

outpatient clinic did not elicit a true picture of morbidity. The possibility that the doctor and being in a clinic inhibit a patient's inclination to report side effects led us to produce a questionnaire and to arrange for a sympathetic, non-medical member of the team to distribute and explain it. The women were asked to complete the form at home in the hope that they would then express their reactions to the treatment more accurately.

We recommend that this method is a more appropriate one of assessing side effects, and similar experiences were reported by H Bush at a symposium of the Royal College of Physicians, London, in May 1980. If such questionnaires were more widely used the toxicity of various chemotherapy regimens could be compared more objectively.

Troublesome side effects were much more common and severe in those women receiving the five-drug regimen, and the therapeutic case for using such a combination has to be a strong one. Side effects were also seen in an appreciable number of patients receiving single-agent chemotherapy, and claims that single-agent chemotherapy (using chlorambucil in this dosage) should be used as an adjuvant because it is "non-toxic" should therefore be regarded with caution.

The proportion of patients who had experienced severe side effects in the trial was considerable; hence such treatment is justifiable only if it will result in a substantial increase in prognosis. A major ambition of doctors should be to improve the wellbeing of patients. Any treatment which causes distress or illness should be given only when there is good evidence of

future benefit. The results of this survey contributed to our decision to stop this study of adjuvant chemotherapy.

We are grateful to Miss Rosemary Fisher for her valuable advice in designing the questionnaire and thank the patients for their help and interest.

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Prophylaxis of infection after appendicectomy: a survey of current surgical practice

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Summary and conclusions

Two hundred and eighty questionnaires were sent to junior surgical staff throughout England inquiring about their use of systemic antibiotic prophylaxis, topical antibacterial agents, and surgical drainage in appendicectomy. One hundred and seventy-five (63%) replies were received from 81 of the 87 hospitals included in the survey. Prophylactic systemic antibiotics were used by 78 surgeons (46%) when operating on a normal appendix but by 168 (99%) when the organ had perforated. Most surgeons started antibiotics before operation, but proportionately fewer did so when the appendix was gangrenous or perforated. Patients with severe contamination tended to receive longer courses of antibiotics, although the duration of administration varied considerably. Metronidazole was included in over 95% of all the prophylactic regimens and was often combined with other drugs when the appendix was gangrenous and perforated. Topical antibacterial agents were applied to the wound routinely by only 45 surgeons (26%), although 106

(61%) used them sometimes. Povidine-iodone was the agent most commonly used. Only 98 surgeons (56%) ever drained appendicectomy wounds, while 135 (77%) sometimes drained the peritoneal cavity.

Evidence suggests that present methods of giving systemic antibiotic prophylaxis should continue, but that topical agents and surgical drainage are perhaps unnecessary when surgeons are confident of the efficacy of the systemic treatment used.

Introduction

Over the past 20 years many reports have assessed different methods of reducing infection after appendicectomy. The techniques examined have included surgical drainage, the application of topical agents to the wound, and the administration of prophylactic systemic antibiotics. Although the general principle of systemic prophylaxis is now well established, opinion seems to vary widely regarding which patients require antibiotics, the optimum time to start the drugs, and the duration of administration. Furthermore, topical agents are still commonly used, although whether they confer much benefit compared with systemic drugs is not entirely clear.

The impact on everyday surgical practice of results of studies on antibiotics in appendicectomy has not been assessed. I therefore sent 280 questionnaires to junior surgical staff asking for details of the prophylactic measures used in their unit to prevent infection after appendicectomy.

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Methods

The questionnaires were addressed to the registrar or senior house officer of 280 consultant general surgeons throughout England. These are the members of a surgical team who usually perform appendicectomies and supervise prescription of any prophylactic antibiotics. To minimise any bias due to common local policies 20 questionnaires were sent to each of the 14 health regions in England. No hospital was

TABLE I—Use of prophylactic systemic antibiotics in appendicectomy

State of appendix	No (%) using antibiotic	No (%) not using antibiotic
Normal	78 (46)	92 (54)
Inflamed	97 (57)	73 (43)
Gangrenous	147 (86)	23 (14)
Perforated	168 (99)	2 (1)

TABLE II—Time of starting antibiotics

State of appendix	No (%) starting antibiotics:		
	Before operation	At operation	After operation
Normal	73 (93)	3 (4)	2 (3)
Inflamed	83 (86)	9 (9)	5 (5)
Gangrenous	97 (66)	41 (28)	9 (6)
Perforated	107 (64)	52 (31)	9 (5)

TABLE III—Duration of administration of systemic antibiotic prophylaxis. (Figures are numbers (%) of responders)

State of appendix	No of doses				No of days					Not stated	Total
	1	2	3	4	2	3	4	5	≥7		
Normal	47 (60)	3 (4)	7 (9)	1 (1)	9 (12)	6 (8)		3 (4)		2 (3)	78 (100)
Inflamed	33 (34)	2 (2)	13 (13)	2 (2)	15 (15)	13 (13)	1 (1)	14 (15)	3 (3)	1 (1)	97 (100)
Gangrenous	15 (10)	5 (3)	15 (10)	5 (3)	18 (12)	18 (12)	2 (1)	47 (32)	16 (11)	6 (4)	147 (100)
Perforated	4 (2)	2 (1)	8 (5)	13 (8)	17 (10)	23 (14)	4 (2)	68 (41)	25 (15)	4 (2)	168 (100)

TABLE IV—Types of antibiotics used in systemic prophylaxis. (Figures are numbers (%) of responders)

	State of appendix			
	Normal	Inflamed	Gangrenous	Perforated
Metronidazole alone	73 (94)	84 (87)	65 (44)	31 (18)
Metronidazole + ampicillin		4 (4)	28 (19)	39 (23)
Metronidazole + cephalosporin	3 (4)	5 (5)	32 (22)	52 (31)
Metronidazole + gentamicin			11 (7)	30 (18)
Metronidazole + others	61	5 (3)		12 (7)
Cephalosporin alone	2 (3)	2 (2)	2 (1)	
Gentamicin alone		1 (1)	1 (1)	
Ampicillin alone			2 (1)	1
Penicillin + streptomycin		1 (1)	1 (1)	1
Ampicillin + gentamicin				1
Ampicillin + cephalosporin				1
Total	78 (100)	97 (100)	147 (100)	168 (100)

sent more than four questionnaires, regardless of the number of surgeons listed on its staff. Thus six or seven hospitals in each health region received questionnaires. Because a registrar or senior house officer may work for more than one consultant recipients were asked to return any unused questionnaires. Subsequent telephone contact, however, indicated that this had not always been done.

Four questions were posed. (1) Do you ever use prophylactic systemic antibiotics in appendicectomy? (2) What drugs/dose/route do you use in patients with a normal/inflamed/gangrenous/perforated appendix? (a) before operation? (b) at operation? (c) after operation? (3) Do you use a topical wound antiseptic or antibiotic, and if so what and when (always/sometimes/never)? (4) Do you ever (a) leave the wound open? (b) drain the peritoneum? (c) drain the wound?

Results

Of the 280 questionnaires sent, 175 (63%) were returned. The geographical distribution of surgeons who did not return their

questionnaire was fairly uniform, and at least one reply was received from 81 of the 87 hospitals in the survey.

Prophylactic systemic antibiotics—Five of the 175 responders stated that they were participating in trials of prophylactic antibiotics but gave no further details. They were therefore excluded from the results, leaving 170 questionnaires for analysis. The state of the appendix was graded as normal, inflamed, gangrenous, or perforated. Table I shows the numbers of surgeons using antibiotics in each state. Table II shows the times of starting systemic antibiotic prophylaxis. Preoperative antibiotics were supplemented by additional drugs at or after operation for a gangrenous appendix by 29 surgeons (17%), and for a perforated appendix by 55 (32%). Table III shows the number of doses or duration of antibiotic treatment. When a varying duration was specified (for example, three to five days) the shorter period is quoted. Table IV summarises the many different antibiotic regimens that were used. Metronidazole was included in 97%.

Topical agents—Of the 175 questionnaires analysed, two did not include a reply to this section. One hundred and six surgeons (61%) sometimes used a topical agent, but only 45 (26%) did so routinely. Altogether 118 preferences were stated, as some surgeons specified alternatives: povidone-iodine was used by 74 (63%); polyantibiotic spray by 19 (16%); ampicillin powder by seven (6%); noxythiolin by five (4%); hydrogen peroxide, chlorinated lime (Eusol), Milton antiseptic, and malic acid mixture each by two (7%); and cephalosin, cephradine, chloramphenicol, chlorhexidine plus cetrimide, and water each by one (4%).

Wound drainage—Questions on wound drainage were designed to ascertain whether any of the techniques were completely unacceptable to the surgeon. Table V presents the replies.

Discussion

PROPHYLACTIC SYSTEMIC ANTIBIOTICS

This survey confirms that systemic antibiotic prophylaxis is now common practice. Although the regimens used vary appreciably, considerable areas of agreement are apparent.

The surgeons who gave antibiotics when removing a normal

TABLE V—Use of surgical drainage in appendicectomy. (Figures are numbers (%) of responders)

	Wound left open	Peritoneum drained	Wound drained
Sometimes	57 (33)	135 (77)	98 (56)
Never	116 (66)	38 (22)	75 (43)
Not stated	2 (1)	2 (1)	2 (1)
Total	175 (100)	175 (100)	175 (100)

appendix almost always did so (93%) before the operation and were generally those who gave such prophylaxis to all patients undergoing appendectomy. The number who claimed to administer preoperative prophylaxis increased with the severity of appendicular inflammation (although how some differentiated between a normal and an inflamed appendix before operation was not clear). The number who started antibiotics at the time of operation also rose with the severity of inflammation, although many surgeons maintain that these drugs are not then prophylactic. Since contamination of the abdominal wound occurs at operation, however, such drugs must be prophylactic against postoperative wound infection. Studies^{1 2} have shown clearly that the efficacy of systemic antibiotics was greatest if they were in the circulation when the bacteria lodged in the tissues and decreased progressively until they became of no real value when started three hours thereafter. Although these studies indicated that antibiotics are most effective when given preoperatively, they also showed that little is lost by starting them within about one hour after bacterial lodgement. Those who started giving antibiotics postoperatively (3-6%) still offered their patients some benefit if the drugs were started within three hours.

Quite apart from raising the apparent paradox between diagnostic acumen and indications for operation, the group that gave preoperative antibiotics only when the appendix was diseased prompts the important question of the value of prophylactic antibiotics when a normal appendix is removed. Ninety-two surgeons (54%) stated that they did not use antibiotics in such cases. Several studies,³⁻⁵ however, clearly document infective complications after normal appendectomy, and these include not only wound infections but also occasionally pelvic abscesses. The incidence of such infections is appreciably reduced by prophylactic antibiotics, which would seem to justify protecting this group of patients.

The large proportion of surgeons (43%) who did not use antibiotics routinely when the appendix was inflamed is surprising. Even when the appendix was gangrenous 14% still withheld systemic prophylaxis, but when it was perforated only 1% considered antibiotics to be unnecessary.

The choice of antibiotics was fairly unanimous. Metronidazole featured in over 95% of all regimens and was often combined with other drugs when the appendix was gangrenous or perforated. This accords with the findings of clinical studies in appendectomy. The choice of antibiotics was radically influenced when anaerobic organisms were recognised as the pathogens causing infections after appendectomy. Their role was first suggested by Veillon and Zuber in 1898,⁶ and in 1974 Leigh⁷ showed bacteroides to outnumber all other bacteria grown from appendix fossa swabs. This may explain the relative lack of success of some antibiotics.^{8 9} To attack the anaerobic bacteria specifically Leigh *et al*¹⁰ used lincomycin in appendectomy and reduced the incidence of infection with a single preoperative dose. Evidence also suggests that clindamycin is beneficial.⁹ These two antibiotics were not used by surgeons in the present survey. Because of its activity against anaerobes metronidazole has received considerable attention in recent years. Its effectiveness in appendectomy was first noted by Willis *et al*,¹¹ who showed a significant reduction in postoperative infections caused by bacteroides, although some subsequent results¹² indicated that an antibiotic with activity against both aerobes and anaerobes might be more advantageous. Metronidazole is superior to systemic ampicillin¹³ and povidone-iodine spray.¹⁴ An especial attraction of metronidazole is its availability as suppositories, which are both effective and cheap. Most surgeons stated that they used these in preference to the intravenous preparation.

The duration of administration of antibiotic prophylaxis varied considerably, although some broad areas of agreement emerged. A single preoperative dose was used by 60% of those who gave an antibiotic when removing a normal appendix. Single-dose prophylaxis has been shown to be effective,^{9 10 15} although its relative merits when compared with longer courses have not been fully evaluated. It appears to be a reasonable

choice, however, especially in those cases in which contamination is not severe. In the early successful trials of antibiotic prophylaxis in abdominal surgery^{16 17} three doses of antibiotic were given, and several surgeons used this regimen. In some later studies,^{3 11 12} however, much longer courses were given, especially when the contamination was severe,¹⁸ and this practice is widely followed. When the appendix was normal or inflamed only 4% and 18% of surgeons respectively gave five or more days of treatment, whereas the proportions increased to 43% and 56% when the appendix was gangrenous and perforated respectively. Many surgeons stated that they varied the duration of administration of antibiotics postoperatively depending on the clinical state of the patient.

TOPICAL ANTIBACTERIAL AGENTS

Forty-five (26%) of the responders always used a topical antibacterial preparation, and a further 61 (35%) sometimes did so. Povidone-iodine, whose benefit Gilmore *et al*, showed convincingly,^{18 19} was used by 67 (63%) of those who used a topical agent. The second most popular agent was polyantibiotic spray, which was used by 19 surgeons (16%). Documented evidence that the incidence of infection is appreciably reduced by applying this preparation to appendectomy wounds is difficult to find. Neither Longland *et al*²⁰ nor Gilmore and Martin¹⁹ showed any such benefit, and earlier trials produced conflicting results. Ampicillin powder was used by seven surgeons (6%). Its value in preventing infection has been clearly documented,²¹⁻²⁴ although Mountain and Seal²² showed no benefit in patients with more severe contamination. The importance of evidence such as this is hard to assess, however, since many surgeons combine the topical agents with systemic prophylaxis. Some surgeons admit that the visible application of an antibacterial substance to the wound imparts a certain psychological benefit. Noxythiolin was used as a wound application by five surgeons (4%) although its value in this role is doubtful.^{25 26}

Several other topical agents were used, but each by only one or two surgeons. The choice of chloramphenicol is interesting, because Lari *et al*²⁷ showed this drug to be effective against all the organisms recovered from operative and postoperative swabs from a series of children undergoing appendectomy.

SURGICAL DRAINAGE

Peritoneal drainage in appendectomy is associated with increased morbidity.^{3 19} This is not simply because such drainage tends to be used in the more severe cases: Magarey *et al*³ randomly allocated patients to receive peritoneal drainage and still found an increase in both the duration of fever and the number of discharging wounds in the group who received drainage. Despite this evidence most surgeons (77%) drained the peritoneal cavity from time to time after appendectomy.

Drainage of the wound, on the other hand, was practised by substantially fewer surgeons (56%), although some evidence suggests that it is beneficial. Vinnicombe⁸ and Everson and Nash²⁸ stated that wound drainage reduces the incidence of infection, although Gilmore and Martin¹⁹ found no such prophylactic value. There is no evidence, however, that wound drainage is attended by any adverse effects.

CONCLUSION

On the basis of the published evidence, giving prophylactic metronidazole to all patients before appendectomy would seem reasonable, and nearly half of the surgeons who replied did this. If a normal appendix is found no further drugs need to be given. If there is considerable contamination another antibiotic should

perhaps be added, and a number of doses given after operation. This practice was followed by nearly a third of surgeons, although a similar proportion began antibiotic treatment only at the time of operation for a gangrenous or perforated appendix.

Applying povidone-iodine to the wound is a simple measure that confers some protection against wound infection and was used occasionally by nearly half of the surgeons in the survey. The available evidence is against peritoneal drainage (which was used by 77%), but a wound drain may be advantageous, although only 56% of the surgeons ever inserted one.

It is possible that topical agents and surgical drainage may be largely abandoned by those who are confident of the efficacy of the systemic antibiotic prophylaxis used.

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SHORT REPORTS

Papillary carcinoma of the thyroid in two brothers after chest fluoroscopy in childhood

Thyroid carcinoma rarely occurs in young men. The occurrence of papillary thyroid cancer in two brothers of similar age therefore suggested some common aetiological factor. A family history back to the grandparents and their siblings yielded no evidence of thyroid disease or of multiple polyposis. Both brothers, however, had been exposed to radiation from cardiac screening in childhood.

Case histories

Case 1—A 33-year-old man presented in 1973 with a painless nodule in the left lobe of the thyroid. He was euthyroid and otherwise fit. At operation a papillary carcinoma in the left lobe of the thyroid and an enlarged retro-cervical lymph node containing carcinoma were removed. He was subsequently treated with ¹³¹I and remained well with no recurrence.

Case 2—A younger brother of case 1 was 38 when in 1979 he noticed a nodule in the left lobe of the thyroid. He was euthyroid and otherwise well. At operation a papillary carcinoma was found without evidence of spread beyond the thyroid. Near-total thyroidectomy was carried out followed by ¹³¹I treatment. He remained well without recurrence.

Sections from the thyroid tumours showed similar appearances (figure). Each was a well-differentiated thyroid papillary carcinoma, in places appear-

ing encapsulated. The adjacent thyroid tissue showed normal architecture and normal colloid-containing follicles. Inquiry disclosed that the two brothers had undergone detailed fluoroscopic examination of the heart at 11 and 9 years of age respectively because their mother had cardiac disease. The examinations had been carried out abroad, before image intensification was available, and no details of exact radiation exposure were available.

Comment

Familiar multiple polyposis (Gardner's syndrome) may be associated with the development of papillary thyroid carcinoma in siblings,¹ but this was excluded in our patients by the negative family history and absence of clinical features (appearances on sigmoidoscopy and barium enema were also normal). The only relevant history was the irradiation that each had received at fluoroscopy. Martin and Olson² concluded that irradiation of the thyroid during cardiac investigations is not negligible and may appreciably increase the risk of cancer.

The association of radiation with the development of thyroid cancer, often some 20-30 years later, is well recognised, though the dose has usually been in the range 2-5 Gy (200-300 rads).³ An increased incidence of cancer may, however, occur after much lower doses, and Pochin⁴ suggested an induction rate of 1% per Gy (1% per 100 rads). Using data on chest fluoroscopies⁵ as carried out at about the time that our patients were so investigated, we estimate that their thyroids had probably received a radiation dose of 0.2-0.3 Gy (20-30 rads). The eventual appearance of papillary cancers 22 and 28 years later confirms