A THERAPEUTIC AUDIT AT AUTOPSY

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- 1 A survey of one hundred patients submitted to autopsy has been carried out to assess the contribution of investigational procedures, surgery and drug therapy to death.
- 2 In nineteen patients drug therapy, usually appropriate and necessary therapy, was thought to have contributed to death. In five patients failure to continue therapy properly contributed to death.
- 3 The survey was not representative either of patients dying in hospital or in the community, but it suggests that a larger and more comprehensive survey should be undertaken.

Introduction

There has in recent years been increasing concern about adverse reactions to drugs (Wade & Beeley, 1974). Some believe the hazards of drugs are underestimated and others that they are exaggerated to such an extent that patients are denied therapy which they need. There is wide acceptance, however, that the use of many valuable and effective drugs is inevitably accompanied by hazards. In this paper an attempt is made to place the contribution of drugs to the cause of death in context with the contribution of investigational procedures and other forms of therapy.

Methods

One hundred randomly selected autopsies performed at the Queen Elizabeth Hospital, Birmingham between January and October 1974 were attended. The history, clinical findings, treatment and pathology were discussed with the doctors responsible for the care of the patient and with the pathologists. The medical records of the patients were studied. Information not available from these sources, as for instance details of therapy given to the patient before admission to hospital, which had not been recorded at the time of admission, has not been used. Attempts to obtain such information showed that it was often incomplete or unreliable. For each patient an attempt was made to assess the contribution to the immediate cause of death of the investigation or treatment the patient had received, and whether this was a definite, probable or merely possible contribution.

Results

In the first ten months of 1974, 608 patients died in the Queen Elizabeth Hospital and 245 autopsies were performed. The number of patients submitted to autopsy varied greatly in different hospital units. Of the sixty-eight patients who died in wards responsible mainly for malignant disease, eleven (16%) came to autopsy, while of the eleven patients who died in the artificial kidney unit nine (82%) came to autopsy.

In forty-nine of the one hundred patients studied the investigational procedures, surgery or therapy were considered to have contributed to the cause of death, but this contribution was often small in relation to the part played by the serious diseases from which many patients suffered. The dominant factors, other than disease, contributing to deaths are listed in Table 1.

Investigational procedures

There were four patients in which investigational procedures were definitely the cause of death. In two diagnostic oesophagoscopy caused death, in one patient by causing massive haemorrhage from a carcinoma of the stomach and in another patient with a carcinoma of the bronchus by causing oesophageal perforation. Abdominal aortography precipitated a fatal myocardial infarct in one patient and a patient with severe malabsorption died from peritonitis after an exploratory laparotomy. There were two patients in which the investigational procedures probably contributed to death. One was a patient who had a delayed anaphylactic reaction to the contrast medium used

Table 1 Factors other than disease contributing to death: 100 autopsies

Investigational procedures	6
Pulmonary embolism	6
Surgery	15
Steroid or immunosuppressive therapy	10
Other drug therapy	6
Failure to continue therapy properly	5
None of the above factors	52

in intravenous pyelography, and another patient died of septicaemia following an exploratory laparotomy.

Pulmonary embolism

There were six patients who died of pulmonary embolism which followed deep venous thrombosis while they were immobile in bed. Three were patients confined to bed after a recent myocardial infarct, one patient was grossly overweight, one had recently had a cholecystectomy and one had extensive carcinomatosis.

Surgery

There were fifteen patients in which surgery was thought to have contributed to death. This was considered definite in five patients; one died of

haemorrhage after a transurethral resection of the prostate, one developed acute renal failure after an operation for a perforated peptic ulcer and three died as a direct result of surgery, done to by-pass an occluded coronary artery, to replace an aortic arch by a graft and to resect a ventricular aneurism.

Surgery was assessed as probably contributing to death in eight patients, three developing myocardial infarcts, one septicaemia and one pneumonia and empyema during or after surgery. One patient died of a haemorrhage from an anastomatic ulcer after a partial gastrectomy.

There were three patients all of whom had renal transplants in whom it was thought surgery had possibly contributed to death, two dying from cardiac arrest and one developing disseminated intravascular coagulation postoperatively.

Drug therapy

There were sixteen patients in whom drug therapy was thought to have contributed to death. There were eight patients in whom treatment with corticosteroids or immunosuppressive drugs was considered to be a probable cause of death and two others in which it was thought to be a possible cause. In one patient who had had a renal transplant, death was due to peptic ulceration and haematemesis but in the other nine patients death

Table 2 Deaths: Contribution of therapy

<i>Patient number</i>	<i>Age (years) and sex</i>	<i>Therapy</i>	<i>Comment</i>	<i>Probability</i>
47	35 F	Anticoagulants	Renal failure and hypertension. Recent cholecystectomy and pulmonary emboli. Intracerebral haemorrhage.	Probable
61	48 F	i.v. fluids	4 years malabsorption. Recent deterioration. Laparotomy followed by septicaemia and diarrhoea. Given 9.5 litres of i.v. fluid in 12 hours.	Probable
86	58 M	i.v. fluids	Henoch-Schönlein purpura. Admitted dehydrated and in renal failure. Given 8 litres of i.v. fluid in 10 hours.	Probable
23	78 F	Blood transfusion	Slow recovery from partial colectomy. 3 weeks post-op. given 3 pints blood. Abrupt deterioration.	Possible
55	60 M	Diamorphine	Total gastrectomy for cancer of stomach. Diamorphine (15 mg.) i.m. a few minutes before death.	Possible
78	52 F	Halothane	Firm diagnosis not possible, but operations with halothane anaesthesia in April 1974, June 1974 and August 1974. Died with jaundice.	Possible

was due to infection, which usually began quietly and insidiously so that its presence even though anticipated was not always suspected until it overwhelmed the patient.

There were six patients in which other drug therapy was thought to have contributed to death (Table 2). In one patient anticoagulant therapy caused an intracerebral haemorrhage. In two patients excessive intravenous fluid infusion was thought to have been a probable factor and in one deterioration followed a blood transfusion. Death followed a few minutes after an i.v. injection of diamorphine (15 mg) in a patient who had recently had a gastrectomy for a cancer of the stomach and in another patient halothane was considered as a possible cause of a fatal jaundice, although a firm diagnosis was not possible.

Three other patients who died of cerebral infarction are excluded from Table 2. There was a suspicion in all of them that the use of psychotropic drugs had by causing hypotension contributed to their death. The circumstances of their death suggested this but it would be wrong to attach too much importance to the observation at this time; it is felt that this problem deserves further investigation.

Failure to continue therapy appropriately

There were five patients in which failure to continue therapy appropriately contributed to their death (Table 3). One had received radioactive iodine for thyrotoxicosis from some other medical centre. She had failed to attend follow-up clinic for reasons unknown to us and she died shortly

after admission with florid myxoedema which must have been present for a considerable length of time. There was one patient who was given massive doses of frusemide for many weeks before she was admitted to die grossly dehydrated with a serum sodium of 99 mEq/litre. There were two hypertensive patients whose failure to take therapy contributed to their death. There was one young man with Addison's disease who became dissatisfied with treatment, abandoned it and died.

Discussion

This series of autopsies is not representative of all deaths which occur in hospital and is certainly not representative of deaths which occur in the community. In most patients in this survey the indications for investigation, operation or therapy were clear and the risks seemed reasonable in the context of the diseases from which the patients suffered. Moreover in many patients the surgery and drug therapy that were required were often complicated and recognized as being hazardous. Although assessment is difficult and subjective it seemed that most patients would have died sooner or suffered more if they had not received the treatment given.

The six deaths in which investigational procedures contributed to death are a reminder that the morbidity and mortality associated with such procedures does not receive the attention it deserves. Similarly, despite the teaching of Richard Asher (Asher, 1972) the hazards of bed rest are often underestimated. At least one of the deaths

Table 3 Deaths: Failure to continue therapy appropriately

<i>Patient number</i>	<i>Age (years) and sex</i>	<i>Comment</i>	<i>Probability</i>
41	62 F	Failed to attend follow-up clinic after radioactive iodine therapy for thyrotoxicosis. Died with florid myxoedema.	Definite
100	60 F	Long history of cardiac failure. Given massive doses of diuretics. No check on electrolytes. Admitted with serum sodium of 99 mEq/litre.	Definite
63	46 M	Malignant hypertension. Disliked side-effects of antihypertensive drugs and did not take them.	Probable
25	25 M	Addison's disease since childhood. Began to dislike therapy. Death in Addisonian crisis.	Probable
22	41 M	Alcoholic with malignant hypertension and renal failure. Probably seldom took tablets.	Possible

might have been avoided if the risk of immobilization in bed had been borne in mind.

The finding that surgery contributed to the death of fifteen patients is not surprising for, as is to be expected in a teaching hospital, many of the operations were major procedures of a type which would never have been attempted a few years ago and in which a high mortality is to be expected.

It is a reflection of our times that the number of deaths, twenty-one, to which drug therapy or failure to continue drug therapy properly was thought to have contributed, outnumbered those to which it was thought surgical treatment made a contribution. This was mainly due to the increasing aggressive use of immunosuppressive and cytotoxic drugs and corticosteroids to control malignant disease or inhibit immune reactions to transplants.

It was a surprise to find such a high proportion of deaths in which a failure to continue treatment or a failure of supervision of therapy was a cause. In these days of modern drugs which often require a complicated regimen of administration communication between the doctor and the patient and his family is becoming increasingly important, as is good communication between medical staff in the hospital service and their colleagues in general practice.

Several previous studies have been undertaken to ascertain the part played by adverse reactions to drugs. Lou, Campbell, Henderson, Napke & Mikael (1974) in a brief report from the Registry for Tissue Reactions to Drugs, Ottawa, found that adverse reactions to drugs contributed to the death of thirty-six of one hundred patients studied in

one hospital in Ontario. Gotti (1974) collected the reports of a large number of autopsies done at a number of different centres and noted that adverse reactions to drugs were of importance but not necessarily the cause of death in 8% of autopsies. Shapiro, Slone, Lewis & Jick (1971) in the comprehensive Boston Collaborative Study believed that 3.6% of deaths in 744 medical patients were caused by drug therapy.

Caranasos, Stewart & Cluff (1974) found that more than 6% of 177 patients admitted to medical wards with drug-induced disease died. In their study these patients constituted 2.9% of all admissions; they excluded patients who had attempted suicide by self-poisoning and patients with complications following the abuse of drugs.

The survey here reported confirms that the contribution of drugs to death from investigational procedures and death is not negligible. More complete reporting by clinicians and pathologists might lead to a more precise appreciation of the risks and lead to an improvement in patient care. There would seem to be a strong case for a further more comprehensive survey to be carried out with collaboration from a number of medical centres. Such a survey might be undertaken under the aegis of the Committee on Safety of Medicines.

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