AN OUTBREAK OF SALMONELLA HEIDELBERG INFECTION IN A GENERAL MEDICAL UNIT

Treatment with Ampicillin and Neomycin

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On the 18th August, 1963, an elderly woman, who was a patient in a general medical unit at the Belfast City Hospital, developed severe diarrhœa. This was the beginning of an outbreak of *S. heidelberg* infection which lasted two and a half months; nineteen persons became infected, five had symptoms and there was one death.

The Ward Unit.

The unit consists of a male and a female ward, each with thirteen beds. The wards are on the upper floor of a forty-year-old building which is separate from the main hospital. They are connected by a landing to which stairs mount from the ground floor, where there are small casualty wards. A small kitchen also opens from this landing. Items such as bread and butter and toast are prepared here by the domestic staff for the patients, for themselves, and for the nurses, who take a light breakfast in the unit. Main courses are brought from a central kitchen and served from heated trolleys. At the time of the outbreak there were three doctors, nineteen nurses, and six domestics working in the unit.

Bacteriological Methods.

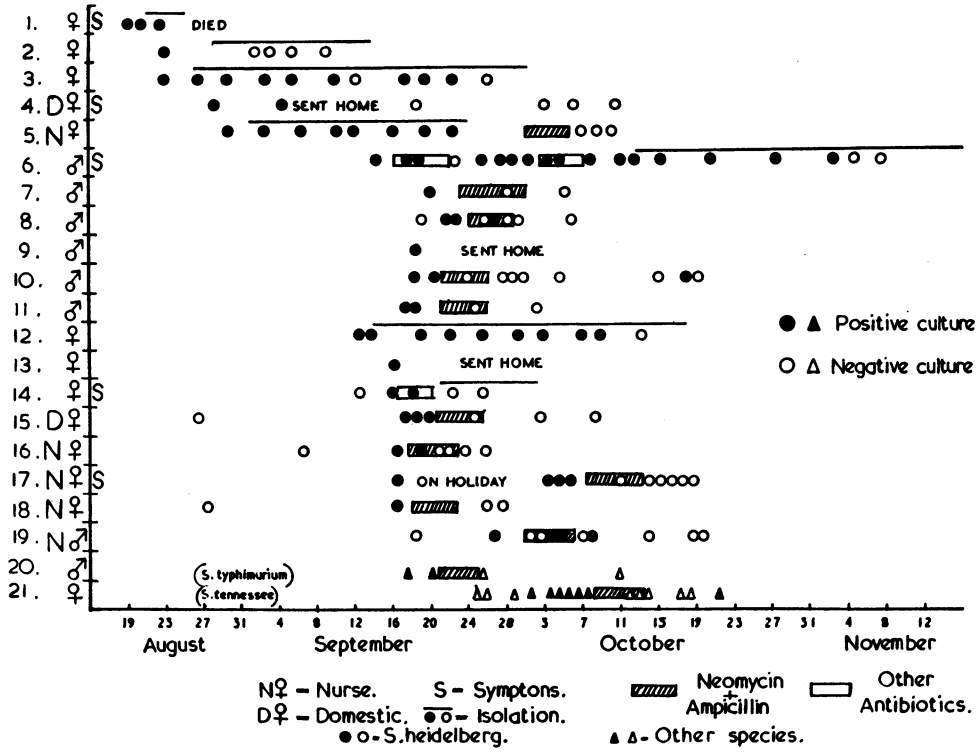
The bacteriological investigations were carried out at the laboratories, Belfast City Hospital. All fæcal samples submitted from patients and staff were examined as recommended by Hobbs and Allison (1945). Primary plating was performed on two selective media:

(a) Wilson and Blair's bismuth sulphite agar, prepared from the Oxoid brand powdered modification of this medium;

(b) Leifson's desoxycholate-citrate agar, as modified by Hynes (1942), to which 1 per cent. sucrose had been added (Murdock, 1954).

Secondary plating was performed on the same two media after overnight incubation in selenite F enrichment medium (Hobbs and Allison, 1945). The primary and secondary sets of plates were both examined after twenty-four and forty-eight hours. Suspicious colonies were inoculated into tubes of composite media (Gillies, 1956) and into tubes of dulcite and lactose. Strains which gave the biochemical reactions of the salmonella group after incubation for twenty-four hours were then tested with the appropriate antisera and their identity determined.

Disc sensitivity tests were carried out. These indicated that the strains of *S. heidelberg* were resistant to sulphonamides and tetracycline, while they were sensitive to neomycin, ampicillin, streptomycin, chloramphenicol, colomycin, and kannamycin.



The Outbreak.

The outbreak started on 18th August, and the unit did not return to normal working until 8th November (see figure). There were two phases.

Phase One.

Five persons were infected in this phase. The first case was a 70-year-old woman with myelomatosis and senile dementia. She had been an in-patient for seven months and was very disabled, being unable to walk. On 18th August she developed diarrhœa. Culture of her fæces next day revealed *S. heidelberg* infection. She was transferred to an isolation hospital, where she died on 25th August.

As soon as the presence of salmonella infection was recognised, one fæcal specimen was taken from each female patient and from each member of the medical, nursing, and domestic staff. Positive results were obtained from two further female patients, one nurse, and one domestic (Cases 2-5). The two patients and the nurse, who were all symptomless, were transferred to the isolation hospital. The domestic worker was supervised by her general practitioner in

her own home. By early October three consecutive negative cultures had been obtained from the nurse and the domestic, and they were allowed to resume work. One patient was returned to the ward to continue medical treatment on 13th September, having had four negative fæcal cultures. The other patient was discharged from the isolation hospital to her home.

When no further cases had occurred by early September, it was felt that the outbreak had come to an end.

Phase Two.

On 14th September an 86-year-old *man* (Case 6), who had just recovered from a severe attack of pneumonia, developed diarrhœa. Within twenty-four hours he had become critically ill and required intravenous fluids on account of extensive fluid loss by diarrhœa. Culture of his fæces revealed *S. heidelberg* infection, but he was too ill to transfer for isolation and was barrier-nursed in the ward.

The recrudescence of the disease suggested dissemination by a member of the ward staff. The following action was taken:—

(i) Both wards were closed for admissions. However, due to an oversight, one woman (Case 21) was admitted during the night of 24th September. It was rather disturbing to find salmonellæ isolated from her fæces on 1st October, but reassuring when the organism was identified as *S. tennessee*. She had no gastro-intestinal symptoms and had presumably been carrying the organism on admission.

(ii) Three fæcal specimens were requested from each patient and member of staff.

(iii) By arrangement with matron, nurses working in the unit were not transferred, and no fresh nurses were sent to the unit.

At this time there were twenty-two other patients in the unit, and twenty-six members of staff had duties there. Thirteen of these were found to be excreting the organism—five male patients, three female patients, four nurses, and one domestic. One of the patients, a woman who was recovering from an exacerbation of chronic bronchitis, had acute diarrhœa and vomiting with severe weakness, and one nurse and the domestic had marked malaise.

In addition, one man (Case 20), who had been admitted on 11th September, was found to be carrying *S. typhimurium*. He had no symptoms attributable to this organism.

Thus eleven patients in all (including the two excreting *S. typhimurium* and *S. tennessee* respectively) were found to be infected in this second phase of the outbreak. They were dealt with as follows:

Transferred for isolation without treatment	1
Discharged for supervision at home	2
Treated and discharged after negative cultures	4
Treated, but transferred for isolation on failure to disinfect	2
Treated and transferred to other units after negative cultures	2

The decision where to treat a symptomless patient was governed by the home circumstances. The two ill patients were kept in the unit until their acute symptoms had subsided and were then transferred for isolation.

The ward sister and three nurses who were carrying the organism were symptomless and were given ambulant therapy. It was felt better to keep them on duty, rather than to bring in fresh staff. They did not handle patients' food. The domestic (Case 15), responsible for food handling, was sent home on treatment.

The standard treatment used in this second phase of the outbreak was a five-day course of neomycin and ampicillin—one gram, four times daily, of each. The ampicillin was used in an attempt to eliminate organisms carried in the biliary tract.

The figure shows the fæcal results of all infected persons and the period of treatment.

By 22nd September there were only four female patients in the unit. These were all free of infection and were transferred to a small downstairs ward. The male ward became completely empty on 12th October. The wards were fumigated with formalin, and their walls washed with 1 in 40 cresol solution (Edgar and Lacey, 1963), and subsequently repainted. The opportunity was taken to thoroughly clean and modernise the kitchen.

The female ward was reopened for admissions on 15th October and the male ward on 8th November. Since then no further cases of salmonella infection have appeared.

TABLE 1.

SALMONELLA INCIDENTS IN ENGLAND AND WALES, 1951-1962[a]

YEAR	TOTAL	ENDOGENOUS SALMONELLA TYPES[b]			EXOGENOUS SALMONELLA TYPES[c]		
		S. typhimurium	*S. enteritidis*	*S. newport*	*S. anatum*	*S. bredeney*	*S. heidelberg*
1951	1711	1236	99	71	11	1	–
1952	2142	1604	145	40	10	4	–
1953	3171	2438	126	50	30	3	11
1954	3576	3038	70	35	20	20	16
1955	5383	4276	126	66	50	14	77
1956	4412	3245	199	97	78	55	136
1957	4278	2973	158	88	75	52	269
1958	4952	3406	113	118	55	50	308
1959	5132	3241	119	319	54	41	182
1960	4105	2943	145	54	17	3	118
1961	3855	2544	90	61	31	14	289
1962	2846	1864	93	64	19	103	133

a. Derived from Reports, Mon. Bull. Minist. Hlth. Lab. Serv. (1954, 1955a, 1955b, 1956, 1957, 1958b, 1959b, 1960, 1961b, 1962, 1963).

b. Endogenous salmonella types are those which were known to occur in the United Kingdom before 1940.

c. Exogenous salmonella types are those which were unknown or uncommon in the United Kingdom before 1940.

Discussion.

Historical Review.

S. heidelberg was first identified some thirty years ago (Habs, 1933). It was not isolated in Great Britain until 1953 (Report, 1955a), but within four years it had become second only to *S. typhimurium* as a cause of food-poisoning (Report, 1959b). Since then the annual number of food-poisoning incidents attributed to this organism has remained high (Table 1).

Despite its prevalence, the source of infection in most cases remained unknown until recently (Report, 1959b). Large-scale surveys of imported egg products (Report, 1958a), organic fertilisers (Walker, 1957; Report, 1959a), animal feeding-stuffs (Report, 1959a; Report, 1961a), and raw meat (Hobbs and Wilson, 1959) produced only very occasional isolations of *S. heidelberg*, although these products were often heavily contaminated with a large number of other salmonella serotypes. However, within the last few years *S. heidelberg* has been isolated from a number of animals, particularly pigs and cattle (Taylor, 1963) and the organisms have been found with increasing frequency in sausages and other made-up meat products (Reports, 1962 and 1963; Taylor, 1963). Two milk-borne outbreaks have recently been described (Knox et al., 1963; Hutchinson, 1964).

TABLE 2.

Isolations of S. Heidelberg in Northern Ireland, 1954-1963[a]

1954	1955	1956	1957	1958	1959	1960	1961	1962	1963
0	35	11	33	11	4	4	23	3	20[b]

a. Information obtained from the records of The Laboratories, Belfast City Hospital, Belfast, 9.

b. Including nineteen isolations from present outbreak.

S. heidelberg was first discovered in Northern Ireland in 1955, and the annual isolations since then are shown in Table 2. Newell (1959) quotes unpublished data (Newell and Murdock), which suggested that the organism was introduced to Northern Ireland in a feeding-stuff for pigs which was imported early in 1955. This agrees with the later findings mentioned above, and strengthens the probability that pigs and pork products are one of the main sources of human infection with this organism in the British Isles.

Several outbreaks of salmonella infection are reported every year in hospitals and other institutions, and it has been recognised that in a number of cases the infection is probably not food-borne, but that cross-infection may play a part in its transmission (Report, 1954; Joint WHO/FAO Expert Committee on Zoonoses, 1959). Rubbo (1948) and Mushin (1948) described a hospital outbreak affecting children caused by *S. derby*, while an outbreak due to *S. enteritidis* was reported by Poole and Ardley (1958) and one due to *S. typhimurium* by Datta and Pridie (1960). Recent hospital outbreaks caused by *S. heidelberg* were described by Primavesi (1956) and Edgar and Lacey (1963). The incident described

by Primavesi was explosive in nature, being associated with contaminated sausage locally prepared from pigs which were found to be infected with *S. heidelberg*.

Newell (1959) mentioned that *S. heidelberg* had been implicated in many large outbreaks in hospitals and other institutions, and discussed possible reasons for this association. He also stated that probably a smaller number of these organisms was required to cause an infection than was the case with most of the other types of salmonella.

Such is the background to the present outbreak, several aspects of which are felt to be worthy of comment:

Infectivity.

In the present outbreak, the high degree of infectivity of the organism is confirmed by its recrudescence after the initial outbreak, and by the high infectivity rate among those at risk. It is of interest that only five of the nineteen persons infected with *S. heidelberg* had symptoms.

Mode of Spread.

As seen from the figure, each phase began in an "explosive" manner. This is suggestive of a food-borne spread. The fact that all who were infected had eaten food prepared by the domestic staff in the unit kitchen suggests that this food was the source of infection. This idea is supported by the fact that the doctors, who took no meals in the unit, were not involved in the outbreak. In fact, two domestics (Cases 4 and 15) were found to be carrying the organism—one in each phase of the outbreak—and it seems reasonable to suppose that they may have been responsible for disseminating the infection.

Treatment.

In the second phase of the outbreak, fourteen persons with salmonella infection were given antibiotic treatment. Apart from the first two cases, a standard treatment was given—five days of neomycin and ampicillin, one gram four times daily of each. The periods of treatment in relation to fæcal results are shown in the figure. Two persons reported mild bowel upsets attributed to the drugs, but no other adverse effects were observed.

The patients who were isolated were not given antibiotic therapy. An opportunity was thus given to assess the effect of the antibiotic therapy in this condition.

For purposes of comparison, only the cases infected with *S. heidelberg* will be considered. Ten of these received the combined treatment, and all but two became negative during or immediately after therapy. One of these two (Case 10) yielded a positive culture after six consecutive negatives in a four-week period. He was sharing the ward with a carrier (who was being barrier nursed) and reinfection cannot be excluded.

In contrast, of five persons who were not treated initially, all but one continued to excrete the organism for considerable periods—three weeks or more. Two of these—who were nurses—were subsequently given the combined treatment, and promptly became negative.

All but one of the above persons were symptom-free. The two groups cannot be compared statistically, but it would appear that the antibiotic combination used considerably shortened the duration of the carrier state.

There are a number of references to the use of ampicillin alone in the treatment of salmonella infections (Stewart et al., 1961; Ross et al., 1962; Bullock, 1963). These show that, while ampicillin is highly effective against a number of strains of salmonella *in vitro*, it is less effective *in vivo*. Stewart et al. (1961) suggest that this is due to concentration of ampicillin in the bile, and that, because of an enterohepatic circulation, the drug does not reach the lower ileum in effective concentrations. Bullock (1963) confirmed in humans that the drug is concentrated in the bile and suggested that it might thus be effective in biliary carriers. Sleet et al. (1964) report moderate success in treating paratyphoid fever with ampicillin.

It is suggested that, when neomycin and ampicillin are combined, the neomycin effects rapid disinfection of the gut, while the ampicillin prevents carriage of organisms in the biliary system. It would appear reasonable to expect that this drug regime might be of value in the treatment of infections due to other species of salmonella, including the enteric fever group.

In fact, a preliminary communication by Pettersson (1964) refers to the use of these two drugs in an outbreak of *S. typhimurium* infections. A different drug regime was used, but again the carrier state appeared to be shortened, though acute symptoms were not affected.

"Iceberg" Effect.

Of the nineteen infected cases, only five had symptoms, and in only three of these was the condition incapacitating. These three were all patients with markedly impaired resistance. Of the forty-eight persons tested in the second outbreak, two were found to be carrying other species of salmonella. These facts suggest that for every obvious case of bacterial food poisoning there are many inapparent infections. It would appear that there is a considerable incidence of subclinical salmonella infections in the general population.

Criteria for Negativity.

From the figure it can be seen that one or two negative fæcal cultures by no means excluded infection. However, apart from the carrier of *S. tennessee*, there was only one case (Case 10, referred to under "Treatment") where the finding of three consecutive negative results was followed by a further positive result. It would appear that three negative fæcal cultures provide a reasonable indication of freedom from infection in an outbreak.

Bacteriological Methods.

An analysis has been made of the relative performances of the selective media used for the isolation of salmonella organisms during this outbreak.

Salmonellæ were detected in the fæces of nineteen persons (excluding the single isolations of *S. typhimurium* and *S. tennessee*). Only the first isolation from each case or symptomless excreter has been considered. In nine instances both the

selective media were positive, while there were five positives on desoxycholate-citrate agar only and five positives on Wilson and Blair's medium only. Thus, if either of these media had been used alone, only fourteen positives would have been obtained instead of nineteen.

The value of the enrichment procedure with selenite F was also demonstrated, as approximately 50 per cent. more positives were obtained on the secondary plates than on the primary plates, the increase being fairly evenly distributed between both the selective plates (desoxycholate and Wilson and Blair). However, there were one or two instances with each medium where positive primary plates were followed by negative secondary plates.

Although the numbers considered here are small, the findings agree closely with those of Cook, Frisby, and Jebb (1951), who analysed the isolations of more than six hundred salmonellæ over a three-year period. They emphasised the value of using more than one selective medium, and of combining direct plating and enrichment techniques in order to obtain the maximum number of positive results.

Summary and Conclusions.

1. An outbreak of *S. heidelberg* infection, presumably food-borne, affected nineteen patients and staff in a 26-bedded medical unit. One patient died.
2. The history of infections with this organism is reviewed, and its high degree of infectivity emphasized.
3. Simultaneous therapy with neomycin and ampicillin shortened the duration of the carrier state.
4. The large proportion of symptomless carriers (fourteen out of nineteen cases), together with the finding of two incidental infections with other species of salmonella, indicates that there may be a high incidence of sub-clinical salmonella infections in the population.
5. It is suggested that at least three negative fæcal cultures are needed to exclude the carrier state.
6. The use of two selective media, and the combination of direct plating and enrichment techniques, increased the number of successful salmonella isolations.

We wish to thank Professor O. L. Wade and Dr. V. D. Allison for their guidance in the preparation of this paper. We are also grateful to Dr. W. P. Ferguson and Mr. W. N. MacDonald for their help in the bacteriological investigations.

References.

Bullock, W. E. (1963). *Am. J. Med. Sci.*, **246**, 42.

Cook, G. T., Frisby, B. R., and Jebb, W. H. H. (1951). *Mon. Bull. Minist. Hlth. Lab. Serv.*, **10**, 89.

Datta, N., and Pridie, R. B. (1960). *J. Hyg. (Camb.)*, **58**, 229.

Edgar, W. M., and Lacey, B. W. (1963). *Lancet*, **1**, 161.

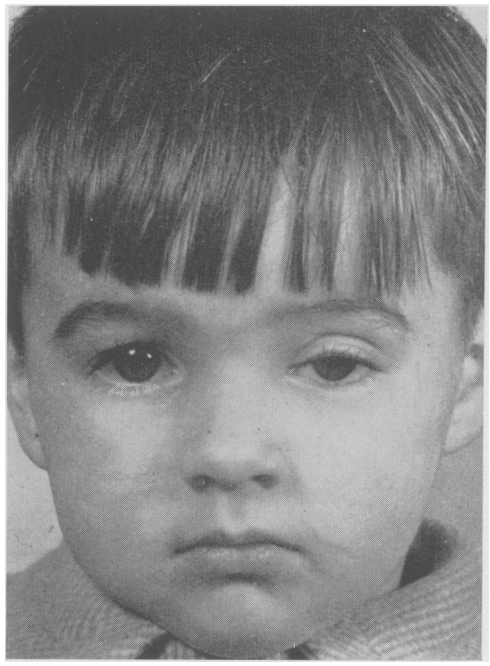
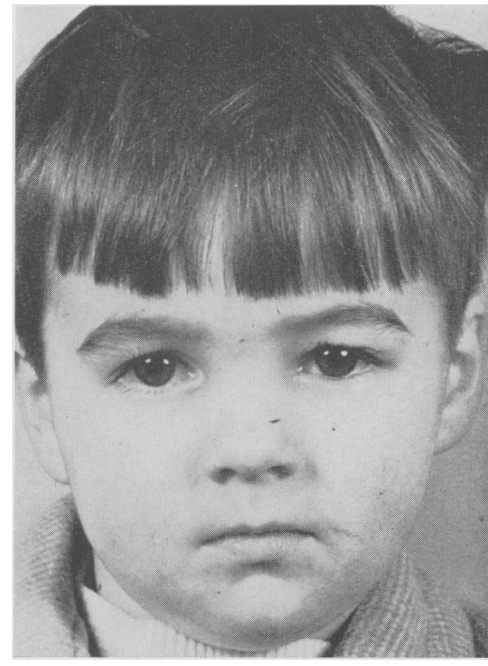


FIG. 1.

PTOSIS

FIG. 1A.

PTOSIS



Correction of left congenital ptosis by the tranconjunctival resection of the levator aponeurosis (Bowman).

PLATE I

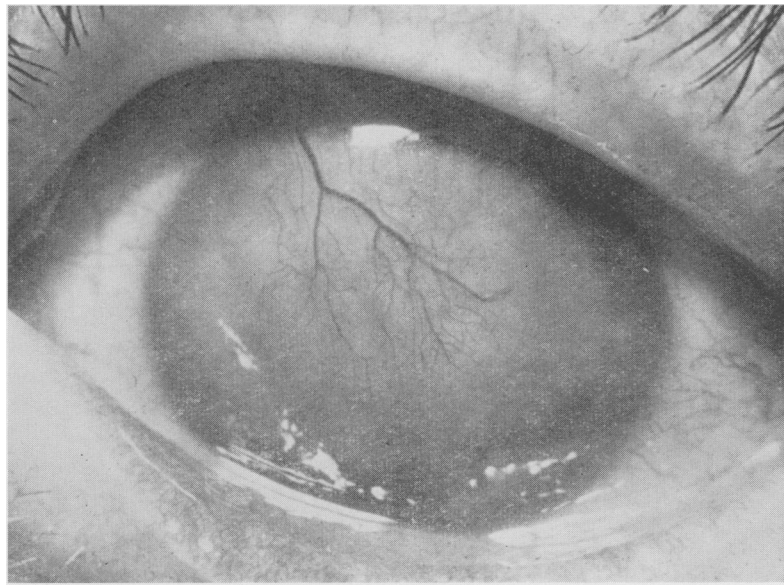


FIG. 2.

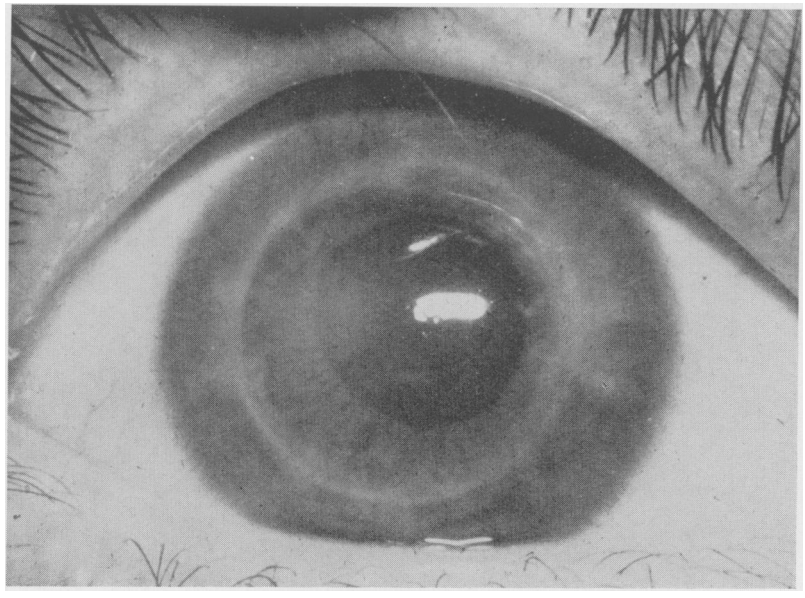


FIG. 3.

CORNEAL GRAFT:
A successful penetration corneal graft after lime burns which gave normal vision.

PLATE II

FIG. 4.

REGIONAL EYE BANK VAN:

The van is fitted with surgical, bacteriological, and preservation equipment, and it is used for the collection of donor eyes at home and in hospital.

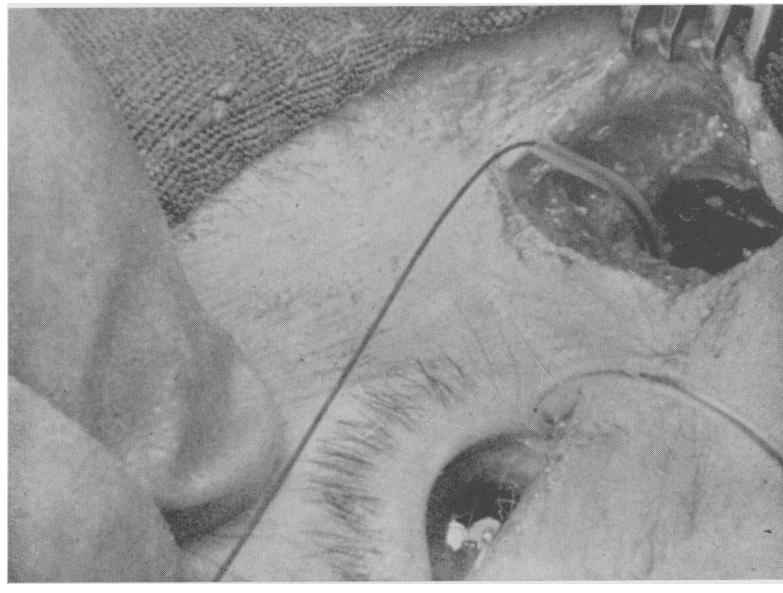


FIG. 5.

POLYTHENE TUBE INTUBATION:

Polythene tubes are used in combination with cystorhinostomy where severe strictures have been formed in the lacrimal passages after fracture, infection or removal of the lacrimal sac.

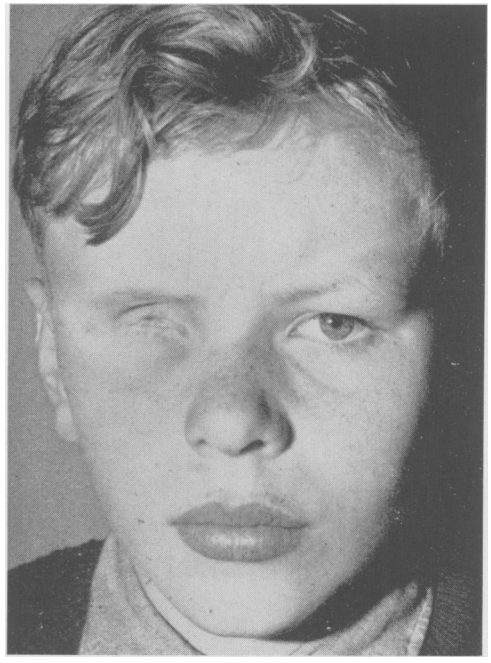


FIG. 6.

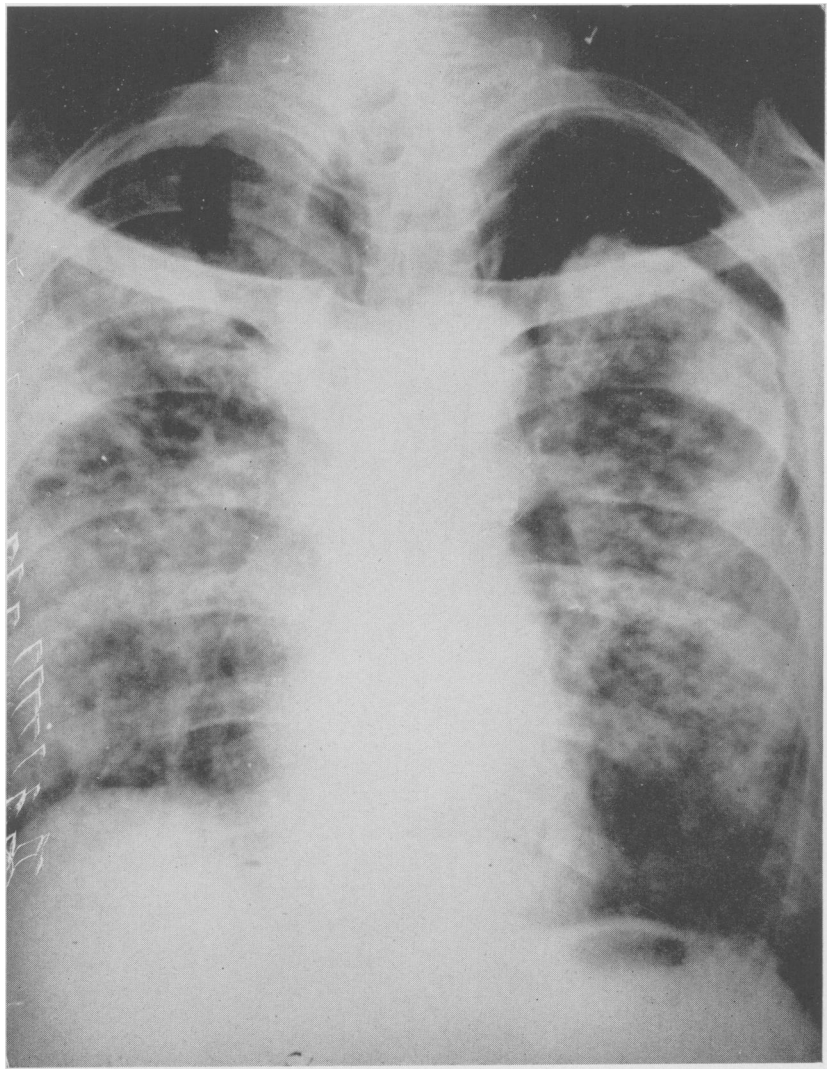
SOCKET RECONSTRUCTION BEFORE OPERATION.

The left socket shows severe contraction after radium therapy.

FIG. 6A.

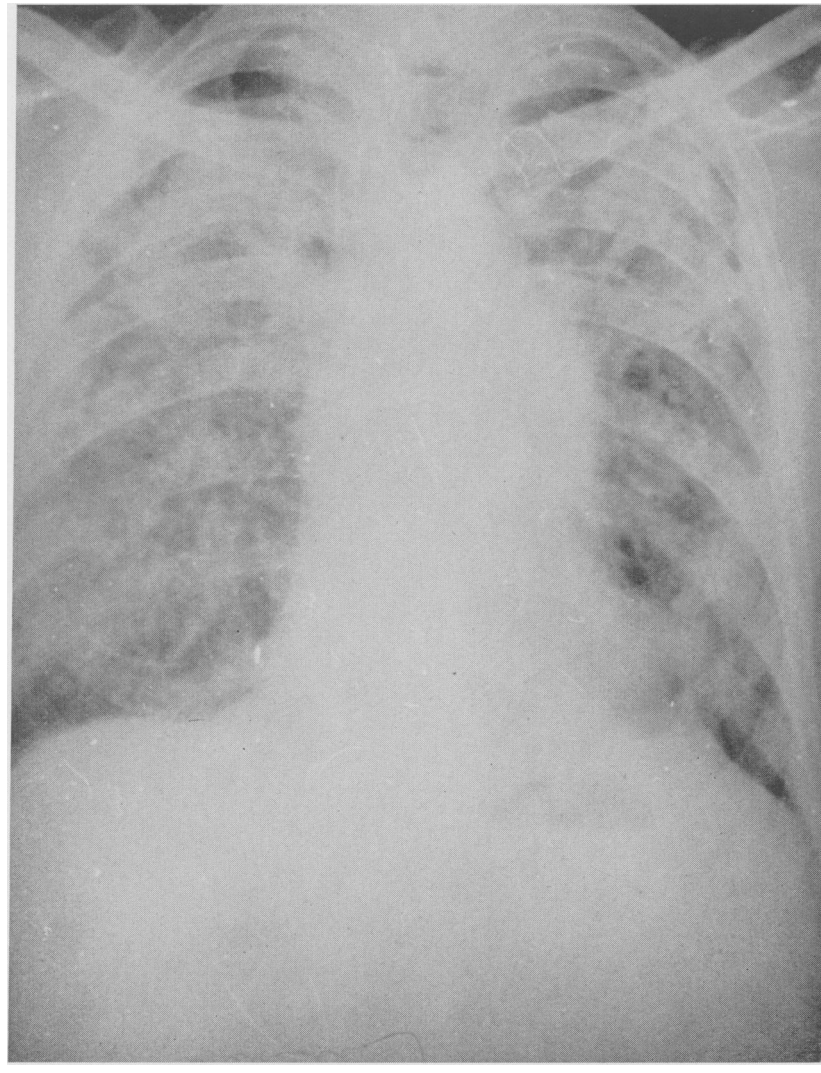
The same socket has been completely excised and a spectacle prosthesis fitted.

PLATE IV



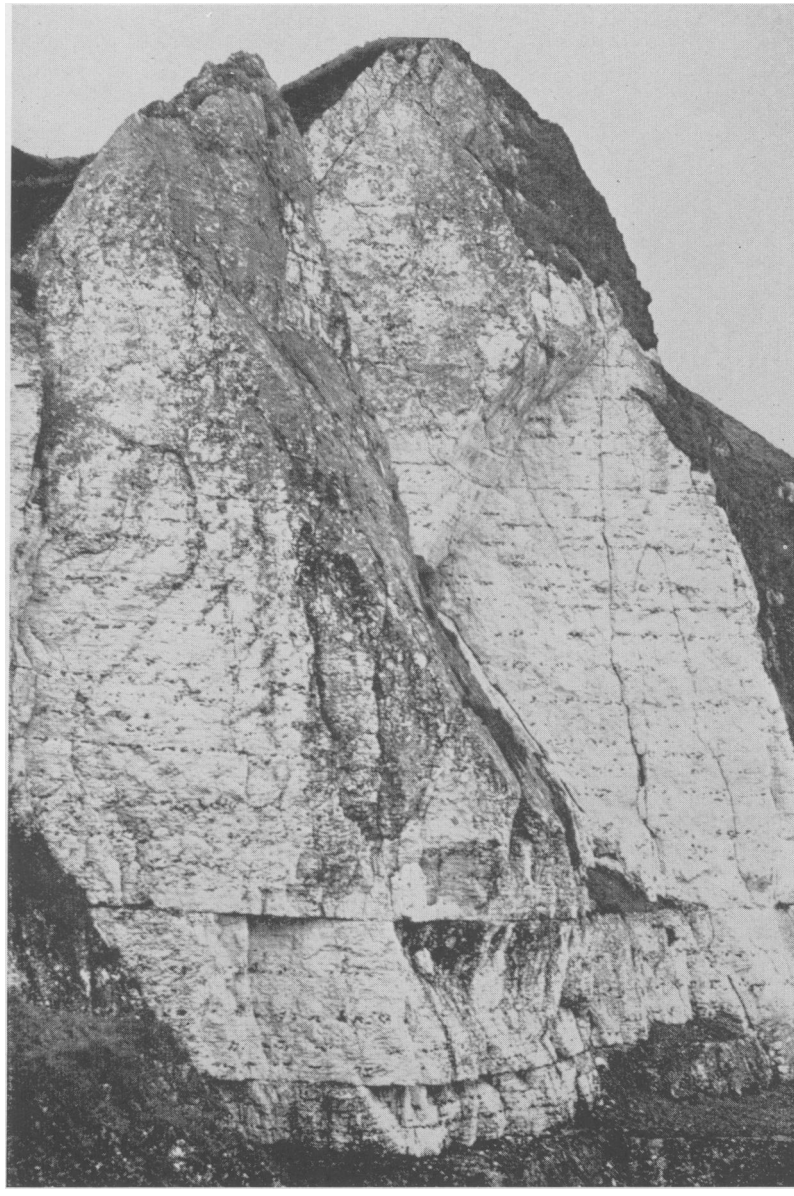
Extensive pulmonary fibrosis after six and a half years' exposure to flint dust as seen in Case 1.

PLATE V



Pulmonary fibrosis due to silicosis in Case 4. Death ensued in only three years after initial exposure to the dust.

PLATE VI



Horizontal parallel row of flints ("widow-makers") seen in the limestone strata.

PLATE VII

GILLIES, R. R. (1956). *J. clin. Path.*, **9**, 368.
HABS, H. (1933). *Zbl. Bakt.*, **130**, 367.
HOBBS, B. C, and ALLISON, V. D. (1945). *Mon. Bull. Minist. Hlth. Lab. Serv.*, **4**, 12 and 63.
HOBBS, B. C., and WILSON, J. G. (1959). *Mon. Bull. Minist. Hlth. Lab. Serv.*, **18**, 198.
HUTCHINSON, R. I. (1964). *Brit. med. J.*, **1**, 479.
HYNES, M. (1942). *J. Path. Bact.*, **54**, 193.
JOINT WHO/FAO EXPERT COMMITTEE ON ZOONOSES (1959). *Wld. Hlth. Org. techn. Rep. Ser.*, **169.**
KNOX, W. A., GALBRAITH, N. S., LEWIS, M. J., HICKIE, G. C., and JOHNSTON, H. H. (1963). *J. Hyg. (Camb.)*, **61**, 175.
MURDOCK, C. R. (1954). *Mon. Bull. Minist. Hlth. Lab. Serv.*, **13**, 43.
MUSHIN, R. (1948). *J. Hyg. (Camb.)*, **46**, 151.
NEWELL, K. W. (1959). *Bull. Wld. Hlth. Org.*, **21**, 279.
PETTERSSON, T. (1964). *Brit. med. J.*, **1**, 562.
POOLE, P. M., and ARDLEY, J. (1958). *Mon. Bull. Minist. Hlth. Lab. Serv.*, **17**, 147.
PRIMAVESI, K. A. (1956). *Med. Klin., Berl.*, **51**, 1103.
REPORT (1954). *Mon. Bull. Minist. Hlth. Lab. Serv.*, **13**, 12.
Ibid., 1955a, **14**, 34.
REPORT (1955b). *Mon. Bull. Minist. Hlth. Lab. Serv.*, **14**, 203.
Ibid. (1956), **15**, 263.
Ibid. (1957), **16**, 233.
Ibid. (1958a), **17**, 36.
Ibid. (1958b), **17**, 252.
Ibid. (1959a), **18**, 26.
Ibid. (1959b), **18**, 169.
Ibid. (1960), **19**, 224.
Ibid. (1961a), **20**, 73.
Ibid. (1961b), **20**, 160.
Ibid. (1962), **21**, 180.
Ibid. (1963), **22**, 200.
ROSS, S., LOVRIEN, E. W., ZAREMBA, E. A., BURGEOIS, L., and PUIG, J. R. (1962). *J. Amer. med. Ass.*, **182**, 238.
RUBBO, S. D. (1948). *J. Hyg. (Camb.)*, **46**, 158.
SLFET, R. A., SANGSTER, G., MURDOCH, J. M. (1964). *Brit. med. J.*, **1**, 148.
STEWART, G. J., COLES, H. M. T., NIXON, H. H., and HOLT, R. J. (1961). *Brit. med. J.*, **2**, 200.
TAYLOR, J. (1963). *Ann. Inst. Pasteur.*, **104**, 660.
WALKER, J. H. C. (1957). *Lancet*, **2**, 283.