

## HAND INFECTIONS TREATED WITH PENICILLIN

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THE choice of method of using penicillin is at present largely conditioned by very short supplies, a state of affairs which is likely to continue for a long time. There can be little doubt that the best way of attacking susceptible pyogenic organisms with penicillin is to bring it to the infected tissues by the blood-stream. This, however, demands a great expenditure of penicillin compared with that necessary for local application.

It has already been shown that chronic pyogenic infections can be successfully treated by appropriate local application, and a few more acute suppurative lesions have been treated with good results (Florey and Florey 1943). Clark, Colebrook and others (1943) and Bodenham (1943) have shown that pyogenic cocci can be removed from infected burns. Pulvertaft (1943) has demonstrated that some chronically infected war wounds can be freed from streptococci and staphylococci by local application.

It appeared desirable to ascertain more fully the possibilities of using penicillin in acute pyogenic infections. Acute infections of the hand were chosen, because they are common in industry and cause much permanent disability, or at best considerable loss of working time. The number of cases available allowed a comparison between those treated with penicillin and those treated by routine methods. The complicated structure of the hand permitted observation of the effects of penicillin application on skin, areolar tissue, blood-vessels, nerves, muscles, tendons, synovial membranes of tendon sheaths and joints, and bone. The results of healing of wounds have in the last analysis to be judged by return of function, and the hand afforded an admirable structure for observations on this important point.

Special attention was paid to: (1) the arrest of sepsis and bacterial infection; (2) the after-effects attributable to arrest or persistence of sepsis; and, in the penicillin cases, (3) possible deleterious effects of the drug; and (4) the most suitable methods of administration.

### METHOD OF INVESTIGATION

The cases were grouped according to the site of the infection.

Group	No. of cases in:	
	"control" series	penicillin series
1. Paronychia .. ..	26	26
2. Pulp infection .. ..	27	28
3. Web-space infection .. ..	9	9
4. Tendon-sheath infection .. ..	11	11
5. Miscellaneous abscesses .. ..	12	12
6. Septic lacerations .. ..	5	6
7. Miscellaneous lesions .. ..	12	18
	102	110

Throughout this paper "series" will refer to the two major classes, "control" and "penicillin-treated." "Group" will refer to both control and treated cases in one clinical class—e.g., pulp infection.

To eliminate personal bias alternate cases were taken for penicillin treatment, although, as will be seen, this was not entirely satisfactory when dealing with small numbers. Observations were made at operation and thereafter daily on both series in the acute phase, and afterwards not less than twice a week till healing was well advanced. The investigation was not considered complete till full function had been regained or till a sufficient period had elapsed to make this unlikely—i.e., up to 6 months from operation.

The duration of expectant treatment and the choice of site and method of approach at operation were in the hands of the surgeons, the same team operating on both series of patients. The postoperative care of outpatients of both series was left in the hands of one investigator, but inpatients remained under the full charge of the hospital staff, only the dressings of the penicillin-treated patients being done by the investigator.

It is necessary here to define the term "controls." Though the surgical methods were the same in both series (except for 3 patients in group 5), the patients of the "control" series received various local applications and some of them were given sulphonamides by mouth at various stages. They were not controls in the sense of receiving treatment in every particular the same except for the administration of the drug. They might better be called "contrasts," since the results of penicillin treatment were contrasted with the results of the various method accepted at the present time.

### TREATMENT

**Local applications.**—For the purpose of the investigation, treatment was considered to start at the time of operation. Controls were packed with paraffin gauze at operation and later with eusol preparations. Inpatients were given saline baths in which they were encouraged to move the hand. As the wounds became superficial, sulphanilamide powder, sulphathiazole cream, or gentian violet and sulphanilamide were sometimes applied. Dressings were carried out once or twice every 24 hours, according to the amount of discharge, till wounds were far advanced towards healing.

The penicillin-treated wounds were powdered evenly at operation with the calcium salt of penicillin and packed with gauze soaked in penicillin paste (lanette wax 12 parts, arachis oil 25 parts, water 55 parts, with penicillin added to make a strength of 150 or 250 units per c.cm. prepared as recommended by Clark and others (1943). A layer of fine-mesh soft-paraffin gauze was placed over the wound to prevent the drug soaking out into the dressings. Treatment with penicillin at the time of operation was considered essential, because far better access to the infected parts could be gained than at subsequent dressings. A bloodless field was obtained by means of a sphygmomanometer cuff, to facilitate application of the powder. Dressings were repeated every 24 hours for a minimum of 5 days. In 3 cases surgical procedure was adapted to the use of a penicillin solution instead of the paste. In the absence of slough, and where access to infected tissues at the first operation had been adequate, penicillin treatment was not continued after the end of the first week, except for a light dusting of penicillin as a preventive against further infection when the dressing was changed. Further dressings were seldom necessary after the first week except for readjustment or for purposes of observation.

**Other treatment.**—Sulphonamides by mouth were used in the more severe control cases but only in 3 of the penicillin series, where 16 g. was the largest amount given. Rest in bed and local heat were ordered on occasion, irrespective of the series. After the 5th day the patients were taught to move the joints and encouraged to do so, provided that no exacerbation of infection followed.

Attention was paid to factors liable to influence the prognosis, such as age, sex, severity and extent of lesion, type of tissue involved and amount of destruction, duration of sepsis and of expectant treatment, concomitant disease, and nature of the infecting organism. An attempt was made to assess these factors. They have been disregarded in the groups where they appeared to equalise one another but they are discussed in the groups where they differed widely.

### ASSESSMENT OF RESULTS

**Bacteriological examinations.**—In the great majority of cases the infecting organisms were either Lancefield's group A streptococci (referred to throughout as "*Strep. pyogenes*"), coagulase-positive staphylococci (referred to as "*Staph. aureus*"), or both. The tabulated results refer to infection by these organisms. The few results with infections by other species—e.g., micrococci, hæmolytic streptococci other than groups A, B, C or G (referred to as "hæmolytic streptococci") and coliform bacteria, are dealt with in the text.

The following criteria were adopted in classifying changes in the degree or type of infection.

Persistence of infection: continuous series of heavy or moderate growths from swabs.

Diminution of infection: reduction of the growth of infecting organisms on a direct plate from the swab to less than 20 colonies.

Reinfection : reappearance of growth after at least two successive negative swabs.

Swabs for bacteriological examination were taken at operation, and thereafter, for reasons of convenience, twice a week on fixed days from inpatients and once a week from outpatients, till healing had taken place or the wound was many weeks old. A swab might therefore be taken on any day from the 1st to the 5th after operation, but for purposes of this comparison "second swab" refers to that taken on or after the 5th day. The changes in growth in the group tables refer to swabs taken up to and including the 8th day.

*Arrest of sepsis and bacterial infection.*—In open wounds a simple check on the arrest of sepsis was provided by the results of the bacteriological examinations, which were considered therapeutically satisfactory if there was a disappearance or diminution of the infecting organisms. Clinically, the loss of pain, redness, swelling, fever and pus formation were all taken into account, but for purposes of statistical comparison the disappearance of pus was found to be the most satisfactory. Pain was subject to emotional influences, redness of the skin in controls was sometimes obscured by soaking, swelling due to inflammatory oedema of the tissues merged insensibly in the longer lasting control infections into a firm thickening, obscuring the time limit of active inflammation, while pyrexia was present in only a few cases. That disappearance of pus is not due to an inhibitory action of penicillin on leucocytic activity has been shown experimentally (Abraham et al. 1941) and clinically by its continued formation during penicillin administration in the presence of coliform organisms. In the tables "drying" indicates the time when a scab had formed. When patients were not seen daily, drying was considered to have taken place half way between the two last days of observation.

*After-effects of arrest or persistence of infection.*—Spread of infection, appearance of granulations and epithelial ingrowth, separation of sloughs, return of movement, loss of digits and time of healing were all studied. Particular attention was directed to the most essential criterion of success—recovery of function. As will be seen, the various clinical groups brought out different aspects of the comparison between control and penicillin-treated cases. In all groups except paronychia, where healing involved little beside the growth of epithelium, the healing process took an obviously different course in the control and penicillin-treated series. For this reason the time of healing under the conditions imposed by current surgery was by no means a criterion of the arrest of sepsis.

Experience with Various Lesions

PARONYCHIA

This group (table I) included infections by *Staph. aureus* and *Strep. pyogenes*, both separately and combined. It comprised infections which had already lasted from one day to six weeks. Expectant treatment in the shape of sodium sulphate compresses and splinting with plaster had been carried out in half of each series. Other factors affecting the prognosis also appeared to be equal.

TABLE I—PARONYCHIA : ARREST OF SEPSIS AND RECOVERY

	Bacteriological findings : number of cases										Days till dry	
	Total	Initial organism				Growth by 8th day					Mean	SD
		<i>Staph. aur.</i>	<i>Str. pyo.</i>	Both	Neither	Pr	Dm	Dp	Healed*	Not done		
Control	26	9	3	14	0	23	0	0	2	1	15.5	± 8.2
Penicillin	26	5	5	14	2†	2	11	9	4	0	7.7	± 3.2
Difference .. . . .											7.8	± 2.6

SD = Standard deviation. Pr = persistence. Dm = diminution. Dp = disappearance. \* Healed = before 2nd swab.

† = (1) micrococci, heavy growth; (2) hæmolytic streptococcus, not group A.

TABLE II—PULP INFECTIONS : ARREST OF SEPSIS

	Bacteriological findings *: number of cases						Days to disappearance of pus			
	Total	Initial org.	Growth by 8th day				Cases†	Mean	SD	
			<i>Staph. aur.</i>	Pr	Dm	Dp				Healed‡
Control	27	27‡	24	1	0	1	1	21¶	14.2	± 12.8
Penicillin	28	28	4	5	18	1	0	22	1.4	± 2.7
Difference .. . . .								12.8		± 2.9

\* Including osteitis cases. † Excluding osteitis cases. ‡ 1 case with hæmolytic streptococcus not group A, B, C or G. ¶ 2 cases not recorded. § Before second swab.

TABLE III—SIMPLE PULP INFECTIONS : RESULTS

	Dry			Epithelialised			Full movement			
	Cases	Days		Cases	Days		Cases	Days		
		Mean	SD		Mean	SD		Mean	SD	
Control	23	20.7	± 13.0	19*	29.7	± 13.5	22*	25.7	± 19.5	
Penicillin	22	10.8	± 4.8	20*	21.7	± 8.7	19*	11.7	± 4.3	
Difference			9.9	± 2.9		8.0	± 3.7		14.0	± 4.3

\* Remaining cases did not report for examination.

At operation, bilateral incisions were made at the angles of the nail fold and as much nail as was considered necessary was removed. Controls were dressed with a paraffin gauze wick inserted between fold and nail bed. In the treated series penicillin powder (about 100 units in 10 mg. of the Ca salt) was inserted below the fold and spread over the nail bed, followed by a penicillin paste gauze wick (150–250 units per g.). After-treatment consisted in daily dressings till the nail bed showed signs of drying. All wounds were wiped over with 1% 'Cetavlon'; a eusol and paraffin dressing was applied to the controls, and in the penicillin-treated cases, penicillin paste was applied for two or three days, followed by a dusting of penicillin powder at subsequent dressings, if necessary, to prevent reinfection.

This group exemplifies a superficial infection. Even in the less amenable cases the infection persisted on the nail bed rather than under the fold. There was little evidence of pus in either series and drying was therefore considered an adequate clinical criterion of the arrest of sepsis.

*Results.*—Treated cases not only dried in half the time of the controls but showed less variability in their course. Persistence of pain was greatly reduced, and the time for full epithelialisation and restoration of movement of the finger followed the same relation to the control cases as did the time of drying. As regards the choice of time for operation, in the control series there was little difference in the course of healing whether surgery was early or late, but among the penicillin cases the time of drying was shorter and less variable when surgical interference was early.

PULP INFECTION

This group (tables II and III) was confined to deep infections of the soft tissues of the pulp, all merely subcutaneous abscesses being excluded. The number treated in both series was the same but osteitis was present in 6 penicillin cases and in only 4 of the controls. The very different prognosis necessitated the exclusion of these cases from the statistical comparison. They will be dealt with later among infections of bone.

Sex and age incidence differed in the two series. Sex did not appear to affect recovery, but the inclusion of 2 cases over 45 years old in the control series may have weighted the scales in favour of penicillin. Surgery consisted in a lateral incision through the soft tissues of the terminal phalanx extending almost to the opposite side but leaving the skin there and at the tip intact. Paraffin gauze packing was inserted into control wounds and subsequent dressings were the same as for paronychia. Penicillin cases received 300–500 units as dry powder (30–50 mg.) and a gauze pack liberally supplied with the paste. Subsequent daily packings (for 5 days) consisted of paste only in mild cases, but where slough,

signs of tendon-sheath irritation or osteitis were present dry powder was also inserted.

**Results.**—In this series, as in paronychias, variability in the course of healing was much greater in the controls. Pain was so constant a feature that it was thought of value to compare its persistence after operation in the two series. Since these were outpatients the emotional influence of different dressers was eliminated, as was also any knowledge that one set of patients was receiving different treatment from the other. Pain and throbbing in all but 3 control cases lasted for 1–9 days where there was a simple pulp infection and up to 21 days where there was osteitis. Of the penicillin cases, 19 suffered no pain at all, gaining immediate relief after operation, and the longest period of pain among the remaining 8 was 4 days. Pus was constant in the control series and drying followed comparatively rapidly when it disappeared. It was seen in only 5 of the penicillin cases and was scanty when it did appear.

Expectant preoperative treatment was carried out in half of each series. Though numbers were small, its value for control cases is possibly shown by arranging the cases according to the duration of sepsis. The post-operative course varied considerably more in those operated on after 1–3 days of symptoms than in those operated on at the end of a week, provided they escaped bony involvement. By contrast, the penicillin cases showed much the same time and variation in drying, whether operated on early or late.

WEB-SPACE INFECTION

The general factors affecting prognosis in this group (tables IV and V) differed little in the two series. In 1 control and 3 penicillin cases two spaces were involved. There was one thenar-space infection in each. Expectant treatment was carried out in more than half the cases, operation being performed when pus had reached the subcutaneous tissues. Incision into the web was sometimes accompanied by incision in the palm over the sinus left by a penetrating wound. In the thenar-space infections an incision was made on the dorsum of the hand and a way opened between the muscles to the space.

Most patients were treated in the ward with rest in bed and heat cradles when necessary. The controls in this

TABLE VI—TENDON-SHEATH INFECTION: ARREST OF SEPSIS

	Bacteriological findings: number of cases								Days to disappearance of—					
	Total	Initial organism				Growth by 8th day			fever		pus			
		Staph. aur.	Str. pyo.	Both	Nil	Pr	Dm	Dp	Mean	SD	Mean	SD		
Control	11	6	1	2	2*	11	0	0	10	12.0	± 8.8	40.4	± 21.4	
Penicillin	11	4	3	2	2†	0	6	4	11	3.7	± 2.6	5.9	± 5.8	
										Difference	8.3	± 4.0	34.8	± 7.0

\* Staph. aureus cultivated by 2nd day in both cases.

† No pathogens cultivated.

‡ In 1 case (excluded) fever disappeared in 106 days and pus in 113 days.

TABLE VII—TENDON-SHEATH INFECTION: RESULTS

	Complications							Further opn.	Loss of digit	Movement of digit by 6 months			Full movement in rest of hand		Healing			
	Number of cases									Cases	Full	Im-paired	Use-less	Days		Cases	Days	
	Total	Soft-tissue extension	Death of tendon	Arth-ritis	Osteo-myelitis	Pulp infec-tion		Mean	SD					Mean	SD			
Control	11	10	7	2	1	0	9*	5	0	4	2	9†	41.4	± 36.7	11	58.9	± 30.3	
Penicillin	11	0	0	0	0	1	1	0	5	4	2	11	7.3	± 3.3	10‡	34.1	± 18.6	
													Difference	34.1	± 12.3		24.8	± 10.9

\* 15 operations in all.

† 2 control hands, full function not returned at 180.

‡ 1 treated wound not healed at 180.

TABLE IV—WEB-SPACE INFECTIONS: ARREST OF SEPSIS

	Bacteriological findings: number of cases					Days to disappearance of—				
	Total	Initial org.	Growth by 8th day			pus		swelling		
			Staph. aur.	Pr	Dm	Dp	Mean	SD	Mean	SD
Control	9	9	9	0	0	15.7	± 16.0	13.1	± 13.6	
Penicillin	9	9	0	3	6	3.6	± 3.33	7.7	± 5.2	
						Difference	12.1	± 5.3	5.4	± 4.9

TABLE V—WEB-SPACE INFECTION: RESULTS

	Total cases	Complications: number of cases							Full movement		Healed (days)		
		Soft tissue extension	Tenosynovitis	Death of tendon	Osteitis	Arthritis	Further opn.	Loss of finger	Mean	SD	Mean	SD	
Control	9	3	2	2	1	1	3*	2	24.7	± 17.3	34.2	± 20.3	
Penicillin	9	1†	0	0	0	0	1	0	10.4	± 8.3	18.8	± 6.5	
									Difference	14.3	± 2.1	15.4	± 7.1

\* 5 operations in all.

† spread to a 3rd web space.

instance received saline soaks followed by eusol packing. One case received oral sulphathiazole—26 g.—after operation. Penicillin treatment followed the usual lines. Cetavlon as a preliminary wash was not used in the ward dressing station.

**Results.**—In the milder cases the healing time did not differ greatly in the two series, though the controls passed through a stage of more severe inflammation. In the more serious infections there was a well-marked difference. Variability in prognosis was again a feature of the controls, and early return of the use of the hand with no further loss of tissue the most striking feature of the penicillin series.

TENDON-SHEATH INFECTION

This group (tables VI and VII) was studied with the greatest attention, since among the examples of more severe sepsis it approached most nearly to a clinical entity. Tenosynovitis occurring as a complication in other groups was excluded, as was also suspected tendon-sheath infection which did not give evidence at operation of increased fluid or perforation of the sheath by a septic sinus. A clinical rather than bacteriological criterion was adopted since a subcutaneous abscess or sinus was always present, and when this was explored first the swab from the tendon sheath was likely to be contaminated from the wound. In 4 cases—2 in each series—where the accompanying sites of infection were not opened at the first operation, swabs of the turbid fluid from the sheath were negative. These sheaths were clinically morbid and in the control series gave subsequent evidence of a very severe infection.

The sexes were distributed equally between the two series—9 males and 2 females in each—and ages approximated closely. Second and third digits were equally represented; there was one fifth digit in the penicillin series and no thumb in either.

The severity of the lesion was judged by the type of fluid in the sheath (clear but in excess, turbid or frankly purulent); condition of tendons; and by extension into other spaces. By these standards 4 control and 6 penicillin cases were severe. Bronchitis and thrombophlebitis complicated one control; one severe penicillin case had to be treated as an outpatient after the 4th day.

Operation consisted usually in exploration of any previous sinus, followed by a lateral incision along the digit affected, retraction of blood-vessels and nerves, and opening of the sheath along the length of the digit, bridges being left opposite the interphalangeal joints. The sheath was opened near its root by a second incision in the palm. Web spaces were incised when pus had tracked into them.

Five controls received a sulphonamide by mouth—sulphathiazole 26–39 g. in 4 after operation (followed in one bronchitic patient by sulphamezathine 60 g.), and sulphanilamide 25 g. in one streptococcal case before operation. One penicillin patient with a streptococcal infection—the most severe—received sulphanilamide 10 g. for two days before operation. His temperature was rising; redness, swelling extending well up the forearm, lymphangitis, and axillary adenitis were well-marked by the time operation was carried out. The sulphanilamide had had no obvious effect.

Controls were dressed as for web-space infections, twice a day where there was copious pus, and one received local applications of sulphathiazole cream. Plaster was used after the 7th day in one control and during the lengthy convalescence of another. It was applied to one penicillin-treated hand for a few weeks when healing was much delayed. Ascorbic acid in sufficient quantities to appear in the urine was given to 4 controls and to a penicillin patient who was one of the least severe cases and the quickest to heal (15 days).

Penicillin treatment followed the same lines as in other groups—at operation a liberal dressing of the dry Ca salt (40–100 mg. of a 10 unit per mg. preparation) was spread over all parts of the wounds, followed by a packing of paste (150 or 250 units per c.cm.) on gauze. Dressings were not repeated more than once in 24 hours and in the later cases were discontinued by the end of the first week. When slough persisted and bacteriological reports indicated the presence of *Staph. aureus* or *Strep. pyogenes* dressings were continued but less frequently. These infections were so severe that there was a tendency to overdose, but even so, the longest involved the use of only 13,000 units; other cases received 2500–7000 units.

All patients were given instruction and encouragement to move their fingers after the 5th day, though this was temporarily suspended in those controls which showed signs of exacerbation.

**Results.**—The course in the controls was, as usual, difficult to predict, infections which appeared mild at operation sometimes progressing to much slough formation and even loss of a digit. Pus was copious in nearly all controls and slough a prominent feature. The control case shown separately in table VI had a most persistent mixed infection with many exacerbations and extensions of inflammation and sloughing. Though he received 30 g. of sulphathiazole he had intermittent fever for 106 days, pus persisted for 113 days and his wound was not healed till 119 days. Pus was always scanty in the penicillin patients and only distinguished with practice from the residues of paste dressings; the times in the table represent the upper limit at which there was any chance of pus being present.

Though sepsis was arrested before the end of the first week in 10 of the penicillin patients, and controlled in the eleventh, which had a persistent slough, healing time varied within wide limits. In milder cases it was as short as 2–3 weeks, in one severe case longer than 24 weeks (see general discussion later). The early return of movement was again a prominent feature and appeared to go hand in hand with the reduction in swelling. Dorsal swelling after operation was well-marked in both series, but, whereas it took from 5 to 82 days to subside in the controls, the oedema insensibly merging into a firm thickening of the whole hand, the longest period for which it persisted in the penicillin cases was 16 days and the shortest 1 day.

Another aspect of the comparison, not too easy to assess, was general health. These patients with severe sepsis were ill, suffering from fever, loss of appetite, pain and often sleeplessness; when sepsis persisted their pallor and even loss of weight were obvious. Penicillin patients were fit enough to be asking to go home in the second week; their dressings were often painful but apart from this they appeared to recover rapidly from their infection and to suffer little pain.

Where frank pus had not developed in the sheath at the time of operation, penicillin patients regained the full use of the hand and affected finger in 4–6 weeks without recourse to finger-exercise classes, and were ready and anxious to return to work. Even in the 6 patients, whose tendon sheaths had contained pus at operation, penicillin treatment alone appeared to achieve as much as the continuation of remedial exercises in control cases long after their discharge from the wards. (Of the 3 penicillin patients in this group whose remedial exercises were prolonged, none showed any definite benefit.) It appeared as if the rapid resolution of sepsis had accomplished the same task as was achieved in control cases by weeks of exercises after healing.

**Return to employment.**—The data from the tendon-sheath infection also make it possible to measure the value of penicillin treatment as a means of accelerating the patient's return to useful employment; it is noteworthy that the average absence from work of 10 control patients was  $100 \pm 50$  days and that of all the treated patients  $54 \pm 19.5$  days. End-results, observed up till 6 months from the first incision, are compared in fig. 1.

Three tendon sheaths which were explored during the period of this investigation and which showed no evidence of infection at operation gave an indication of the length of time in which healing and functional recovery might be expected to take place in this situation in the absence of sepsis. In 2, healing took place in 15 and 23 days and function returned in much the same time. The third, whose wound became infected with *Staph. aureus* from a subcutaneous abscess, was completely healed in much the same time, but complete function was only regained after 57 days.

#### ABSCESSSES

This group (table VIII) comprised well-formed and circumscribed abscess cavities in various parts, including dorsum and palm of the hand, forearm, arm, axilla, groin and back of the neck. As far as possible the same sites were included in each series. Three-quarters of each series had received expectant treatment and in some resolution was obviously taking place (cultures from one control were negative and another showed only scanty growth); the value of using a bacteriostatic drug at this

TABLE VIII—ABSCESSSES. ARREST OF SEPSIS: HEALING

	Bacteriological findings : number of cases								Days till disappearance of pus		Dry	
	Total	Initial organisms				Growth by 8th day			Mean	SD	Mean	SD
		<i>Staph. aur.</i>	<i>Str. pyo.</i>	Both	Sterile	Pr	Dm	Dp				
Control	12	9	2	0	1	9	1	2	9.6	$\pm 7.8$	23.6	$\pm 10.3$
Penicillin	12	8	1	3	0	1	4	7	3.4	$\pm 1.8$	20.8	$\pm 10.9$
									6.2	$\pm 2.8$	..	..
			..	..	..	..	..	..				

stage was not likely to be great. In one penicillin patient, infected above and below the dorsal fascia of the hand, adequate access was only obtained at a second operation, and times have been measured from then.

Three abscesses—in the glands of axilla, groin and occiput respectively—were treated by injection of penicillin solution. The abscess was incised at the uppermost part in relation to the patients' position in bed, loculi were opened and the contents evacuated. Rubber tubing,  $\frac{1}{4}$  in. in diameter, was placed in the wound so that its extremity reached to the lowest part of the cavity, the wound was sewn up and the rubber tubing sutured to the skin. Firm dressings were applied, the

TABLE IX—BACTERIOLOGICAL FINDINGS IN SEPTIC LACERATIONS AND MISCELLANEOUS GROUP

Cases of septic lacerations	Total	Initial organisms				Growth by 8th day		
		Staph. aur.	Str. pyo.	Both	Coli-form	Pr	Dm	Dp
Control ..	5	2	0	3	..	5	0	0
Penicillin ..	6	1	2	3	..	0	3	3
<i>Miscellaneous cases</i>								
Control ..	12	10	0	2	0	12	0	0
Penicillin ..	18	10	2	5	1	2	8	8

distal end of the tubing being brought through them. Penicillin, 500 units per c.cm., was then injected into the cavity. Injection preceded by aspiration was repeated 12-hourly for 4 or 5 days. At the end of that time the dressings, tubing and stitches were removed. A dry dressing under elastic plaster was applied and left in situ till the mouth of the sinus had dried.

**Results.**—Healing time, and in some cases cessation of pus were much the same in the two series, but, as in other groups, the amount of pus formed was much less under penicillin treatment. In the abscesses injected with penicillin solution the skin edges healed by primary union. When the dressings were removed induration of surrounding tissues had subsided and cultures were free of the initial organism. There were no painful dressings, so characteristic a feature of septic cases.

SEPTIC LACERATIONS OF HAND

The septic lacerations in the penicillin series were of such severity that certain aspects are worth describing, but in this and the following group the only comparison of value is bacteriological (table IX). Clinically, each case was different and comparison is impracticable. The penicillin cases, with one exception, had the most serious infections introduced into the ward during the time of the investigation. All had open suppurating wounds which involved more than one tissue. There were 3 with compound fractures, 2 with suppurating joints and 4 with tendon-sheath infections, one with a necrotic terminal phalanx and another with suppuration and necrosis in the deeper planes of the palm. Injury had occurred 12-17 days earlier and was treated by excision, suture and plaster splinting. Signs of infection did not develop for upwards of a week and the cases were treated expectantly for from 2 to 8 days. No sulphonamides were given. By the time they came to operation the 5 inpatients had fever, considerable swelling of the hand, and ragged, purulent and sloughing wounds.

Hanging distal segments of digits were removed at operation in 2 instances but were retained in the remaining cases, including the necrotic finger. Treatment with penicillin followed the usual lines. Intensive treatment was given for 6-10 days, followed by paste only until all dead tissue had separated. No case received more than 13,000 units.

Adequate access to all sites of infection was obtained at the first operation in all patients but one, and he demonstrated well its necessity when penicillin is applied locally. An open suppurating terminal interphalangeal joint, with the tendon sheath perforated near its insertion and the middle phalanx stripped of part of its periosteum, was found at the first operation. Incisions were made on both sides of the joint, penicillin being applied in the usual way. Though pus ceased to collect in the wounds there was evidence of its presence in the tendon sheath by the 3rd day. This was then opened on the finger only, but,

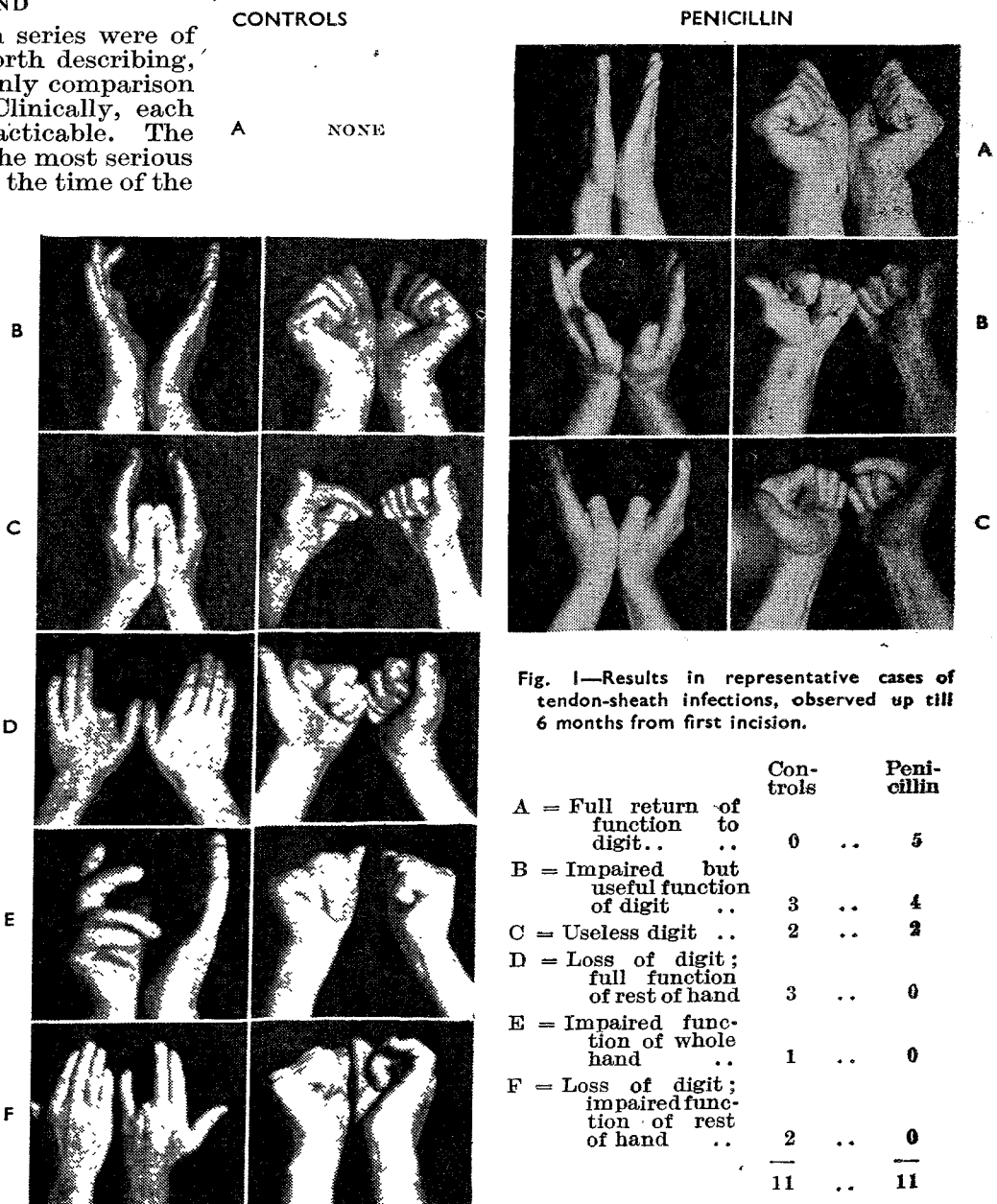
though these wounds were free of pathogens and pus by the 7th day, perforation of the sheath had occurred in the palm and led to the collection of pus in the thenar and first web spaces, reaching as far as the level of the carpal tunnel. When these cavities were finally opened all wounds became free of pus and pathogens within 4 days and remained so for weeks without further treatment.

**Results.**—The table showing the arrest of bacterial infection has some interest, although only one control case was comparable in severity or extent of damaged tissue to those treated with penicillin.

Once sepsis has been controlled the difficulty of regaining full function of the hand, even after the removal of infected digits, is the major therapeutic problem. The period of many months spent in treating such loss of movement is well known to all concerned with the surgery of the hand. It is regrettable that the control series is not of value as a comparison, but patients who had had more severe injuries, comparable to those in the penicillin series, were seen during the period of this investigation, and on them these facts were readily demonstrated.

The results of the penicillin treatment may be set out in a general way, as follows:

(1) In 4 cases full function of all parts of the hand, other than the digit primarily affected, had returned in 2-3 weeks. The most severe case—compound fracture of phalanx, tendon-sheath infection, and sloughing and suppuration in all planes of the middle palmar space as far as the carpal tunnel—regained full movement in 2 months without special physical therapy. In the only similar case seen in the preceding year the patient had not closed his fist completely 12 months after sepsis was first apparent. The 6th penicillin patient was



suffering from disseminated sclerosis, but, in spite of this and of having two suppurating wounds communicating with separate tendon sheaths, he regained full flexion in 3 months. Of 2 similar untreated cases seen in the hospital, a young man of 20 had not regained full function of remaining parts till 5 months from operation and a man of 43 could not grip after 8 months. (The one control case of this group which can be considered comparable had not regained full movement, in spite of removal of the digit, after 4 months.)

(2) Apart from projecting fragments of bone, none showed sequestrum formation.

TABLE X—WHOLE SERIES: INITIAL INFECTING ORGANISM

—	Total	<i>Staph. aur.</i> alone	<i>Str. pyo.</i> alone	<i>Staph. aur.</i> and <i>Str. pyo.</i>	Hæmolytic strep.	Micrococci	Coliform
Control	102	74*	6	21	0	1	0
Penicillin	110	66†	13	27	1	2*	1

\* 3 first isolated 2nd day from operation.

† 1 " " " " " " " "

(3) Apart from the case with a necrotic phalanx, there was no loss of a digit after penicillin therapy was begun or of any other tissue in fingers or hand.

Further results worth noting were: tendons declared at operation to be dead regained their function; ankylosis occurred in cases with arthritis without any sequestrum formation, and movement in adjoining joint returned so that useful digits were preserved. More than one surgeon had warned these patients that they would lose their fingers.

#### MISCELLANEOUS GROUP

These were mainly septic wounds (fig. 2) or surfaces of some weeks' or months' duration where treatment with penicillin was not related to the time of operation. A bacteriological comparison is the only one of value (table IX).

This group does no more than indicate the value of penicillin in such conditions as chronic septic dermatitis; in preparing infected surfaces for skin-grafts or stumps for amputation, and in preventing the extension of a septic process.

#### General Considerations

##### BACTERIOLOGICAL OBSERVATIONS

Bacteriological comparison was applicable to all cases of both series. Table X summarises the original infecting organisms. Changes in or persistence of original growth from first swabbing till healing had taken place are shown in table XI.

The response to the drug in almost all penicillin cases led to an attempt being made to find the earliest time at which bacteriological evidence of the arrest of sepsis could be obtained. It was not practicable to swab all cases daily, so that an exact date for the arrest of infection cannot be stated. By the 8th day practically all cases which had not healed had been swabbed a second time and this day is therefore selected for comparison, although growth from the majority of penicillin wounds was scanty or absent before then (table XI).

The body appears to be quite capable of dealing with a scanty growth of organisms in open wounds once granulations have formed. This is borne out by the observations on the controls in which pus formation had ceased, the wound was superficial and healing was progressing though pyogenic cocci could still be cultivated from the surface.

**Reinfection.**—Organisms reappeared in cultures after disappearing from some of the penicillin-treated wounds. (The instances of disappearance from control wounds were so few and so late that a comparison is valueless.) It is impossible to say whether this reappearance was an indication that infection had not been completely eliminated or that a fresh infection had been added. When it occurred during penicillin administration the former interpretation was given. In the 5 instances where this happened inadequate access or the presence of dead tissue had prevented the complete elimination of infection.

**Newly appearing infection.**—This was found in some wounds of both series but it is noteworthy that, whereas *Strep. pyogenes* was the most usual secondary invader in

TABLE XI—WHOLE SERIES: GROWTH DURING COURSE, AND BY THE 8TH DAY

—	Total cases	Growth during course					Growth by 8th day		
		Pr	Dm	Dp	Not done	Healed*	Pr	Dm	Dp
Control ..	102	73	14	10	2	3	93	2	2
Penicillin ..	110	4	23	78	1	4	9	40	56

\* Healed before second swab.

control wounds, among penicillin-treated wounds it was coliforms. The clinical significance of the former is difficult to assess, though they were commonly found in the more serious infections of the outpatient groups. Though penicillin-treated wounds appeared to be more susceptible to infection by coliforms, no effect on the clinical course was noted in the outpatient groups. In the more widely open wounds of the 5 ward patients epithelium seemed to grow more slowly and even to disintegrate when newly formed. Daily applica-

TABLE XII—NEW-APPEARING INFECTION

—	Total cases	<i>Staph. aur.</i>	<i>Str. pyo.</i>	Coliform
Control ..	21	3	16	2
Penicillin ..	21	4	1	16

tions of sulphonamide powder removed these organisms in 5 days, though they returned after discontinuance in the two cases which were not already healed (table XII).

**Persistence of growth.**—Table XI shows there were 9 treated cases whose wounds showed no response to penicillin by the 8th day. These were:

(a) Two paronychias which were healed in the same time as other penicillin-treated cases, though the amount of penicillin used was not sufficient to remove all the bacteria.

(b) Five cases in which dead tissue was present, usually where bone was involved. When the slough disappeared or the projecting bony fragment separated the organisms also vanished. Signs of inflammation, however, subsided as quickly in these cases as in those without slough.

(c) Two where surgical access was inadequate. Further incisions were followed by the disappearance of organisms within a few days.

#### PROGRESS OF WOUNDS

The earliest and most striking difference noted between the two series was in the pus formation. Pus did not appear or was scanty and had completely ceased to form within a week from operation in all but 6 cases among the penicillin series. In the controls, with the exception of 1 case, it continued for anything from 3 to 113 days.

Where incisions were made directly into well-formed abscess cavities lined with granulation tissue in the penicillin series slough was very much less than and separated as rapidly as in control wounds. Once separated there was no further formation.

Where incisions were deepened through inflamed tissue which had not reached the suppurating stage other differences were noted. They were seen in pulp-infection wounds but still better in the larger incisions made for tendon-sheath infections. Though free bleeding at the time of dressing obscured the surfaces of the control wounds for the first few days, there was no apparent difference between the two series in the early stages; sharp-edged, steep sided wounds passed into more open gutters with varying degrees of slough formation on the surfaces.

In the controls thick pus had appeared by the 2nd to the 4th day and was greeted with relief by the dressers. It was followed by softening and separation of sloughs but fresh sloughs continued to appear, both on the surface and in the depths of the wound. The sides of the wound continued to swell, and gaped to a considerable degree, till the digit looked like a fat split sausage. Granulations grew exuberantly over the whole surface, filling the wound and rising above the level of the surrounding skin.

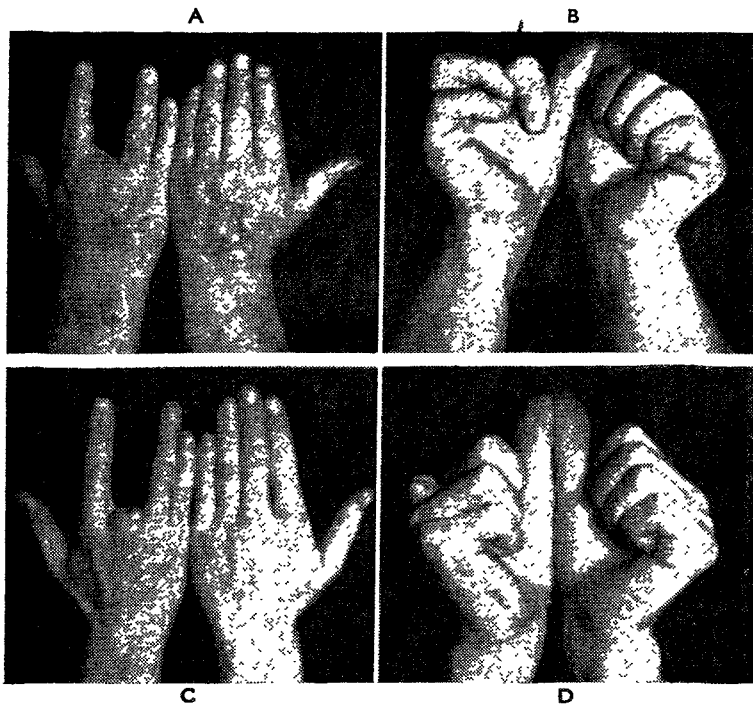


Fig. 2—Right palmar sepsis

A and B, controls; following laceration of palm and tendon-sheath infection; hand cannot grip 52 weeks after first incisions in spite of prolonged massage and remedial exercises. C and D, penicillin-treated; following compound fracture of proximal phalanx and tendon-sheath infection; hand closed fully 8 weeks from incisions and removal of digit without remedial exercises.

In penicillin-treated cases, if pus formed at all it was so scanty as seldom to be distinguishable from the penicillin paste residue. The small amount of bleeding during early dressings added to the lack of pus formation made the "dirty" stage of the wound appear much longer than in the control series, whereas in reality granulation tissue began to form at the same time in both. Slough, if it did form, did not disappear in bulk but remained on the surface of the wound in the more severe cases till well into the healing period. Gaping of wound walls sometimes occurred, but was of much less extent than in the controls, and granulations remained smooth and moist and were not abundant. Wounds which healed rapidly did not gape more than  $\frac{1}{2}$  in. and the granulation tissue was sufficient to bridge this gap, but when healing

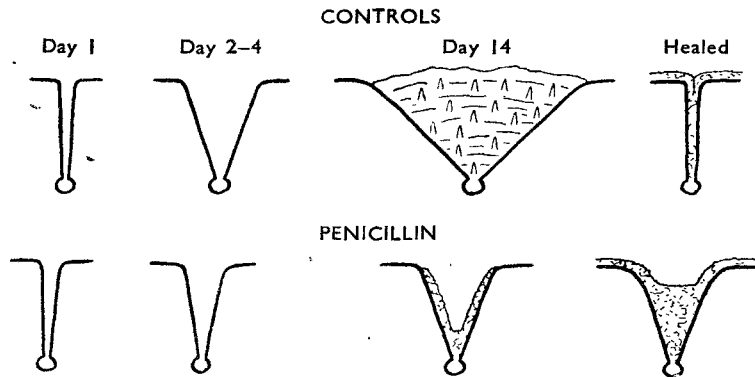


Fig. 3—Diagram showing abundance of granulation tissue in control wound, and lack of it in penicillin-treated wound, which therefore depends on epithelial growth for closure.

took more than 3 weeks the gap grew wider. In these cases it appeared that the newly formed fibrous tissue was not sufficient to draw the edges together as was obviously the method of healing in the controls, where epithelium merely had to bridge a narrow gap to complete the process. In the penicillin wounds epithelium grew down into the wound and later across the gap between the two sides, eventually forming a smooth valley along the side of the digit. Scars so formed were soft, seldom puckered and not tender. Final closure of the wound, therefore, depended mainly on contraction of granulation tissue in the controls and on epithelial growth in the penicillin cases (fig. 3).

Pulp-infection wounds demonstrated this difference particularly well. No packing was used in the penicillin

cases after the 5th day so that wound walls fell together readily but the skin layer always retracted further than the subcutaneous tissue. Even though subcutaneous tissues remained in apposition, epidermis had to grow over an oval area about 3 mm. wide before healing was accomplished.

SWELLING

An increase in the swelling of surrounding parts was very obvious on the day after operation. This occurred in both series and in all groups except possibly paronychia. Where infection had reached the palm, dorsal swelling was prominent. Its subsidence was taken as a useful index of the diminution of the infection. The tendon-sheath infections again form the best series for comparing this, for it was a well-marked and constant accompaniment of the condition. The controls showed a wide variation in the degree and times of increase and of subsidence of swelling. It disappeared in the 3 mildest by the end of the 1st week, in others it continued for 14-100 days. When the oedema disappeared a firm generalised thickening remained which persisted in some cases for weeks or months. Penicillin cases all showed an increase of swelling on the 1st day after operation and in 2 cases on the 2nd. All were subsiding between the 2nd and 4th day, subsidence being complete in 3-16 days.

SPECIAL TISSUES

*Tendons.*—The majority looked pearly and taut when sheaths were opened. One of each series appeared to be sloughing at the time of operation, granulations were growing on a few, and in 3 of the penicillin patients the tendons were so lax and lustreless as to be considered non-viable by the surgeon. In the 11 primary and 3 secondary infections of the control cases death of the tendons occurred in 9. Destruction of the tendons in some cases extended into the palm beyond the sheath and even into extensor tendons as well. Survival of all tendons, even those suspected of being non-viable, occurred in the penicillin-treated patients, as evidenced by return of movement at all joints. In the cases treated at later stages, however, when there were granu-

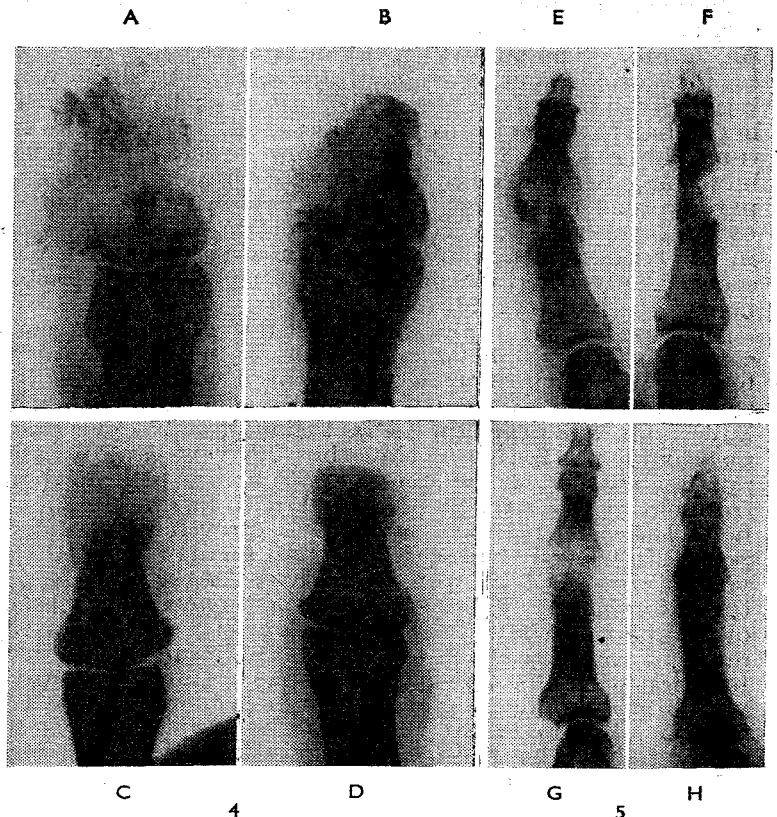


Fig. 4—Osteitis of terminal phalanx. A and B, controls; C and D, penicillin-treated.

A, 7 weeks from first incision. B, 22 weeks from first incision. C, 1 1/2 weeks from incision. D, 6 weeks from incision.

Fig. 5—Osteo-arthritis of interphalangeal joint. E and F, controls; G and H, penicillin-treated.

E, 6 weeks from injury; 2 weeks from first incisions, before sequestrectomy. F, 12 weeks from injury; 8 weeks from first incisions. G, 3 weeks from injury; 1 1/2 weeks from incision. H, 11 1/2 weeks from injury; 10 weeks from incision.

lations and thick pus in the sheath, movement was impaired, and in the 2 most severe cases almost lost.

**Bones.**—There was evidence of bony involvement in 7 controls and 11 of the penicillin cases. Sequestra had to be removed from 4 of the controls. Apart from projecting bony fragments no sequestra were removed from the penicillin series. Radiograms demonstrated the same well-marked rarefaction of bone after penicillin therapy as was noted in an earlier investigation (Florey and Florey 1943), so much so that reports received from radiological departments were at variance with the clinical condition. Recalcification of bone occurred readily in spite of the great amount of absorption. In the most severe pulp infection the whole head of the terminal phalanx had re-formed 6 weeks after operation (fig. 4). In 2 of the mildest control infections healing of the bone took about the same time, but in the 2 more severe controls the head of the terminal phalanx had not re-formed in 16 and 26 weeks respectively. Swelling of the digit and aching after much movement occurred for months after healing in 4 of the controls, necessitating amputation of the terminal phalanx in one instance. It was not met with in any of the penicillin cases.

**Joints** were involved in only 5 cases (fig. 5). Three penicillin cases and one control became ankylosed. The other control had to have his digit removed because sepsis had spread to tendons and caused their death.

### Discussion

There can be little doubt from these series that the local application of penicillin can arrest sepsis rapidly in the hand. That it can be controlled between the first application and at latest the third day and completely overcome by the end of the first week may be claimed, provided always that adequate access has been secured and all dead tissue removed. Although, after incision, swelling of the part increases, spread of infection is not necessarily the cause, since surgical trauma on already inflamed tissue or circulatory disturbances, consequent on the use of a tourniquet at operation and tight bandaging afterwards, may be responsible.

It must be emphasised that for all but 3 of the present series there was no modification of the usual surgical procedure. The surgeon must decide whether to make his incision at an early stage of inflammation, thus opening up fresh planes of tissue to its spread, or to wait in the hope that the infection will be localised. If he waits he runs the risk of the inflammatory process producing increasing destruction. In the penicillin series, among paronychias and pulp infections prognosis was better or at least not altered when incision was early, and in the tendon-sheath infections return to normality was secured only when incision was performed early, that is, before pus had formed.

Because of the rapid disappearance of pus the considerable interval between its cessation and complete healing in penicillin cases as compared with controls led to the question whether the drug delayed healing. The impression was based on the fact that though septic cases may exude pus for a long time they dry very rapidly after pus has ceased; sometimes the problem is to keep them from closing over till pus has ceased to form. In superficial lesions, where only epithelial growth was needed, penicillin halved the mean time and greatly reduced the variability. But as wounds became larger and deeper the difference grew less. The dependence on a wealth of granulation tissue for knitting together septic wounds must be foregone when surgery is contemplated in conjunction with effective bacteriostatic action. The great variability in healing time among penicillin-treated tendon sheaths may therefore be at least partly accounted for by the lack of the stimulus of infection to fibroblastic growth.

In assessing the viability of tissue at operation somewhat revised standards are required when a bacteriostatic drug is used. Further destruction is prevented, and, as exemplified by some tendons in this series, tissue considered dead by ordinary standards is capable of returning to functional activity when the effect of sepsis is rapidly eliminated.

The end-results of infections of the hand cannot be assessed in terms of healing time alone. Among the controls it was often months after the original wounds

had healed before a man had an effective hand with which to work, whereas some penicillin cases felt so little disturbed by their wounds that they insisted on returning to work while these were still open. Among the pulp and tendon-sheath infections alone (35 penicillin-treated compared with 35 controls), the actual working time saved by penicillin treatment was 1000 days. (Insufficient data made an assessment of the corresponding figure for all the groups impossible.) The quick return of function would seem to be a result of small formation of fibrous tissue because resolution occurred before the fibroblast reaction had become extensive. Movement returned as soon as excess inflammatory fluid had been absorbed from the inflamed tissues. Movement was slowest to return in the most severely affected digit, but in the severe cases more movement was possible before than after complete healing had taken place—that is, before granulations had turned into fibrous tissue.

As to the best methods of administration, the type of preparation used was governed by the surgery. Open wounds had to be treated by some means that would retain the drug in situ. For this reason and because of its ease in handling a dry preparation of the Ca salt was used, but as it rapidly dissolved in the tissue fluids the action was prolonged by the use of a weaker paste in addition. Packing was only employed in order to convey the preparation to all parts of the wound. This method had two disadvantages—the possibility of damaging wound surfaces by the initially high concentration of the Ca salt, and the keeping of the wounds open. About half the patients complained of burning, but not if paste or solution was used alone. The preparation used contained not more than 1% of penicillin and the impurities present may have accounted for any ill effect on the cut tissues.

It seems well worth while exploring further the possibility of closing or partially closing abscesses after evacuating the pus, penicillin solution being instilled for the next 4–5 days. The 3 cases so treated did well, no disadvantage being apparent from this method, but it was not tried in any other cases.

A major advantage gained by penicillin treatment for the patients and staff was the great reduction in the number of dressings required. Once pathogenic bacteria had been eliminated further dressings were only needed as a protection.

The great economy effected by local application as compared with general administration was well demonstrated. Not more than 500,000 units was used to treat 100 cases locally. This is about a quarter to half the amount needed to treat a single severe and well-established staphylococcal infection systemically.

### Summary

A comparative study of 212 acute infections, mainly of the hand, has been made. About half were treated by current methods and the other half by local penicillin application, superimposed on the usual surgical procedures.

The great majority of control cases remained septic for well over a week and nearly three-quarters were infected till their wounds healed. In the penicillin-treated series, given adequate access and removal of dead tissue, sepsis by clinical and bacteriological criteria was eliminated within a week.

In the penicillin-treated cases pus was scanty and often absent from operation onwards. No further destruction of tissue apart from the superficial layers of the wound was seen, and this only rarely. Relief of pain and throbbing and improvement in general condition have been striking, and penicillin has effected a great saving in the number of dressings.

Mean healing time has been considerably reduced by penicillin treatment, but a few cases have shown undue prolongation of healing. Other factors may have affected this result.

In cases of inflammation of bone penicillin treatment led to rapid rarefaction concurrently with improvement in clinical condition. Reformation of bony tissue took place readily.

The rapid return of mobility to infected parts was one of the most striking features of the penicillin series, but

complete normality was not regained after tendon sheaths had contained frank pus.

Harmful effects of the dry impure calcium salt on wound surfaces not protected by granulation tissue cannot be excluded. Some patients complained of burning when the dry salt was used.

Among chronic cases penicillin proved of value in preparing infected surfaces for skin-grafting and infected stumps for amputation, and for procuring complete healing in chronic dermatitis.

The total amount of penicillin used to treat over 100 cases was not more than 500,000 units.

Complete figures for 35 of the penicillin-treated cases showed a saving of about 1000 man-days of working time as compared with the controls.

These results have been obtained by careful attention to technique and consistent 24-hourly dressings for a minimum period of 5 days.

We are indebted to Mr. William Gissane, clinical director of the Birmingham Accident Hospital, for providing facilities for carrying out the clinical work; to Mr. T. W. Howat and Mrs. O. Müller, in whose departments most of the work was done; and to the other surgeons and staff of the hospital, and members of the Sir William Dunn School of Pathology, Oxford.

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## REHABILITATION OF THE CHEST CASE

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THE science of rehabilitation of patients suffering from injuries of bones, joints and muscles has developed along well-defined lines. It aims at the return to optimum function of the injured member and the restoration of the general health in the shortest possible time. Since such patients rarely have any serious lesion of the vital cardiac and respiratory systems, their return to full health depends essentially on the rapidity with which normal muscular tone, maximum joint movement and firm bony repair can be established.

Patients who have sustained a chest injury or have suffered from an inflammatory condition of the lung or pleura, or who are recovering from a thoracic operation, require a form of rehabilitation which though basically the same in principle as for other conditions often differs in detail. The respiratory system is primarily damaged; the cardiovascular system is secondarily affected, either by alteration in the intrathoracic mechanics, or by toxæmia, as well as by the long confinement to bed which has been necessary in a high percentage of such cases.

These patients, if discharged from the hospital wards to the usual type of convalescent home, take long to recover. They are rarely given graduated exercises, although they may eventually be sent to join a physical training course where they are expected to undertake severe exercise for which they have not yet developed the necessary respiratory or cardiac tone. The PT instructor as a rule has no specialised knowledge of this type of case, and the patient may receive much harsh criticism for his inability to perform exercises of which he is incapable. For the most rapid and complete return to normal of chest cases, rehabilitation must be undertaken by a team of workers specially trained in respiratory exercises, with knowledge of the physiology and anatomy, and able to detect the first signs of respiratory and cardiac embarrassment.

The following is an account of the methods adopted and the investigations made in a rehabilitation centre attached to a chest surgical unit, which undertakes the final recovery of all traumatic and operation cases. The centre is also available to outside civilian and Service

hospitals, who can send in their chest surgical patients who may have not been primarily transferred to the unit for treatment, or patients recovering from inflammatory conditions of the lung—e.g., pneumonia. These facilities have been well utilised.

#### CAUSES OF DISABILITY

The symptom of which almost every patient complains when he enters the rehabilitation centre is dyspnoea after varying degrees of exertion.

In a normal subject the increased oxygen utilisation of muscular effort results in the formation of more carbon dioxide. The consequent rise in the hydrogen-ion concentration of the blood stimulates the respiratory centre, the breathing becomes deeper and more rapid, and as a secondary result the cardiac output is increased. This hyperpnoea does not become noticeable until the pulmonary ventilation is about twice that at rest. When the subject becomes unpleasantly conscious of his respiratory movements, and of a "shortness of breath," then the condition of dyspnoea has supervened. The nearer the pulmonary ventilation approaches to the vital capacity, the more intense is this dyspnoea. In patients with a damaged respiratory system, the vital capacity is diminished, and dyspnoea is experienced correspondingly earlier. The reduction in the vital capacity is due mainly to mechanical factors, affecting the thoracic cage, pleura and lung, and to the reflex results of pain.

(a) *Weakness and inefficiency of the respiratory musculature.*—Long rest in bed, causing varying degrees of atrophy, supplements the disability resulting from damage to the muscles by wounds or incisions. After trauma or operation, full muscular action is temporarily or permanently hindered by intramuscular fibrosis and intermuscular adhesions; moreover, the nerve supply of segments or of whole muscles may be interrupted. Adhesions may limit the movement of the diaphragm or so distort it that efficient action is impossible.

(b) *Damage to the bony structures of the thorax.*—The loss of portions of ribs causes a diminution in size of the section of the thorax to which they are related, and on inspiration that part of the chest does not expand to the normal amount. Irregular new formation of bone in these areas has the same effect on the thoracic cage, particularly if there are bony connexions between adjacent ribs. If the periosteum has been lost, permanent paradoxical respiration may develop over the wound area. Malunion of fractured ribs, particularly in the region of the neck and angles, may result in a considerable dropping of the anterior segments, with consequent reduction of normal pulmonary expansion.

(c) *Thickening and adherence of the pleura.*—When there has been a total involvement of the pleural cavity by an empyema, the vital capacity is much reduced, for the thickened parietal pleura fixes the internal aspect of the ribs and the normal widening of the lateral and anterior sections of the intercostal spaces on inspiration cannot take place. In consequence the chest wall moves only as a solid block and as such is ineffective. At the same time the thickening of the visceral pleura reduces the expansibility of the lung tissue. Furthermore, during the reparative processes the organising fibrous tissue contracts, drawing the ribs still further down into the position of expiration, and producing a considerable flattening of that side of the chest. There is an alteration in the shape of the ribs, both in their longitudinal curve which becomes flattened, and their cross-section which becomes triangular. A localised empyema will result in proportionately less interference with expansion.

In a non-infective pleural process such as a hæmothorax, the pleural space becomes obliterated and replaced by many fine adhesions. It seems that production of the maximum pulmonary ventilation in a lung depends upon the visceral layer being able to slide freely upon the parietal layer during inspiration, since the thoracic cage does not expand equally in all directions (Best and Taylor 1939). When the two pleural layers are adherent, though not necessarily thickened, the expansion of the lung is irregular, as it is produced by a direct pull through the adhesions, and not by a diffuse suction equally distributed over the surface by the rise in the negative intrapleural pressure. Thickening of the diaphragmatic pleura and diaphragmatic adhesions produce an even greater effect upon the movement of the