in this unit (Gett *et al.*, 1971). Consolidation is defined as 'opacities (homogeneous or irregular) in part or whole of a lung field with an air bronchogram'. Bacteraemic shock is a convenient label to describe a clinical syndrome which strongly suggests widespread organ damage due to bacterial toxins with or without bacteraemia (Levin, 1973). The clinical signs and abnormal test results are listed in Table 1.

Temperature was measured electrically with an electrode placed in the rectum and one strapped to the big toe. Haematological and biochemical measurements were made daily. Metabolic balance was maintained by the methods devised in this unit (Jones and Sechiari, 1963; Jones and Peaston, 1966). Acute renal failure was treated by means of frequent haemodialysis. Before July 1973 antibiotics were started only when there were signs of bacterial toxaemia and sometimes when the chest radiograph showed consolidation or collapse. After July 1973, a standard regimen of antibiotics was used according to the policy to be described. The concentration of gentamicin in the serum was measured by a plate diffusion technique, based on the method of Bennett *et al.* (1966).

PATIENTS

These were divided into two groups. The first group comprised all four patients with thoracic and other injuries admitted during a 10-month period (September 1972 to June 1973). All four had injuries requiring IPPV and all developed clinical features of bacterial toxaemia and died. Twenty patients were admitted over the next two years (July 1973 to September 1975) and 16 of these satisfied our criteria for treatment with antibiotics and formed the second group. Fourteen required IPPV and tracheostomy. The four patients who did not receive antibiotics all survived.

Results

FIRST GROUP

In each of the four patients, the respiratory tract was colonised by Gram-negative bacilli and, although repeated blood cultures were negative, features suggesting bacterial toxaemia appeared in all the patients. It was found that in each case a rapid rise in body temperature, white cell count or blood sugar preceded the clinical diagnosis of bacterial toxaemia by a period of at least 48 hours. The mean values for these parameters just before this rapid rise were—a rectal temperature of 38·5°C, a white cell count of $11{\cdot}0\times10^9$/l, and a blood sugar of 11·2 mmol/l. The number of observations were too few for statistical analysis, but it seemed possible that these values could be used to formulate an antibiotic policy for such patients.

Antibiotic policy

This was based partly on the signs described above and on additional criteria. They were: Gram-negative bacilli in stained films of the tracheal aspirate together with radiological evidence of consolidation or absorption collapse; laparotomy. The latter was included because of the high risk

Table 1 *Clinical signs and abnormal test results associated with severe toxaemic infection*

System	*Signs*	*Tests*
Cardiovascular	Warm hypotension	Increased cardiac output; reduced peripheral resistance; raised blood lactate
	Cold hypotension	Reduced cardiac output; increased peripheral resistance; raised blood lactate
Respiratory	Respiratory distress syndrome of adults	Hypoxaemia, hypocapnia, alkalosis; chest radiography normal or shows pulmonary infiltrates
	Respiratory failure	Hypoxaemia, hypercapnia, acidosis; apnoea; pulmonary oedema on radiograph
Blood	Bleeding	Hypofibrinogenaemia; thrombocytopenia; increased radiofibrinogen catabolism
Renal	Acute renal failure	Uraemia; increased plasma/urine osmolality
Hepatic	Jaundice	Hyperbilirubinaemia; raised SGOT and SGPT
Gastrointestinal	Haemorrhage	Hypotension; tachycardia; low central venous pressure
	Paralytic ileus	High gastric aspirate; absent bowel sounds; dilated bowel and fluid levels on abdominal radiograph
Central nervous	Drowsiness, lethargy, confusion, and coma	

of bacteraemia (*British Medical Journal*, 1975) or increased absorption of bacterial toxin from the intestine (Caridis *et al.*, 1972). The resulting list of indications was grouped under three headings as shown in Table 2; the policy was tested out on the second group of 16 patients.

Table 2 *Indications for starting antibiotics*

	I	Gram-negative bacilli in stained films of the tracheal aspirate together with radiological evidence of consolidation or absorption collapse
or	II	Two of the following:
		a Rectal temperature of 38·5°C or more
		b White blood cell count of $11{\cdot}0 \times 10^9$/l or above
		c Blood glucose level of 11·2 mmol/l (200 mg/100 ml) or above
or	III	Laparotomy

The antibiotics given were gentamicin and lincomycin (Table 3), each as bolus injections intravenously. They were chosen because in combination they have a wide range of activity against aerobic and anaerobic Gram-negative and Gram-positive bacteria. To combat primary infection due to fungi, or indeed infection secondary to the antibiotics, nystatin was routinely administered into the trachea and the stomach. When previous bacterial monitoring suggested the presence of *Ps. aeruginosa* carbenicillin was added. The dose of gentamicin was adjusted to give peak and trough levels of 5–15 μg/ml and 5 μg/ml respectively. The antibiotics were given for at least seven days and stopped according to one or more of the following criteria: weaning from the ventilator, return of the temperature and white cell count to normal, and a blood sugar in the range of 5·6–11·1 mmol/l without the need for insulin.

SECOND GROUP

Each of the 16 patients was colonised by one or more bacterial pathogens as shown in Table 4, which also lists the indications for starting the antibiotic regimen. Organisms were not cultured from the blood in any of the 16 patients. Ten of the patients recovered and six died. Two deaths were caused by brain damage from head injury, one from biliary peritonitis, and one by progressive pulmonary oedema (post-traumatic pulmonary insufficiency) due to fat embolism and saline excess. The remaining two deaths occurred in patients with clinical features of bacterial toxaemia. Patient 5 (Table 4) was given antibiotics after a laparotomy. Antibiotics were stopped on day 7 but on day 10 new indications appeared (I. IIa,b of Table 2). Antibiotics were restarted but clinical signs of toxaemia appeared on day 15 and the patient died the next day. The bacteria isolated were sensitive to the antibiotics given. In patient 8, clinical signs of toxaemia appeared on the second day and preceded by one day the indications (I, IIa of Table 2) selected for initiating antimicrobial therapy. Antibiotics were started on the third day but the patient died the following day. In both groups of patients, this was the only occasion on which the clinical features of toxaemia preceded those criteria chosen for starting antibiotic therapy.

Discussion

Our experience confirms the susceptibility of the injured patient to colonisation by bacterial pathogens and the high mortality when clinical features and tests suggest the onset of bacterial toxaemia (Walter, 1971; Caridis *et al.*, 1972). It is accepted that the criteria used to diagnose bacterial toxaemia may also be seen in patients with acute pancreatitis, severe ulcerative colitis or extensive burns, and that circulating endotoxins may or may not be the dominant causative factor. When a clinical diagnosis of bacterial toxaemia is made and bacterial monitoring indicates a Gram-negative infection, then antibiotics are frequently ineffective. In contrast, when infection is due to a Gram-positive organism antibiotics are much more effective although these organisms can also cause toxaemia (MacLean *et al.*, 1967). The dilemma which faces the clinician is when to start antibiotics in such patients. Although the antibiotic policy described has not been tested by a controlled trial, the results are very encouraging. The indications based on body temperature, white cell count, and

Table 3 *Antibiotic regimen used to treat the 16 patients in the second group*

Antibiotic	*Dosage*	*Administration*	
		Frequency	*Route*
Carbenicillin	5 g	6-hourly	Intravenous
Lincomycin	600 mg	6-hourly	Intravenous
Gentamicin	80–240 mg	8-hourly	Intravenous
Nystatin suspension	100 000 units	6-hourly	Intragastric and intratracheal (nebulised by ventilator)

Table 4 *Findings in the second group of patients*

Patient	*Age*	*Injuries sustained*	*Treatment*	*Bacterial pathogen*	*Isolated from*	*Outcome*	*Indications for antibiotics*[1]
1	17	Thoracic	IPPV	*Staph. aureus*	Tracheal aspirate	S	II a, b, c
2	20	Thoracic	IPPV	*Strep. faecalis*	Tracheal aspirate	S	II a, b, c
3	35	Thoracic, limb, and pelvic fractures; fat embolism	IPP breathing; heparin	*Klebsiella* spp	Sputum	S	II a, b
4	20	Torn liver and hepatic duct; limb fractures	IPPV; haemodialysis; laparotomy	*Proteus* spp, *Candida albicans*	Trachael aspirate	D, biliary peritonitis	II a, b
5	70	Thoracic; perforated duodenum	IPPV; closure of perforation	*Klebsiella* spp	Tracheal aspirate	D, bacterial toxaemia	III day 2 I, II a, b day 10
6	38	Thoracic; torn liver	IPPV; partial hepatectomy	*Staph. aureus*	Throat	S	III, II c
7	17	30% burns, soft tissue damage, limb fractures	IPPV; amputation of limb	*Ps. aeruginosa*	Tracheal aspirate, burns	S	I, II a
8	34	Head, thoracic, limb, and pelvic fractures	IPPV	*Ps. aeruginosa*	Tracheal aspirate	D, bacterial toxaemia	I, II a
9	23	Head; inhalation of vomit; limb fractures	IPPV	*Esch. coli*	Tracheal aspirate	S	I, II a
10	44	Head; inhalation of vomit; traumatic pancreatitis	IPPV; haemodialysis; laparotomy; aprotinin; glucagon	*Klebsiella* spp	Tracheal aspirate	D, brain damage	I, II a
11	21	Thoracic; torn spleen	IPPV; haemodialysis; splenectomy	*Klebsiella* spp, *Ps. aeruginosa*	Throat	D, post traumatic pulmonary insufficiency	III
12	22	Head, thoracic, and pelvic fractures	IPPV; peritoneal dialysis	*Ps. aeruginosa*	Tracheal aspirate	D, brain damage	II a, b, c
13	57	Thoracic	IPPV	*Esch. coli*, *Proteus* spp	Tracheal aspirate	S	I, II c
14	10	Head, thoracic, and limb fractures	IPPV	*Ps. aeruginosa*	Tracheal aspirate	S	II a, b
15	34	Soft tissue damage; pelvic crush injury	Haemodialysis; excision of necrotic tissue	*Cl. welchi*, *Bacteroides* spp, *Esch. coli*, *Candida albicans*	Wound Urine	S	III, II a
16	61	Thoracic; torn liver and spleen	IPPV; splenectomy; partial hepatectomy	*Ps. aeruginosa*	Tracheal aspirate	S	III

[1]See Table 2.
S = survived; D = died.

glucose intolerance are, of course, not specific to bacterial infection or toxaemia and can be due to either inflammation or the metabolic response to injury (Taylor, 1965; Walker and Johnston, 1971; Sevitt, 1974).

It would greatly help the clinician to have a laboratory test which would show when colonising bacteria become invasive. Two such tests have been studied, the nitrobluetetrazolium test (Freeman *et al.*, 1973) and the limulus lysate assay for endotoxin (Caridis *et al.*, 1972; Stumacher *et al.*, 1973; Wardle, 1975). Unfortunately, neither test has proved satisfactory in detecting infection in clinical practice (Levin, 1973; Ward, 1974; Elin *et al.*, 1975). We believe that the high death rate from bacterial toxaemia will be reduced only by adopting measures which are designed to prevent bacteria from colonising and subsequently infecting the patient. In the future it may be possible to maintain the immunity of the injured patient or to neutralise circulating endotoxin (Cuevas *et al.*, 1974; Wardle, 1975).

An alternative policy would be to give antibiotics routinely to all patients with severe injuries. Experience has shown that such prophylactic usage leads to harmful infection by resistant bacteria (Price and Sleigh, 1970). It is highly probable that the indiscriminate use of gentamicin or tobramycin would result in the emergence of resistant strains and reduce the available therapy for treating resulting infections. We believe that the most effective policy is to use antibiotics according to readily available criteria such as those described.

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