

TABLE III—Average durations of stay of patients admitted with appendicitis to 22 major hospitals in Wales during 1976 and numbers of such patients*

Health district	Average stay in days in each hospital	No. of patients admitted
A	7.3	283
B	6.7	362
C	6.0	177
D	6.0	139
E	7.6	222
F	7.5	177
G	6.7	392
H	6.6	213
I	9.9	291
J	7.4	102
K	†	99
L	9.4	324
M	6.0	265
N	7.8	262
O	9.2	160
P	8.9	174
Q	8.1	306
	6.9	199
	†	†
	7.4	329
	8.1	207
	8.5	91
	9.3	211
Total	7.6	4985

*Ninety-six percent of patients admitted to hospitals in Wales were admitted to these 22 major hospitals.

†Districts I and O contained no major hospitals.

health district in south Wales with another in north Wales. Furthermore, the large variation in admission rates analysed by day of the week implies that, although appendicitis is generally considered to be an emergency necessitating immediate admission, there is some freedom of choice regarding the day of admission. The differences between admission rates on weekdays and at weekends are more likely to be causally associated with the availability of general practitioners and ease of access to hospital than with daily differences in the onset of pain. In addition, the negative association between age-standardised admission rates

and the average durations of stay may be viewed as an indication of the limited physical resources in hospitals—namely, beds, theatres, and surgical and nursing staff—per caput of population. In districts in which many patients consult for appendicitis or where general practitioners refer many patients with appendicitis the hospitals are likely to discharge inpatients earlier in order to clear beds for further referrals. On the other hand, in districts served by hospitals in which the duration of stay is longer the non-availability of beds may produce a “waiting-list effect” and hence may reduce the rate of referral to hospital.

We therefore suggest that much of the variation between districts in hospital admission rates may be explained not by a difference in incidence caused by genetic⁵ or dietary² factors but by differences in hospital admission policies. The other variation observed—that in hospital admissions analysed by day of week—and the negative association between admission rates and duration of stay also provide supportive evidence that the admission to hospital of patients with appendicitis is not entirely governed by the sudden onset of abdominal pain: other contributing factors include the threshold of consultation of each patient, the referral habits of his general practitioner, the availability of hospital beds, and the general expectation of the community based on these factors and on the past admission rates of local hospitals.

This paper is based on a community medicine project by MJC.

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Factors influencing postoperative morbidity and mortality in patients treated with bleomycin*

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Summary and conclusions

Patients treated with bleomycin are at risk of developing the acute adult respiratory distress syndrome postoperatively. In a prospective study of 12 patients who had received bleomycin preoperatively and were under-

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going removal of retroperitoneal lymph nodes or pulmonary metastases several preventive factors were established. These were the use of low concentrations of inspired oxygen during operation and in the immediate postoperative period, careful monitoring of fluid replacement, and restriction of crystalloids in favour of colloids.

Introduction

Bleomycin, an antibiotic synthesised from *Streptomyces verticillus*, is highly effective against many malignant diseases, including dysgenetic neoplasm of the testes.¹⁻³ Among its side effects, however, the most important is interstitial pneumonia occurring during administration of the drug, followed by chronic fibrotic changes in the lung.⁴⁻¹⁰

Bleomycin is extensively used at this centre for metastatic embryonal-cell carcinoma or teratoma of the testicle. Until 1974 the protocol was orchietomy followed by chemotherapy with vinblastine and cyclophosphamide, retroperitoneal node dis-

section, and eventually treatment of the metastases with bleomycin. Current practice is to remove the diseased testicle, administer 200-400 mg bleomycin/m², and six to 12 months later remove the retroperitoneal lymph nodes or pulmonary metastases surgically. With this protocol the lymph nodes show no metastatic disease on removal but are fibrotic and sclerotic. They are large, however, and the operation is usually long and difficult, often including resection of the large bowel, inferior vena cava, and abdominal aorta and removal of one kidney. Blood loss is often 10-15 units or more, and the overall duration of the operation is about six to eight hours.

The first five patients who received bleomycin according to the new protocol developed severe respiratory distress three to five days after removal of the retroperitoneal lymph nodes or pulmonary metastases. Despite mechanical ventilatory support, positive end-expiratory pressure, and, in one case, eight days of extracorporeal membrane oxygenation all five patients died from inexorably progressing interstitial pneumonia. Necropsy in each case disclosed increased lung size and weight and abnormal amounts of interstitial fluid. Microscopical and ultra-microscopical examination of the lung showed interstitial fibrosis, destruction of types I and II pneumocytes, and alveolar wall and capillary damage, all consistent with the general diagnosis of adult respiratory distress syndrome. Cultures for bacterial and viral pathogens were sterile in vivo and at necropsy.

We thought that two factors might have been related to the high postoperative mortality rate in bleomycin-treated patients. One was a disproportion of crystalloid to colloid replacement, with resultant pulmonary interstitial oedema. The other was the concentration of inspired oxygen, as pulmonary lesions similar to those found at necropsy have been reported in patients with "oxygen toxicity." To test the validity of these assumptions fluid replacement was carefully monitored and relatively low fractional concentrations of inspired oxygen (F_IO₂) were used in the operative and postoperative periods in a series of patients who had previously received bleomycin treatment. The results are presented here.

Methods

We chose 12 patients for the prospective study who matched closely the five patients who had died. Matching was for age, bleomycin dosage, incidence of pulmonary problems while taking bleomycin, residual pulmonary function at surgery, preoperative

blood gas tensions and duration and extent of surgical procedures (see tables I and II). None of the 17 patients had at any time received chemotherapeutic agents besides bleomycin, or pulmonary irradiation.^{8,9} No patient had a history of pulmonary disease before the administration of bleomycin. In all patients, both survivors and non-survivors, anaesthesia was induced with thiopentone and maintained with nitrous oxide and oxygen, a narcotic, and a muscle relaxant. Ventilation was controlled with a volume-cycled ventilator (model 300/DO; Ohio Surgical Equipment, Wisconsin, USA), with tidal volume and rate adjusted to maintain the P_aCO₂ at 4.7-5.3 kPa (35-40 mm Hg).

In the 12 patients studied prospectively the F_IO₂ concentration was maintained at 0.22-0.25 throughout surgery, often being controlled with an oxygen analyser (model 200 oxygen monitor; Ohio Medical Products, Wisconsin). Blood gas tensions were determined several times during the operation. A Swan-Ganz catheter was inserted immediately before operation, permitting measurement of pulmonary artery and capillary wedge pressures and cardiac output. Crystalloids were administered at 3-4 ml/kg/h. The volume of colloids (5% purified protein fraction or fresh frozen plasma) and whole-blood replacement was based on the cardiac output, pulmonary capillary wedge pressure, and hourly urinary output. Volumetric and gravimetric methods were used to measure blood loss. After operation the patients were returned to the special care unit, where they were maintained on room air or a F_IO₂ concentration of 0.24 regulated by Ventimask. The variables measured in the groups of survivors and non-survivors were compared by Student's *t* test for paired data.

Results

The 12 patients studied had an uneventful postoperative course. They were discharged from the special care unit within 48 hours and left the hospital 12-25 days after operation. In contrast, the initial five patients had entered the special care unit three to five days after operation owing to pulmonary complications and died despite treatment.

Although survivors and non-survivors were closely matched for preoperative variables (table I), three differences existed post-operatively (table II). The first was the inspired oxygen concentration administered during the operation and in the immediate postoperative period. The mean F_IO₂ concentration was 0.24 in the survivors compared with 0.39 in the non-survivors (*P* < 0.001). Secondly, the survivors received a mean of 3.87 ml crystalloids/kg/h intraoperatively and the non-survivors 5.86 ml/kg/h (*P* < 0.05). The survivors received more colloids than the non-survivors, although the difference was not significant. Hourly fluid balance (crystalloid intake minus urinary output) was 303 ml/h in the non-survivors and 126 ml/h in the survivors (*P* < 0.05). Thirdly, the mean preoperative alveolar-arterial oxygen pressure difference (P_A-a_O₂) was higher than the normal

TABLE I—Preoperative details of survivors and non-survivors

Case No	Age in years	Bleomycin dosage (mg)	Interval between bleomycin treatment and surgery (months)	Interstitial pneumonia during bleomycin treatment	Preoperative vital capacity (% predicted)	Preoperative carbon monoxide diffusion (% predicted)
<i>Survivors</i>						
1	15	480	8	Yes	74	60
2	29	340	10	No	92	58
3	19	699	6	No	72	48
4	27	1108	7	No	96	55
5	21	765	11	Yes	88	98
6	30	532	11	No	61	62
7	32	779	9	No	94	67
8	18	579	8	No	80	81
9	32	301	12	No	96	60
10	34	575	10	Yes	80	68
11	15	616	8	No	98	75
12	54	421	10	No	65	58
Mean ± SE of mean	27.6 ± 3.65	599 ± 64	9.2 ± 0.5		83 ± 3.7	61.7 ± 2.8
<i>Non-survivors</i>						
13	31	420	7	No	60	55
14	25	560	12	No	94	61
15	27	135	10	Yes	91	50
16	21	595	9	No	67	68
17	54	420	10	No	90	60
Mean ± SE of mean	31.6 ± 5.83	426 ± 181	9.6 ± 0.8		80.5 ± 7.0	58.8 ± 3
P	NS	NS	NS		NS	NS

TABLE II—Operative and postoperative data on survivors and non-survivors

Case No	Operation	Duration of operation (h)	Intraoperative fluid (ml/kg/h)		Excess crystalloids (ml/h)*	Intraoperative F ₁ O ₂	PA-aO ₂ (kPa)	
			Crystalloids	Colloids			Preoperatively†	Postoperatively‡
<i>Survivors</i>								
1	RND	7.1	3.9	4.2	26	0.24	5.8	6.9
2	PM	2.0	4.2	4.0	82	0.25	3.8	4.7
3	RND	6.0	4.9	4.7	86	0.24	4.1	7.0
4	RND	5.9	4.2	1.7	301	0.24	4.6	3.6
5	RND	8.4	4.0	2.2	248	0.26	4.8	8.4
6	RND	6.5	3.9	5.3	64	0.25	4.9	6.3
7	PM	2.8	3.4	3.2	307	0.25	4.0	6.8
8	RND	5.8	3.7	2.1	56	0.24	2.5	1.3
9	RND	6.0	3.2	1.8	23	0.25	2.9	7.2
10	RND	6.3	3.8	2.1	20	0.24	4.6	2.3
11	RND	7.1	3.1	3.2	36	0.22	4.8	3.1
12	RND	5.8	4.2	3.1	268	0.22	2.6	3.2
Mean ± SE of mean		5.74 ± 0.55	3.87 ± 0.14	3.21 ± 0.38	126 ± 34	0.24 ± 0.003	4.1 ± 0.3	5.0 ± 0.7
<i>Non-survivors</i>								
13	PM	2.1	4.4	1.4	317	0.40	5.8	15.0
14	RND	7.3	8.0	3.2	440	0.35	2.2	8.9
15	RND	6.8	4.0	0	171	0.40	5.5	14.0
16	RND	6.0	6.5	1.9	245	0.40	3.8	17.4
17	RND	7.1	6.4	5.4	327	0.42	6.2	22.7
Mean ± SE of mean		5.86 ± 0.96	5.86 ± 0.74	2.38 ± 0.91	303 ± 37	0.39 ± 0.01	4.7 ± 0.7	15.6 ± 2.2
P		NS	0.05	NS	0.05	0.001	NS	0.005

RND = Retroperitoneal node dissection. PM = Removal of pulmonary metastases.

*Crystalloid intake minus urinary output. †Measured on room air. ‡Cases 1-12 measured on F₁O₂ concentration of 0.21-0.24; cases 13-17 measured on F₁O₂ concentration of 0.3.

Conversion: SI to traditional units—PA-aO₂: 1 kPa ≈ 7.5 mm Hg.

range of 0.7-1.3 kPa (5-10 mm Hg) in both survivors and non-survivors (4.1 and 4.7 kPa (30.9 and 35.4 mm Hg) respectively), but the difference between the groups was not significant. After operation, however, PA-aO₂ was unchanged in the survivors (5 kPa (37.9 mm Hg)) while greatly increased in the non-survivors (15.6 kPa (117.2 mm Hg); $P < 0.005$).

Statistical analysis by Pearson's product moment formula showed that the postoperative F₁O₂ concentration correlated linearly with the intraoperative concentration ($P < 0.001$) but not with the volume of crystalloids administered.

Discussion

At this centre during 1970-4, 100 patients with a mean age of $26.4 \pm \text{SE}$ of mean 1.13 years underwent retroperitoneal node dissection or multiple wedge resection of the lung for dysgenetic neoplasm of the testes. None had received bleomycin before operation. Inspired oxygen concentrations during operation and in the postoperative period ranged from 0.35 to 0.40. Postmortem examination of seven patients who died within 30 days of operation disclosed no evidence of pulmonary lesions compatible with the adult respiratory distress syndrome. The first five patients with similar disease who six to 12 months before operation had received bleomycin treatment according to the new protocol described died within 12 days after surgery in respiratory failure. At necropsy gross and microscopic findings of the lungs in these patients were characteristic of those attributed to the adult respiratory distress syndrome. It was suggested that the bleomycin treatment itself or in conjunction with other factors had resulted in this postoperative respiratory complication. Pulmonary lesions associated with bleomycin treatment and their relation to age, dose, and irradiation have been described.⁴⁻¹⁰ The changes include intra-alveolar exudate, hyaline membranes, interstitial fibrosis, squamous metaplasia of type I and later type II pneumocytes, and increased interstitial fluid in the alveolar-capillary space.

Although only six of the entire group of 17 patients studied (survivors and non-survivors) had developed moderate to moderately severe respiratory distress during bleomycin treatment, all had some restrictive disease and impaired carbon monoxide diffusion capacity (table I). The preoperative PA-aO₂ was also greater than normal (table II). Probably, therefore, residual pulmonary effects from bleomycin were present despite the

absence of clinical and radiological evidence preoperatively.

The pulmonary lesions of oxygen toxicity described by Winter and Smith¹¹ were strikingly similar to those resulting from treatment with bleomycin. Although the inspired oxygen concentration in the non-survivors was lower than that usually associated with oxygen toxicity, possibly even these concentrations over a long period have a synergistic, detrimental effect in the presence of pulmonary tissue injured by bleomycin. On this basis the F₁O₂ was reduced to a concentration similar to or slightly above that of room air during the operation and postoperative period.

The preoperative PA-aO₂ in all 17 patients was measured on a F₁O₂ concentration of 0.21. The postoperative PA-aO₂ was determined in the survivors on a F₁O₂ concentration of 0.21-0.24 and in the non-survivors on a concentration of 0.30. Pontoppidan *et al*¹² showed that the PA-aO₂ is modified by the inspired oxygen concentration. In our series the maximum difference between the preoperative and postoperative F₁O₂ concentrations was 0.09. This small change could not account for the large increase in postoperative PA-aO₂ in the patients who died, which was seen in the immediate postoperative period, when the patients had no signs or symptoms of respiratory distress. Although too few patients were studied for definitive conclusions to be reached, the clinical evidence and statistical correlation of the F₁O₂ concentration, PA-aO₂, and survival rate suggest that oxygen administration may play a part in the postoperative upset and death of patients who have received bleomycin treatment a few months before operation. After this initial study was carried out the same relatively low oxygen concentration was used for 85 patients previously treated with bleomycin with no pulmonary complications or deaths.

If oxygen is a factor in the postoperative mortality of these patients its mode of action is unknown. The F₁O₂ concentration used during surgery and in the immediate postoperative period in the non-survivors never exceeded 0.45. There is no evidence that this concentration of oxygen exerts toxic effects, even when used for several weeks.¹¹ We therefore assume that previous bleomycin treatment somehow sensitises the lung to concentrations of oxygen that do not usually produce detrimental lesions.

In addition to being given a lower F₁O₂ concentration the survivors received less crystalloid and more colloid than the

non-survivors, in accordance with the routine advocated by Skillman.¹³ Fluid administration was also carefully monitored with a Swan-Ganz catheter. These factors could account for some difference in pulmonary interstitial fluid between the two groups. The mean volume of crystalloid given to non-survivors, however, was not excessive (less than 6 ml/kg/h). There was also no correlation between the postoperative PA-aO₂, total and hourly fluid gain, or amount of colloid infused.

From this preliminary study we conclude that patients who have previously received bleomycin treatment have a greatly increased risk of developing postoperative pulmonary complications. A factor that appears to lessen this risk is a reduction in the oxygen concentration administered during operation and in the immediate postoperative period. Careful monitoring of fluid replacement, with emphasis on colloids rather than crystalloids, may play an accessory part in decreasing or preventing pulmonary interstitial oedema.

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SHORT REPORTS

Detecting deficient energy and protein intake in hospital patients: a simple record method

Up to half of surgical patients suffer from protein-energy malnutrition.^{1,2} A Danish study³ showed that 85% of all elderly patients in an orthopaedic surgical ward were undernourished during the entire hospital stay. These abnormalities are often unrecognised.² Therefore a simple, inexpensive method for detecting patients who eat poorly is desirable.

Patients, methods, and results

A dietary survey was carried out on 46 consecutive patients aged over 60 admitted to an orthopaedic surgical ward. Two methods were used—(1) the precise weighing method,⁴ and (2) a simple record method. A full-time dietitian was responsible for the first method, in which the intake of nutrients was calculated by a computer program based on Danish food-composition tables.⁵ In the second method each patient was given a food-intake record sheet in the morning. The patient, his relatives, and the nursing staff (but not the dietitian) noted all foods and drinks taken during the day on the sheet—for example, $\frac{1}{2}$ hamburger, 2 potatoes, and $\frac{1}{4}$ helping of sauce; 1 slice of rye bread with cheese; 1 cup of coffee with milk; $\frac{1}{2}$ bar of chocolate; etc. Next morning the completed record sheet was sent to the kitchen, where the energy and protein intake was calculated from food-composition tables. The result was noted on the sheet and returned to the ward together with the supper.

A total of 603 one-day food-intake records were completed. Three-day records were determined as the average of three consecutive days. Nine months after the end of the test period the record sheets for the second month were also calculated by the dietitian, who did not know the results for the earlier calculations. The accuracy of the simple record method was determined by comparing the results with those of the precise weighing method. The percentile probabilities were calculated by a purely empirical method. All the results are shown in the table.

Comment

The accuracy of one-day records was not quite satisfactory, mainly owing to a tendency to underestimate the high energy intakes. The purpose of using the simple record method in a hospital ward, however, should be to find the patients whose food intake is insufficient. The three-day records gave a correct measure of the energy and protein intake in 85-90% of patients. This degree of accuracy is satisfactory for clinical use. It can scarcely be expected that patients or staff in a busy surgical ward can record the food intake more precisely. The calculations in the kitchen from the food-composition tables were made at brief intervals by different members of the staff who never came to the ward. The results could be better if the calculations were made by a dietitian who knew the ward and had a better chance of concentrating on the work. Both in the kitchen and in the ward the routine use of the simple record method increased the interest in and the attention paid to the importance of the patient's proper food intake.

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Probability of correct measurements of the energy and protein intake within the margin of ± 200 kcal and ± 10 g and of misleadingly high and low values (divergence more than 400 kcal or 20 g protein) obtained by the simple record method. The correlation coefficients are given in parentheses

Assessed by	No of records	Correct assessment (%)	Misleading assessment		No of records	Correct assessment (%)	Misleading assessment		
			High (%)	Low (%)			High (%)	Low (%)	
Energy									
One-day records	K D	603 238	57 (0.86)	3	12	399	69 (0.76)	3	2
			64 (0.91)	2	6		166	72 (0.78)	2
Three-day records	K D	311 124	66 (0.92)	1	8	208	85 (0.77)	0	0
			77 (0.93)	0	1		92	85 (0.82)	0
Protein									
One-day records	K D	601 235	64 (0.79)	3	10	421	76 (0.86)	4	2
			67 (0.88)	3	0		172	69 (0.93)	4
Three-day records	K D	307 119	72 (0.86)	0	1	213	87 (0.82)	0	0
			90 (0.93)	1	0		90	90 (0.86)	1

K = kitchen staff. D = dietitian.
1000 kcal \approx 4.2 MJ.