Papers and Originals

Postoperative Clostridial Infections in Britain

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Summary: Eighty-five cases of clostridial infection, including 56 cases of gas gangrene, followed "clean" surgical operations performed in British hospitals in the course of two years. Nearly all the serious infections followed amputations of the leg for ischaemia or other operations on the leg in which a foreign body was implanted. All the infections were sporadic, and the evidence suggested that the infecting organism usually came from the bowel of the patient. Nearly half of the operations were performed in modern theatres with satisfactory ventilation and unexceptionable arrangements for the sterilization of instruments and dressings.

Skin sterilization was often carried out perfunctorily or with agents with poor sporicidal activity. Total eradication of spores from the skin is, however, difficult to achieve, and recontamination may occur during the operation. Hence it is considered justifiable to give penicillin prophylactically to the small group of patients at serious risk from postoperative gas gangrene.

Introduction

Gas gangrene and other clostridial infections are well recognized as a consequence of open injuries due to violence and of surgical operations on the bowel and gall bladder. Less is known about the circumstances under which they occur after "clean" surgical operations, because few surgeons and hospital bacteriologists have had personal experience of many cases. In the absence of this information it is difficult to decide what preventive measures are likely to be appropriate and what action should be taken when a case occurs.

In June 1966 we asked bacteriologists in hospital and public health laboratories who contribute to the weekly Communicable Diseases Report of the Public Health Laboratory Service to include in their reports a reference to each case of clostridial sepsis occurring after a "clean" surgical operation that came to their knowledge. Each of these cases was followed up by correspondence, and a series of questions were asked about the nature of the operation and the circumstances under which it was performed and about the infection and its consequences. The present report concerns cases that followed operations that took place between 1 July 1966 and 30 June 1968.

Definitions

A "*clean*" *surgical operation* was defined as an operation that was not for the treatment of an open injury, and did not involve incision into any part of the gastrointestinal tract or the gall bladder or vagina. Procedures of a surgical nature not carried out in an operating-theatre, such as injections and the insertion of needles into blood vessels and body cavities, were not specifically excluded.

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Clinical infection included not only gas gangrene but also certain localized necrotic or purulent infections. *Gas gangrene* was defined as an acute spreading necrosis of muscle in which gas bubbles were seen, and from which a clostridium was isolated. *Localized necrosis* of skin and adjacent tissues without gas formation and *purulent lesions* were regarded as being due to a clostridium when the organism was the only potential pathogen isolated from a swab collected soon after the appearance or first recognition of the lesion. Other potential pathogens were taken to include *Staphylococcus aureus, Pseudomonas aeruginosa,* all enterobacteria, and all groupable streptococci.

Operative Procedures

In the two years we received information about 85 cases of clostridial sepsis that fulfilled our clinical criteria and followed "clean" surgical procedures; 81 followed surgical operations and four followed a needle puncture (Table I). Eighty-four were due to *Clostridium welchii* and one to *C. septicum.*

TABLE I.—*Postoperative Clostridial Sepsis Reported Between July 1966 and June 1968; Main Classes of "Clean" Surgical Procedure and Clinical Type of Infection*

Surgical Procedure	No. of Cases of			Total Cases
	Gas Gangrene	Local Necrosis Without Gas	Purulent Lesion	
Amputation of leg	39	3	5	47
Other operation on leg	11	0	12	23
Any other surgical operation ..	3	2	6	11
Injection or puncture	3	0	1	4
Total	56	5	24	85

There were 56 cases of gas gangrene, 5 of local necrosis without gas, and 24 purulent lesions. Most of the operations belonged to one of two types—47 (55%) were amputations of the leg and a further 23 (27%) were other operations on the leg; but whereas nearly all (39 out of 47) of the infections following amputations were gas gangrene over half (12 out of 23) of those following other leg operations were purulent lesions.

Further examination of the operations performed on the leg, and of the pre-existing diseases of the patients who had clostridial sepsis, revealed the results shown in Table II. Nearly all the patients who had had amputations suffered from gross arterial insufficiency of the leg; of the 45 patients about whom reliable information was obtained, all but three had arterial insufficiency. In 13 this was due to diabetic arterial disease, in a further 25 there was arteriosclerotic or other chronic obstructive disease of the arteries of the leg, and in four there was acute arterial obstruction due to an embolus. Twenty of the patients already had arterial gangrene or an open ulcer of the leg at the time of operation. Amputation was through the thigh in 28 cases, through the knee-joint in 2, and below the knee in 17.

The other leg operations were nearly all on the hip region (20 out of 23) and involved the implantation of a foreign body (22 out of 23). They were mainly operations for the treatment of fracture of the neck of the femur (13) or for the relief of chronic osteoarthritis of the hip (7). Cases of gas gangrene followed the insertion of a nail or nail-and-plate into the neck of the femur (7), an intramedullary nail into the shaft of the femur (1), and a plate to the upper end of the tibia (1). Operations for the replacement of the head of the femur by a prosthesis, on the other hand, were more often followed by the appearance in the depths of the wound of a local collection of pus. Two of the patients were diabetics.

TABLE II.—*Clostridial Sepsis After Operations on the Leg: Nature of Pre-existing Disease and Clinical Type of Infection*

Disease	Operation	No. of Cases of		
		Gas Gangrene	Local Necrosis Without Gas	Purulent Lesion
Arterial insufficiency:				
Diabetic	Amputation	10	2	1
Other chronic	Amputation	22	1	2
Embolic	Amputation	4	0	0
Not arterial	Amputation	2	0	1
Unknown	Amputation	1	0	1
Arthritis of hip	Prosthesis	1	0	6
Fracture neck of femur ..	Prosthesis	2	0	0
Fracture neck of femur ..	Nail or nail-and-plate	7	0	4
Fracture shaft of femur ..	Nail	1	0	0
Other		1	0	1

The other operations or procedures considered to have been complicated by clostridial sepsis are listed in Table III. There were two cases of gas gangrene of the muscles of the flank in diabetic patients who had undergone lumbar sympathectomy for the treatment of arterial insufficiency of the legs, and one that occurred as a terminal event in a patient in whom the external iliac arteries and subsequently the aorta had been tied. There was one intracranial abscess after a temporal lobectomy, a local purulent lesion after a frontal craniotomy, and a relatively mild wound infection after an operation for fusion of the lumbar spine. Two local infections followed abdominal operations in which the bowel was believed not to have been penetrated, and, finally, there were two relatively trivial cases of wound sepsis after operations on the urinary tract and a local necrosis of the skin flaps after radical mastectomy that was thought not to have been due to deficient circulation.

TABLE III.—*Other Surgical Operations, Injections, and Punctures Followed by Clostridial Sepsis*

No.	Procedure	Type of Infection
1	Lumbar sympathectomy (arterial insufficiency)	Gas gangrene
2	Lumbar sympathectomy (arterial insufficiency)	Gas gangrene
3	Ligation of external iliac arteries and abdominal aorta (aneurysm of iliac artery)	Gas gangrene (terminal)
4	Laparotomy: division of adhesions	Local necrosis and faecal fistula
5	Radical mastectomy	Local necrosis of skin
6	Temporal lobectomy	Purulent: abscess in tumour space
7	Frontal craniotomy	Purulent: wound sepsis
8	Fusion of lumbar spine (rheumatoid arthritis)	Purulent: wound sepsis
9	Relief of strangulated hernia	Purulent: wound sepsis
10	Nephrectomy	Purulent: wound sepsis
11	Excision of neck of bladder	Purulent: wound sepsis
12	Intramuscular injection	Gas gangrene
13	Intramuscular injection	Gas gangrene
14	Superficial venepuncture	Gas gangrene
15	Paracentesis of pleural effusion	Clostridial empyema with gas

The four infections that followed puncture wounds included three cases of gas gangrene (two of the buttock and one of the arm) and one case of clostridial empyema. Two followed intramuscular injections, but in only one was the injected substance a vasoconstrictor. The third followed a diagnostic venepuncture in the antecubital fossa without the formation of a haematoma; the infecting organism was *C. septicum*, the skin of the injection site had been treated only with ether, and the patient was not a diabetic. The fourth followed paracentesis of the pleural cavity.

Clinical

The 85 patients were nearly all elderly; 78 were over 50 years of age and 35 were over 70. They comprised 48 men and 37 women, but there was a preponderance of middle-aged and elderly men who underwent amputations of the leg (31 aged 50–80 years) and of elderly women (15 aged 70–90 years) who had operations on the hip.

The symptoms of gas gangrene usually appeared soon after the operation (Table IV), in 60% of cases by the second postoperative day and in over 90% of cases by the fifth postoperative day. Local necrotic lesions attributed to clostridial infection also appeared during the first week, but on the whole later than gas gangrene. The purulent lesions, however, were in many cases not detected for a considerable time. This was particularly so with the deep abscesses associated with operations on the hip, 8 out of 10 of which were first observed after the fifth day, and one of which remained undetected until the third week after operation.

TABLE IV.—*Time Between Operation and Onset of Clostridial Sepsis*

Type of Lesion	No. of Cases with Onset on Postoperative Day:									
	1	2	3	4	5	6	7	→14	→21	Not Known
Gas gangrene	13	22	9	6	3	2	0	1	0	1
Local necrosis	0	0	1	0	1	0	2	0	0	0
Purulent ..	2	1	4	0	1	5	4	5	1	1

Forty-one of the patients (48%) died while in hospital, but the death of nine was considered not to have been due to clostridial sepsis—eight of the nine survived the initial clostridial infection but died subsequently of some unrelated disease, and one was moribund when the infection began. In one case there was insufficient evidence to determine the cause of death. There remained 31 deaths which were attributable to the clostridial infection, and all of them were in patients who had had gas gangrene (Table V); 28 followed leg operations (19 amputations and 9 operations on the hip), two followed intramuscular injections, and one followed lumbar sympathectomy.

TABLE V.—*Death of Patients with Clostridial Sepsis in Relation to Clinical Type of Clostridial Disease and Operation Performed*

	No. of Cases	No. of Deaths			
		Attributable to Infection	Unrelated Cause	Cause Not Known	Total
Clinical type of sepsis:					
Gas gangrene ..	56	31	5	1	37
Local necrosis ..	5	0	1	0	1
Purulent	24	0	3	0	3
Operations:					
Amputation ..	47	19	4	1	24
Other leg operation	23	9	4	0	13
All other operations	11	1	1	0	2
Puncture	4	2	0	0	2
Total ..	85	31	9	1	41

Most of the deaths attributed to gas gangrene occurred very soon after the appearance of the disease. Twenty-four of the 31 patients died within two days of onset, 22 of acute toxaemia and two while undergoing a further amputation. The disease had a particularly sudden onset and short course in several of the patients who developed gas gangrene after operations on the hip; three of them collapsed suddenly and died within a few hours without the appearance of any local signs, and the diagnosis was first made at necropsy.

Four patients survived the first few days on massive antibiotic therapy, but their condition continued to deteriorate and

they died on the 7th, 9th, 18th, and 35th day respectively. Two others underwent disarticulation of the hip; but their wounds failed to heal and they eventually died of chronic sepsis due to other organisms.

Relatively few of the patients who survived the gas gangrene escaped further surgical intervention (Table VI). Only three were successfully treated with antibiotics or with antibiotics and hyperbaric oxygen, four underwent a local excision of muscle, and 15 had an amputation or reamputation or a disarticulation of the hip. In all, five patients underwent the last procedure—two died of secondary sepsis, one died of an unrelated cause, and two survived.

TABLE VI.—*Outcome of Clostridial Infection*

Outcome		No. of Cases with		
		Gas Gangrene	Local Necrosis	Purulent Lesion
Death:				
Attributable to clostridial sepsis	Acute toxaemia	23	0	0
	Death under anaesthetic	2	0	0
	Late toxaemia	4	0	0
	Secondary sepsis	2	0	0
Moribund at onset of clostridial infection		1	0	0
Cause not known		1	0	0
Survived clostridial infection:				
Antibiotics only		1	4	17
Antibiotics and hyperbaric oxygen only		2	0	1
Further operation	Excision or drainage	4	0	5
	Amputation	15	1	1
Outcome not known		1	0	0
Total		56	5	24

All of the 29 patients with local or purulent lesions survived their infections, and 22 of them made an eventual recovery after treatment with antibiotics or with antibiotics and hyperbaric oxygen. Two patients had reamputations, and five large abscesses were drained surgically.

Distribution of Cases

In general, clostridial sepsis occurred sporadically. Cases were reported from 55 different hospitals; 31 hospitals reported only one case in the two-year period, 20 reported two cases, two reported three cases, and two reported four cases.

The time of occurrence of multiple cases in single hospitals was examined carefully for evidence of outbreaks of infection. There were 11 hospitals in which there were two or more cases of gas gangrene in the course of two years, and in four of the hospitals two cases occurred within one month. This suggested an occasional association between cases. Further inquiry in two of the hospitals revealed no positive information of significance. In the third hospital two cases followed amputations and both occurred almost immediately after the introduction of a new "myoplastic" technique in which the muscles of the stump were tightly constricted during the immediate postoperative period. In the fourth hospital two cases of gas gangrene followed amputations performed within 24 hours, but by different surgeons and in different operating-theatres. Careful investigation by local bacteriologists (see Ayliffe and Lowbury, 1969) showed that the theatres were properly ventilated, that the level of environmental contamination in them was low, and that the sterilizers were in good order and properly operated. It was subsequently found (R. G. A. Sutton, personal communication) that the strains of *C. welchii* isolated from the two cases were serologically different.

None of the cases of clostridial infection could be attributed to the fact that a case of clinical gas gangrene had been operated on in the same theatre during the previous week, and no secondary cases followed operations on the cases of gas gangrene reported in this inquiry.

Conditions in Operating-theatres

Inquiries were made about the conditions under which the surgical operations followed by clostridial sepsis had been performed.

Construction and Ventilation

Information was obtained about the construction and ventilation of the theatres used for 77 of the 81 operations. Fifty-one had been carried out in modern theatres with acceptable types of positive-pressure ventilation, and in all but three cases there was evidence that the ventilation system was working satisfactorily. Two operations were carried out in a theatre adjacent to the site on which a new theatre block was under construction, and the bacteriologist thought there was evidence that contaminated dust may have reached the air of the theatre. The third took place at another hospital at a time when the ventilation plant was not functioning correctly.

The remaining 26 operations were performed under less satisfactory conditions—13 in older theatres with extract-ventilation systems and 13 in rooms with no artificial ventilation. In three instances there was evidence of more serious defects. One operation was carried out in a naturally ventilated room adjacent to a building site. In another, the operations were performed in a similar room opening on to a busy corridor at a time when a large party of visitors passed along the corridor; during the operation the theatre door was opened several times by nurses bringing in and removing trays of instruments. In a third hospital a case of gas gangrene followed an amputation, and *C. welchii* and an aerobic spore-bearing bacillus were isolated from the wound. An old ventilator grille in the roof of the theatre, originally intended for ventilation, had been closed for some years, but recently a hole had been made to allow for the passage of an electric cable, and an unsealed gap had been left which communicated with a loft above the theatre. The loft was found to contain straw contaminated with bird droppings, and *C. welchii* and an identical aerobic spore-bearing bacillus were isolated from it.

Sterilization

We have information about the methods of sterilization of the materials and instruments used for 75 operations. In 73 instances all the utensils and dressings had been autoclaved, but in two the bowls and gallipots were boiled. All surgical instruments used for 49 operations had been sterilized by autoclaving or by dry heat, but all of those used for 10 operations had been boiled; in two instances some had been boiled and in 14 instances some had been treated chemically. The chemical disinfectants used were various: Hibitane (chlorhexidine) or Savlon (chlorhexidine and cetrimide) in alcohol (seven operations); instrument lysol (two operations); formaldehyde in alcohol (one operation); formaldehyde vapour released from metaformaldehyde by warming in a closed tin (one operation); Metaphen (one operation); the chemical used in two instances was unknown.

Regular testing of autoclaves was the practice in all hospitals, and it was stated that satisfactory results had been obtained at times relevant for all except two operations. In one hospital there had been an isolated mechanical failure of an instrument autoclave, and in another there had been repeated failures of the Bowie–Dick test on a dressings autoclave in the previous three weeks, but no action was taken.

Although this part of the investigation showed that a number of the operations had been carried out under unsatisfactory physical conditions, this was by no means always so. Indeed, for 36 out of 75 operations no criticism was made of the construction and ventilation of the operating-theatre or of the methods of sterilization of equipment.

Methods of Skin Preparation

The following substances were used as the main disinfectant in preoperative skin preparation: chlorhexidine or Savlon in alcohol, generally in 70% ethanol (46 operations); Cetavlon (cetrimide) in alcohol, or in water followed by 70% ethanol (four operations); iodine in alcohol (10 operations); Betadine (povidone-iodine) (two operations); Merthiolate (thiomersal) in alcohol (four operations); "orange Dettol" (three operations); 70% ethanol (one operation); other chemicals (two operations); no chemical substance (three operations). The method of skin disinfection used before six operations is not known.

In many instances the exact procedure for skin preparation was not given, but it is clear that there were great variations in the time and care devoted to it. For instance, in 10 cases in which chlorhexidine in alcohol was the main sterilizing agent its use followed repeated cleansing of the skin with detergents during the previous 24 to 48 hours, but in three cases the information was volunteered that a single brief application of it in the theatre was the only preoperative treatment.

Chemoprophylaxis

An inquiry about the prophylactic use of antibiotics was answered satisfactorily in 76 instances. No patient who subsequently developed clostridial sepsis was being treated with adequate doses of penicillin on the day of the operation. Three of the patients received some antibiotic treatment that might have been expected to have some prophylactic effect. One received a daily injection of 1 million units of benzylpenicillin from the second postoperative day until a large abscess containing *C. welchii* appeared in the muscles around the hip joint on the seventh postoperative day. Another had been given full therapeutic doses of ampicillin from the first postoperative day and then developed gas gangrene three days later. A third received tetracycline continuously from the day before operation, but mild sepsis due to a tetracycline-sensitive strain of *C. welchii* occurred on the seventh postoperative day.

Discussion

Table VII is a summary of information obtained from five papers published since 1960 which record large series of clostridial infections in civilian practice. The total number of cases of clostridial sepsis and the number of cases of gas gangrene are shown separately, and the postoperative infections have been reclassified for comparison with our findings. One of these papers (Gye *et al.*, 1961) is concerned specifically with infections following "clean" surgical operations, and records 16 cases in one Australian hospital in seven years. The second (Bornstein *et al.*, 1964) lists all cases of clostridial sepsis seen in an American hospital in three and three-quarter years. The remaining three papers (Brummelkamp, 1964–5; Trippel *et al.*, 1967; Hitchcock *et al.*, 1967) are accounts of cases of gas gangrene sent to special units for hyperbaric oxygen treatment. There is a general similarity in the types of operation that were followed by clostridial infection. From all the accounts, there were 11 cases of gas gangrene following amputations of the leg, eight following other leg operations (nearly all for fractures of the hip), two following intramuscular injections, and only seven following all other surgical operations. In the Australian series half the cases of clostridial sepsis followed "other" surgical operations, but some of these infections were very mild, and similar cases would have been excluded from our series because other potentially pathogenic organisms were also isolated from the wounds.

Mode of Infection

The results of our survey leave little doubt that the overwhelming majority of postoperative clostridial infections are sporadic. There was a slight tendency for cases to be associated in time and place, but this may have been due to factors connected with the surgical technique. In no instance was there evidence that two or more cases had been infected from a common source. This suggests that infection is nearly always from an autogenous source, which exists in all patients because faecal carriage of *C. welchii* is almost universal. The relative frequency of local clostridial infection of the abdominal wall following operations on the bowel or gall bladder (see, for example, Millar (1932), Shapiro *et al.* (1963), and Table VII) suggests that these cases follow direct contamination of the wound with clostridia from the bowel. The fact that operations on the hip and thigh are such a prominent cause of gas gangrene suggests that in these cases organisms may also have come from the intestinal flora. The early onset of symptoms in most cases of postoperative gas gangrene indicates that the organism was introduced into the wound at operation or very soon afterwards. In the hip operations and most of the amputations, therefore, it is likely that the organisms reached the wound from the outside and came from the surrounding skin. Ayliffe and Lowbury (1969) showed that *C. welchii* is present on the skin of the buttock and thigh in a considerable proportion of hospital patients, and that there was a serological resemblance between the faecal and wound strain in three cases of postoperative gas gangrene.

In some of the amputations, however, there was another possible source of infection. In nearly half of these cases arterial gangrene or ulceration of the foot was present, and some of these lesions were probably contaminated with clostridia; this would provide a rich alternative source of infection. It is noteworthy that nearly one-third of the amputations followed by gas gangrene were below the knee. The possibility cannot be excluded that transient bacteriaemia might occasionally result from rough manipulation of the limb in the course of the preparations for operation, and that small numbers of clostridia might in this way reach the operation site from the blood stream.

Predisposing Factors

It is not easy to disentangle the predisposing factors for the development of postoperative clostridial infection. Most of the operations it follows are through grossly ischaemic tissue or involve the implantation of a foreign body. The fact that local

TABLE VII.—*Clostridial Infections recorded in Six Recent Surveys*

Reference	Total No. of Cases	No. of Cases of Clostridial sepsis (in Parenthesis: Cases of Gas Gangrene) following						
		"Open" Injury	Bowel Operation	No Wound or Operation	"Clean" Surgical Procedure			
					Amputation of Leg	Other Operation on Leg	Injection or Needle Puncture	Other Operation
Gye *et al.* (1961) ..	16 (4)				2 (2)	6 (2)	0 (0)	8 (0)
Bornstein *et al.* (1964)	22 (4)	1 (0)	8 (2)	8 (0)	0 (0)	2 (1)	2 (1)	1 (0)
Brummelkamp (1964–5)	(40)	(22)	(2)	(4)	(5)	(2)	(1)	(4)
Trippel *et al.* (1967) ..	(23)	(10)	(6)	(1)	(4)	(1)	(0)	(1)
Hitchcock *et al.* (1967)	(32)	(20)	(4)	(4)	(0)	(2)	(0)	(2)
Present series ..	85 (56)				47 (39)	23 (11)	4 (3)	11 (3)

ischaemia predisposes to gas gangrene following amputation through the thigh is well known (Taylor, 1960) and is in line with the observation that gas gangrene occurs mainly in gunshot wounds in which there is damage to a large artery (Lowry and Curtis, 1947 ; North, 1947), but most amputations in civilian practice are for ischaemia and are of the leg. Similar difficulties are encountered in trying to assess the importance of diabetes as a predisposing factor. In the present series 13 out of 47 infections after amputations but only 2 out of 23 after other leg operations and 2 out of 15 in cases after other procedures were in patients known to be diabetics. This would be consistent with the view that diabetes predisposes to clostridial infection mainly by causing arterial insufficiency, but the two cases of gas gangrene developing after lumbar sympathectomy in diabetics suggests a more specific effect.

The predisposing effect of a foreign body in the wound appears to operate only in the hip region, but its significance cannot be properly assessed without knowledge of the relative frequency of comparable operations in large muscle masses without implants and in other regions. It also appears that contamination of the depths of the wound with clostridia in hip operations is by no means always followed by gas gangrene ; in nearly half of the cases a local collection of pus was formed slowly around the foreign body. Clostridial lesions in some other parts of the body—for example, the brain (Russell and Taylor, 1963 ; and Case 6, Table III), the meninges (Colwell *et al.*, 1960 ; Willis and Jacobs, 1964), and the body cavities (Goldberg and Rifkind, 1965 ; and Case 15, Table III)—are usually purulent. Why clostridia sometimes produce similar lesions in the muscles of the thigh is not clear.

That so many operations followed by clostridial sepsis involve the cutting of bone may also be significant. This suggests that powdered bone itself may provide a suitable anaerobic medium for the initial multiplication of clostridia. In addition to this, other "hidden" predisposing factors connected with the surgical techniques may have existed in some of the operations. Mention has already been made of two cases in rapid succession in one hospital after the introduction of a "myoplastic" amputation technique ; a similar case was reported from another hospital.

Prevention

Since nearly all postoperative clostridial infections are sporadic, the effective preventive measures are those that form part of the hospital routine and not those taken when a case occurs. Indeed, the intense activity that follows such an incident is often ill-conceived and tends to distract attention from essentials. It is common practice to close the operating-theatre and to carry out extensive bacteriological sampling of surfaces and objects in it. *C. welchii* is almost invariably isolated, but a similar result would probably have been obtained if there had not been a case of gas gangrene (Lowbury and Lilly, 1958). Heroic measures may be taken to "sterilize" the operating-theatre, and further swabs may be taken. If the laboratory is technically efficient it will prove difficult to obtain a negative result and there may be great uncertainty about when to reopen the theatre.

Alternatively, a case of gas gangrene may be too easily attributed to the bad construction or inadequate ventilation of the theatre. This survey revealed that in a few instances there were serious defects in a theatre that might have been responsible for an exceptional degree of contamination with clostridia, but in over half the cases the operations had been performed in theatres of modern construction with well-functioning ventilation systems. It is obviously undesirable that operations should be performed under poor physical conditions, which undoubtedly influence the general postoperative sepsis rate, but criticism of the operating-theatre should seldom be the main response to a case of gas gangrene.

Similarly, the survey revealed a number of unsatisfactory sterilization procedures. Boiling of instruments cannot be relied on to destroy clostridial spores, and all except one of the chemical agents used to sterilize instruments (formaldehyde in alcohol) had poor or uncertain sporicidal activity. In some instances the use of inadequate methods could be attributed to the absence of a modern instrument autoclave, but in others it appeared to be due to the surgeon's fear that autoclaving would injure the instruments or would reduce his freedom to have instruments "sterilized" quickly. A comparison of the routine practices of different surgeons suggested that there was little agreement about which instruments must be sterilized chemically. Again, however, no criticism could be made of the sterilization arrangements for over half the operations.

After a case of postoperative clostridial infection it is reasonable that there should be an immediate inspection of the theatre and its ventilation plant, together with a review of the sterilization methods, the temperature charts, and the results of recent tests, and a series of extra tests on the autoclaves. It may even be considered desirable to carry out a ritual cleansing of the theatre by orthodox "domestic" methods, but an extended period of closure and bacteriological tests are seldom necessary. In any case these activities should not divert attention from more important matters concerned with the management of the individual case.

The main risk of serious clostridial disease is confined to a small proportion of the total number of "clean" operations, and special attention should be devoted to these. Apart from details of surgical techniques designed to reduce the amount of devitalized tissue and to avoid anoxia due to tension, measures should be directed to preventing contamination of the wound from the surrounding skin or from other open lesions. It is clear that in the present survey the preoperative sterilization of the skin was often perfunctory, and consisted of a single application of an agent with poor sporicidal activity. Although clostridial spores are relatively resistant to most commonly used antiseptics, a considerable proportion of them may be removed from the skin by vigorous scrubbing with detergent fluids. Repeated ablutions and several applications of antiseptic over a period of two to three days are therefore recommended before elective surgery (Lowbury *et al.*, 1964), but treatment with povidone-iodine, which has good sporicidal activity on artificially contaminated skin, proved much less effective than might have been expected in freeing the skin of patients of *C. welchii* (Ayliffe and Lowbury, 1969), and some cases of gas gangrene in the present series appear to have followed careful preoperative skin preparation. It is doubtful whether any agent can be relied on to destroy all spores on the skin, and a wound may become recontaminated during a long and complicated operation. This possibility might be reduced by the use of plastic adhesive drapes attached to the wound edges.

It is justifiable, therefore, to use antibiotic prophylaxis for the prevention of postoperative gas gangrene after operations in which the risk of this complication is known to be high (Taylor, 1960 ; Johnstone, 1963). The antibiotic of first choice is benzylpenicillin, to which all clostridia are sensitive, and a reasonable dosage would be 500,000 units six-hourly, as recommended by Taylor (1960). Treatment should begin a few hours before the operation but not earlier, and should be continued for five to seven days. According to Traub and Sherris (1968) *C. welchii* is also very sensitive to ampicillin, but one patient of the present series suffered gas gangrene in spite of being given apparently adequate doses of this antibiotic. A considerable proportion of *C. welchii* strains are resistant to tetracycline (Johnstone and Cockcroft, 1968), and erythromycin appears to be the antibiotic of second choice for patients with a history of penicillin hypersensitivity.

The general arguments against the prophylactic use of antibiotics are not of great weight in this case. The risks to the patient of ill-effects from antibiotic "replacement" of the normal flora

or from hypersensitivity reactions are worth taking as an alternative to gas gangrene, and giving penicillin prophylaxis to the small number of patients at serious risk would have a negligible effect on the proportion of patients who receive antibiotics, which is at present at least 30% of all persons admitted to hospital.

Outbreaks of Clostridial Infection

No outbreak of postoperative clostridial infection was observed in Britain during the two years 1966–8, but groups of associated cases may appear, though very rarely. For understandable reasons they are seldom reported in the medical literature. I have heard of four in the past 25 years, and had the opportunity of investigating one personally.

In two weeks four patients undergoing orthopaedic surgery developed gas gangrene. All the operations had been performed by one surgical team, but no cases followed operations performed during the same period and in the same operating-theatre by a second orthopaedic surgeon, who gave prophylactic penicillin to all his patients. The investigation revealed two further significant points. Firstly, the theatre was adequately ventilated but there were defects in the loading of a dressings autoclave so serious that clostridial spores might easily have survived in heavily contaminated material. Secondly, a patient with gas gangrene after a road accident was under treatment in the hospital. He was taken to the operating-theatre three times, and on each occasion a case of gas gangrene developed in a patient operated on within the next 24 hours.

It is clear that under normal conditions the risk to other patients of taking a patient with gas gangrene to the operating-theatre is not great. Many of the patients with gas gangrene in the present survey had amputations and none caused secondary cases. Some contamination with clostridia of instruments and materials in operating-theatres must be relatively common—for instance, in the course of operations on the bowel. Nevertheless, it is possible that the removal of exudate-soaked dressings from a case of gas gangrene may result in a heavy and widespread contamination of objects in the theatre. This seldom appears to cause trouble under normal circumstances, but might lead to a disaster if there is a concomitant sterilizer failure or grossly defective ventilation of the theatre. This suggests that particularly rigid precautions are desirable in operating-theatres in hospitals with hyperbaric oxygen units.

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Control of Sodium Reabsorption*

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Hormonal Control of Tubular Sodium Reabsorption

It is well established that steroids, particularly aldosterone, have a powerful effect on sodium reabsorption in the distal tubule.[122] It is still a matter of some speculation whether another hormone controls sodium reabsorption in the proximal tubule. Most of the evidence which suggests the presence of such a hormone has been obtained in experiments in which the fluid volume of an animal has been expanded with saline, plasma, or blood.

Escape Phenomenon

The first suspicions that there might be some hormonal control of sodium reabsorption other than by aldosterone were aroused by the finding that when the extracellular fluid volume is expanded by the continuous administration of deoxycortone acetate, fludrocortisone, or aldosterone there is an initial diminution of sodium excretion followed within a few days by a rise in sodium excretion to control levels.[2 98 112] This is often referred to as the "sodium escape phenomenon." Smith[103] suggested that this phenomenon was due to a circulating substance which he named a natriuretic hormone X. Nevertheless, the demonstration by Davies and Shock[29] that the standard deviation of individual determinations of inulin clearance from the mean of a series was 5–10% was sufficient to deter most workers from accepting the sodium escape phenomenon as anything but another demonstration that sodium excretion was controlled by small changes in glomerular filtration rate,[123] even when the changes in filtration were so small that they were undetectable.

Effect of Intravenous Saline

The point was not resolved until de Wardener, Mills, Clapham, and Hayter[121] demonstrated that in dogs receiving large amounts of salt-retaining steroids and vasopressin an infusion of saline causes a rise in urinary sodium excretion even

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