STAPHYLOCOCCAL BACTERAEMIA

CLINICAL AND BACTERIOLOGICAL
OBSERVATIONS IN 201 CASES

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A recent survey of the cases of bacteraemia due to *Staphylococcus aureus* at a Danish hospital for communicable diseases showed a striking increase in the frequency of this disease during the last few years.

In order to find out whether this was a local phenomenon, a survey was made of all the cases of bacteraemia diagnosed at the Statens Seruminstitut and the Blegdamshospital. The accompanying Chart shows the number of patients suffering from bacteraemia due to some well-characterized organisms for each of the years 1953-8. The total number of blood cultures examined is given for comparison. It is evident that the most common bacteria isolated are *Staph. aureus*, *Escherichia coli*, and non-haemolytic streptococci.

In a corresponding investigation by Tarnowsky (1944), carried out in the years 1938-42, the dominating organisms were non-haemolytic streptococci, *Staph. aureus*, haemolytic streptococci, and pneumococci. The Chart shows that the two latter organisms have almost disappeared as a cause of bacteraemia, whereas the frequency of *Staph. aureus* and *E. coli* seems to have increased during the last few years.

The present report deals with the cases of staphylococcal bacteraemia in the above-mentioned material diagnosed in 1957 and 1958.

Cases of bacteraemia (1953-8) due to some frequently isolated bacteria. Cultivation performed at Statens Seruminstitut and Blegdamshospital, Copenhagen. The total yearly number of blood cultures is given in hundreds.

It is our purpose to account for the portal of entry, the source of infection, the phage-types, the antibiotic resistance, and some other properties of the isolated *Staph. aureus*, and to examine the influence of these factors on the mortality rate.

Material and Methods

The material comprises 201 cases of bacteraemia due to *Staph. aureus*, diagnosed at the Statens Seruminstitut and the Blegdamshospital. The 201 patients were admitted to 86 special hospital departments all over the country.

Clinical information, comprising diagnoses, signs of presumed or stated staphylococcal infections, possible source of infection, and portal of entry, was obtained through the use of detailed inquiry forms.

Phage-typing was performed at the Statens Seruminstitut, using the technique and the phages described by Wilson and Atkinson (1945) as modified by Williams and Rippon (1952) and Williams, Rippon, and Dowsett (1953).

Resistance to antibiotics was determined by the technique described by Jensen and Kjør (1947) and Dragsted and Erichsen (1953).

Production of alpha-toxin was determined by the method used by Jackson, Dowling, and Lepper (1955).

Production of hyaluronidase was ascertained by using a technique described by Faber and Rosendal (1960).

Egg-yolk reaction was performed as described by Gillespie and Alder (1952).

Results

Sex, Age, and Mortality.—The material comprised 124 males and 77 females. Six patients were under 1 year of age and 25 above 70. The distribution of patients within the in-between age-groups is rather uniform. Eighty-three (41%) patients died: 54 (44%) males and 29 (38%) females. The mortality rate for patients over 30 years was 51%, with only minor deviations for the subgroups, whereas only 19% of the patients under 30 died.

Complicating Diseases.—One-third of our patients had severe primary conditions which may have lowered their resistance. The diseases most frequently encountered were diabetes mellitus (21), generalized affections of the skin (15), and blood diseases (11). For the remaining 18 cases the diagnoses were: cancer (4), ulcerative colitis (3), shock (5), severe renal impairment (3), burns (2), and tetanus (1). Treatment with steroids had been given to 17 of these patients, and to a further three patients with minor disabilities. None of our patients received x-ray treatment. The mortality rate for this group of patients was 50%, as compared with 37% for patients with no complicating diseases.

Origin of Infection.—In 182 cases the information obtained permitted a distinction to be made between infections contracted outside hospitals and hospital-acquired infections. Table I gives the details. Probably a considerable number of the 19 cases in the group of infections of unknown origin were in fact nosocomial infections. The group includes four patients with cutaneous boils appearing shortly after admission to hospital, and several patients with infectious traumatic lesions, many of whom were treated by operations and intravenous infusions.

Patients Infected in Hospital

To give an impression of the character of the hospital-acquired infections, here are a few case reports.

Case 1.—A boy aged 1 month, who had been admitted to a dermatological department for pityriasis, developed bilateral pneumonia and bacteraemia with *Staph. aureus*, phage-type 80, resistant to penicillin and streptomycin. He died 36 hours after the first symptom of the infection.

Case 2.—A nurse aged 38 developed a boil on her nates. One month later she felt heavy pains over her back, which induced her to take large doses of analgesics. In order to break off this habit, she was admitted to a psychiatric department, where the diagnosis of bacteraemia was established (*Staph. aureus*, phage-type 80, resistant to penicillin and sulphonamides). X-ray examination revealed osteomyelitis in the lumbar spine. Complete cure followed antibiotic treatment.

Case 3.—A girl aged 6 years was infected with *Staph. aureus* (phage-type 80, resistant to penicillin, sulphonamides, and streptomycin) during an operation for complete dislocation of one of her hip-joints. Her symptoms were those of meningitis, endocarditis, pericarditis, bilateral pneumonia, and empyema; and several osteomyelitic foci with fistulae were found. Treatment for many months with antibiotics, gamma-globulin, steroids, and staphylococcal antitoxin resulted in eliminating the infection, but left the patient an invalid on account of the deformity in her pelvis.

Case 4.—A 61-year-old man had been treated with steroids for many years for rheumatoid arthritis. Two days after an intra-articular injection with hydrocortisone acetate had been given, he was admitted to hospital in a state of shock with bilateral pneumonia and a heavy pyarthrosis of his right knee. He was cured by intensive treatment with antibiotics and steroids, followed by surgery.

The portals of entry for infections acquired in hospital are given in Table I. The operations include gynaecological operations (7), prostatectomy (5), osteosynthesis (4), urethral catheterization (3), colectomy (2), and 14 miscellaneous operations each represented by one case only: herniotomy, appendicectomy, cholecystectomy, nephrectomy (renal tuberculosis), splenectomy (haemolytic jaundice); operations for stenosis of the mitral valve, paralysis of the urinary bladder, pilonidal fistula, stricture of the urethra, enchondromata, varices of the lower extremities, and malignant tumours of the urinary bladder, the pancreas, and the breast. Four cases originated from haemodialysis, six from intravenous infusions of injections, and in two cases the infection may have originated from traumatic lesions as well as from intravenous infusions and haemodialysis.

The group "miscellaneous and unknown" includes one patient with staphylococcal otitis media complicating pertussis, and one with cancer of the bowel; in the latter case bacteraemia followed oral antibiotic treatment. In 14 cases the portal of entry could not be ascertained with certainty, but in all these cases the infection started after hospitalization for a long period.

From the mortality rates in the present material it is concluded that infections due to surgical procedures have a higher mortality rate than those originating from cutaneous boils or pulmonary infections. The mortality rate for patients infected in hospital is higher than that for those infected outside hospital.

Patients Infected Outside Hospitals

The following are illustrative case-histories.

Case 1.—A woman aged 31 acquired an infection from a scratch on her hand. One week later she was admitted to hospital, unconscious and pyretic. Within a few hours manifest shock developed. From the wound, nostrils, sputum, and blood *Staph. aureus* were isolated (phage-type 80, resistant to penicillin, sulphonamides, and streptomycin). Death followed after two days, in spite of prompt and intensive treatment with penicillin, erythromycin, gamma-globulin, staphylococcal antitoxin, and steroids, and general anti-shock therapy. No hospital contacts could be found.

Case 2.—A 3-year-old girl contracted a boil on her leg and was admitted to hospital a few days later with bilateral pneumonia. She died after two days in respiratory failure, despite tracheotomy and use of a mechanical respirator. Necropsy revealed pyopneumothorax and multiple pulmonary abscesses. *Staph. aureus*, phage-type 80, resistant to penicillin and sulphonamides, was isolated from the blood and sputum. The infection could be traced to a sister of the patient, who had a boil on her leg, acquired during her stay at a home for children with infantile paralysis.

Case 3.—A 19-year-old woman was admitted to hospital unconscious. She had been well until 12 hours before admission, when she had complained of headache. Investigations, including x-ray examination of the lungs and lumbar puncture, showed nothing abnormal. The next morning her condition deteriorated. She was then cyanotic and hypotensive; there was haemorrhage from the vagina and diarrhoea, and tiny pustules and petechia appeared; antibiotic therapy with penicillin, streptomycin, and erythromycin was started, and heavy doses of steroids were given for several days. She was pyretic, so treatment with chlorpromazine, pethidine, and transfusions was tried. She developed signs of oedema of the lungs, on account of which she was ventilated per respirator. In a few days she developed jaundice; blood-urea increased owing to anuria, and left-sided convulsions were observed. A transitory improvement was seen after haemodialysis, but the convulsions returned, and she died 11 days after the onset of the first symptoms. Necropsy revealed multiple cerebral abscesses and septic emboli in the heart and kidneys, ulcerative endocarditis of the mitral valves, pneumonia, and acute enteritis. *Staph. aureus*, phage-type 75/77, resistant to penicillin, sulphonamides, streptomycin, and tetracyclines, was cultured from blood, sputum, faeces, heart, kidneys, lung, and brain.

The portals of entry for the infections acquired outside hospital are given in Table I. One-third of these infections were secondary to cutaneous boils, but in 44 cases the portal could not be settled with certainty.

TABLE I.—Origin of Infection and Portal of Entry in 201 Cases of Staphylococcal Bacteraemia

Origin of Infection	Operations, i.v. Infusions, Haemodialysis, Injections		Cutaneous Boils, etc.		Respiratory Tract		Miscellaneous and Unknown		Total	
	No.	Died	No.	Died	No.	Died	No.	Died	No.	Died
Hospital	47	29 (62%)	31	13 (42%)	0	—	16	10 (63%)	94	52 (55%)
Community	4	2 (50%)	29	9 (31%)	11	4 (36%)	44	10 (23%)	88	25 (28%)
Unknown	0	—	4	1 (25%)	0	—	15	5 (33%)	19	6 (32%)
Total	51	31 (61%)	64	23 (36%)	11	4 (36%)	75	25 (33%)	201	83 (41%)

Most of the patients with primary osteomyelitis and endocarditis belonged to this group. Of the 88 patients, 25 (28%) died.

Phage-types

A total of 222 different strains were isolated from the blood of the 201 patients. The phage-types of these strains are given in Table II. It seems that nearly half of the nosocomial infections were due to phage-types 80 and 52/52A/80, and almost one-fourth to strains belonging to phage-group III. In 34 cases the infecting type was known to be endemic or epidemic in the hospitals concerned.

TABLE II.—Phage-types of 222 Bacteraemia Strains

	Origin of Infection			Total
	Hospital	Community	Unknown	
Phage group I:				
Types 80 and 52/52A/80	51	29	7	87
Other types	8	3	1	12
Phage-group II	10	17	2	29
III	26	19	8	53
N.I. and miscellaneous	3	8	0	11
N.T. (non-typable)	12	6	3	21
Not phage-typed	1	7	1	9
Total	111	89	22	222

N.I. = Not identified.

TABLE III.—Mortality Rate for Bacteraemia Cases Due to Types 80 and 52/52A/80 Compared with that for Bacteraemia Caused by Other Types

Origin of Infection	Phage-types							
	80		52/52A/80		Other Types		Total	
	No.	Died	No.	Died	No.	Died	No.	Died
Hospital	34	21 (62%)	15	7 (47%)	35	22 (63%)	84	50 (60%)
Community	19	8 (42%)	8	1 (13%)	53	14 (26%)	80	23 (29%)
Unknown	6	3 (50%)	1	(0)	10	2 (20%)	17	5 (29%)
Total	59	32 (54%)	24	8 (33%)	98	38 (39%)		

For infections acquired outside hospital the distribution of the various phage-types was more even.

An attempt was made to find out whether there was a higher mortality rate in bacteraemia due to type 80 and 52/52A/80 than in infections caused by other types (Table III). Patients infected with more than one strain have been omitted, as it is impossible to evaluate the individual roles of different strains in these cases.

Table III shows that the mortality rate for patients infected with type 80 + 52/52A/80 did not differ from that for patients infected with other types when groups of the same origin are compared (hospital, community).

Antibiotic Resistance

18% of the strains were sensitive to all antibiotics examined. Antibiotic resistance was most pronounced in hospital strains; nine-tenths of these strains were penicillin-resistant, and one-quarter tetracycline-resistant. Tetracycline-resistance was found in only 6% of strains acquired outside hospital. Fifty-eight out of 94 strains resistant to penicillin + sulphonamides + streptomycin, and 27 out of 38 strains resistant to tetracyclines were nosocomial strains.

Only 3 strains out of 213 were resistant to chloramphenicol, and no strain in this material was resistant to erythromycin.

Types 80 and 52/52A/80 were almost constantly resistant to penicillin, sulphonamides, and streptomycin, whereas chloramphenicol-resistance was found in only one and tetracycline-resistance in only two type 80

strains. Out of 38 strains resistant to tetracyclines 21 belonged to phage-group III. In the group of tetracycline-resistant strains three were sensitive to penicillin and streptomycin, and a further 14 were sensitive to streptomycin. Of these 17 strains with unusual antibiotic patterns, 16 were isolated from six patients with dermatological diseases admitted to departments where tetracycline ointments were often used.

The present material strongly confirmed the prognostic role of the sensitivity of the infecting strains to antibiotics. In Table IV resistance to three anti-

TABLE IV.—Mortality Rate Related to Antibiotic-resistance of the Infecting Strains

Origin of Infection	Penicillin		Streptomycin		Tetracyclines	
	Sens.	Res.	Sens.	Res.	Sens.	Res.
Hospital	6 (17%)	76 (63%)	22 (27%)	60 (71%)	66 (56%)	16 (75%)
Community	26 (19%)	57 (30%)	54 (24%)	29 (31%)	78 (26%)	5 (40%)
Unknown	3 (0%)	14 (43%)	7 (14%)	10 (50%)	15 (40%)	2 (0%)
Total	35 (17%)	147 (48%)	83 (24%)	99 (58%)	159 (40%)	23 (61%)

The figures in parentheses indicate mortality rates.

biotics is considered separately. The total figures show mortality rates for antibiotic-resistant infections one and a half to three times as high as for infections due to strains sensitive to the drugs in question. Resistance to several antibiotics made prognosis still worse: strains resistant to penicillin + streptomycin + sulphonamides were responsible for 90 cases, 53 of which were fatal. Of these 53 cases, 41 were nosocomial infections.

Out of 34 patients infected with organisms sensitive to the three above-mentioned drugs, only 5 died.

From Table IV it also appears that infections caused by resistant strains have a more favourable prognosis when they originate outside hospitals.

Alpha-toxin, Hyaluronidase, and Egg-yolk Factor

Taking mortality in bacteraemia cases as a measure of the virulence of the infecting organisms, we have used the present material to evaluate the pathogenic role of some *in vitro* properties of *Staph. aureus*. Alpha-toxin was produced in measurable amounts *in vitro* by 90% of the strains. The amount of toxin produced by the individual strains varied considerably (Jessen, Faber, Rosendal, and Eriksen, 1959), but showed no correlation to mortality.

The quantitative production of hyaluronidase likewise showed no relation to the clinical course of the cases.

However, a striking difference in mortality appeared when the cases were classified according to the egg-yolk reaction (E.Y.) of the infecting strains (Table V). The difference between the group of patients infected with egg-yolk-positive (E.Y.+) strains (mortality rate 36%) and those infected with egg-yolk-negative (E.Y.-) strains (mortality rate 67%) is highly significant.

TABLE V.—Mortality Rate Correlated to Egg-yolk Reaction of the Infecting Strains

Origin of Infection	Survivals		Deaths		Mortality Rate	
	E.Y. +	E.Y. -	E.Y. +	E.Y. -	E.Y. +	E.Y. -
Hospital	21	8	23	26	52%	76%
Community	47	5	16	5	25%	50%
Unknown	8	3	3	1		
Total	76	16	42	32	36%	67%

The material was closely scrutinized to discover whether this correlation was a primary one, or secondary to any known relevant factor. Only two such factors were shown to be of any importance: the epidemiological origin and the antibiotic resistance of the strains. Both these factors influenced mortality, and it was found that the E.Y.— strains occurred with the greatest frequency among hospital strains (Table V) and among antibiotic-resistant strains (Table VI).

TABLE VI.—Mortality Rates for Infections due to E.Y.-positive and E.Y.-negative Strains Within Groups Uniform in Regard to Penicillin and Streptomycin Resistance

	Survivals		Deaths		Mortality Rate	
	E.Y.+	E.Y.—	E.Y.+	E.Y.—	E.Y.+	E.Y.—
Streptomycin-sensitive	46	5	11	7	19%	58%
Streptomycin-resistant	29	11	28	25	49%	69%
Penicillin-sensitive	21	1	5	0	19%	0%
„ resistant	54	15	34	32	39%	68%

However, these two factors could not completely account for the higher mortality in bacteraemia due to E.Y.— strains. This higher mortality is observed even within groups of patients with infections of uniform epidemiological origin (hospital or community) (Table V). Furthermore, a comparison was made of the mortality rates for groups of patients infected with strains of uniform resistance to each of the antibiotics mentioned and various combinations of these antibiotics, but differing with regard to the egg-yolk reaction. This principle is illustrated in Table VI, where the comparisons are carried out within groups uniform regarding streptomycin- and penicillin-resistance. Corresponding comparisons were made with a view to the origin and the resistance of the strains. In comparable groups it was a constant finding that E.Y.— strains were responsible for higher mortality rates than were E.Y.+ strains.

Antibodies Against Alpha-toxin and Hyaluronidase

Increasing titres of antibodies against bacterial products can be expected 10 to 14 days after the beginning of an infection. In 118 patients surviving 10 days or more, antibodies against staphylococcus alpha-toxin (ASTA-T) and hyaluronidase (ASTA-H) were investigated at weekly intervals. In about 62% of the cases the antitoxin titres were elevated and the anti-hyaluronidase titres in 28%; in 72% of the cases the figures for at least one of the antibodies were elevated.

The antibody values were not correlated with mortality, with affection of certain organs, nor with the type of primary infection or the age of the patients. The values were independent of the *in vitro* production of alpha-toxin and hyaluronidase of the corresponding strains.

In infections due to strains of phage-types 80 and 52/52A/80 and to strains belonging to phage-group II, elevated ASTA-T titres seemed to occur more regularly (74%) than in infections caused by other types, whereas ASTA-H values were independent of the phage-type of the infecting strains.

Discussion

The increase (30%) in the number of specimens of blood received at the Statens Seruminstitut and

the Blegdamshospital (Copenhagen) for examination during the period 1953–8 exceeded by far the 10% increase in the admission rate to Danish hospital departments. This preponderance is probably due to a greater interest in the bacteraemia problem during the last few years. However, the threefold to fourfold increase in the number of *Staph. aureus* bacteraemia cases would seem to indicate a real and considerable increase of this condition, and for the moment *Staph. aureus* is the organism most often isolated as the cause of bacteraemia.

In Australia, Hassall and Rountree (1959) observed a similar increase in 1955, and considered it to be due to the spreading of a particular staphylococcal strain, phage-type 80/81, which they had observed since 1953. The frequent occurrence of this type is now recognized in most parts of the world, and has been reported from England (Williams, 1959) and America (Blair and Carr, 1958), for example.

Phage-typing of staphylococcal strains isolated from boils, abscesses, paronychia, etc., going back to 1949 has shown that at that time type 80, sensitive to all antibiotics, was not infrequent in Denmark (Eriksen and Rosendal, 1960); but the first Danish nosocomial infections due to drug-resistant strains of type 80 were observed in 1954 (Thaysen, Eriksen, and Rosendal, 1957). In Denmark, as in England, type 80 during the last few years has replaced strains belonging to phage-group III as the most common cause of hospital staphylococcal epidemics. It is endemic in many hospitals and is widely distributed throughout the population (Dons, Eriksen, and Rosendal, 1960).

This shift of the predominating strain coincides with the increasing frequency of serious staphylococcal infections, especially nosocomial infections. However, it has not yet been convincingly shown that these two factors are causally related. If such a relation exists, it may depend upon a tendency of this type to cause long-lasting and easily spread infections, especially boils and paronychia, among hospital staff and patients. No difference in virulence—as measured by mortality in bacteraemia cases—could be ascribed to difference in phage-type in the present material.

The actual staphylococcal problem cannot be reduced to a question of the presence of type 80 strains. Only 83 out of 181 strains isolated from cases of bacteraemia belonged to this type or to type 52/52A/80. For nosocomial infections the figures were 49 out of 84 strains. This figure is surprising low, considering the wide distribution of these types.

Hospital-acquired infections probably account for a considerable part of the increase in the total number of staphylococcal bacteraemia cases in the present material, but a retrospective analysis of the epidemiological origin of bacteraemia cases during 5 or 10 years in order to confirm this view has not been possible.

In the two-year period investigated more than half of the infections in which the origin could be settled were nosocomial, and about 50% of these cases were directly caused by major or minor surgical procedures.

The hospital-acquired infections had a much poorer prognosis than infections originating outside hospitals. This bore no relation to the age of the patients, and the difference was found even when comparing patients with no serious complicating diseases to influence their

general resistance. The greater mortality rate when operation sites, etc., were the portals of entry (Table I) might explain some of the difference mentioned. The frequent antibiotic resistance of the hospital strains may also be of significance. It is unlikely, though, that ineffective antibiotic treatment of the cases caused by resistant strains explains the higher mortality rate in the "hospital" group. However, it was impossible to make a detailed evaluation of the treatment given, as the bacteraemia cases originated from 86 different hospital departments; but according to the antibiograms, which in most cases determined the treatment, chloramphenicol and erythromycin were effective in nearly all cases and tetracyclines in far the greater part. The possibility still remains, however, that endemic hospital strains achieve a higher virulence through human passages.

We used the material in an attempt to evaluate the possible influence of some bacterial properties on the mortality rate, being aware of the limited value of estimating the *in-vivo* properties through *in-vitro* experiments.

The production of alpha-toxin and hyaluronidase of the strains could not be shown to influence mortality, whereas a definite correlation could be established between mortality and the E.Y. reaction.

This reaction was introduced by Gillespie and Alder (1952) and Alder, Gillespie, and Thompson (1955). These authors suggested that the causative factor—probably a lipolytic enzyme—might be regarded as a pathogenic property. The reason for this suggestion was the predominance of EY+ strains in staphylococci isolated from boils and other closed purulent infections, and the frequency of E.Y.+ strains from human infections as opposed to animal infections. The first of these two observations has been confirmed by other authors (Tomlinson and Parker, 1956; Parker, 1958; Jessen *et al.*, 1959).

The present material shows a much higher mortality rate in bacteraemia cases due to E.Y.— strains than in cases caused by E.Y.+ strains. This observation is interesting in so far as no single biochemical property has previously been demonstrated to influence mortality in infections with *Staph. aureus*. The proportion of E.Y.— strains was highest in hospital-acquired bacteraemia cases and in strains resistant to antibiotics. This is in accordance with the above-mentioned reports by Gillespie and Alder (1952) and Alder *et al.* (1955).

The relation of the E.Y. reaction to the clinical character of the infection and to mortality in bacteraemia cases seems to encourage further research on biological differences between the two groups of strains. One of these differences seems to be the "serum opacity factor," stated by Tomlinson and Parker (1956) to occur almost exclusively in E.Y.— strains. There is no evidence that the absence of E.Y. reaction should be regarded as a defect due to the development of antibiotic resistance (Jessen *et al.*, 1959).

During recent years the question has arisen (R. E. O. Williams, 1959, personal communication) of whether there is any difference in virulence between type 80 and the closely related type 52/52A/80 (Asheshov and Rippon, 1959; Rountree, 1959). In the present material the proportion of E.Y.— strains and antibiotic-resistant strains was the same among strains of these two types; a comparison of virulence as estimated from an analysis of the mortality rate could not be carried out because of the small number of strains of type 52/52A/80.

The composition of the present material—epidemiologically unrelated cases of bacteraemia—renders it quite certain that the conclusions drawn regarding the frequency, the mode of infection, the mortality rate, the phage-types, and the biochemical properties of the strains are not influenced by particular local conditions in single hospitals or by the predominance of a few endemic or epidemic strains.

Summary

Out of 201 epidemiologically unrelated cases of staphylococcal bacteraemia, 94 were contracted in hospitals, and 88 outside hospitals; in 19 the origin of the infection was unknown.

In hospital-acquired infection the mortality rate was 55%. Of these cases 50% originated from surgical procedures and 33% from cutaneous boils. In half of the cases staphylococci belonging to phage-types 80 and 52/52A/80 were the infecting agents and in a quarter of the cases strains belonging to group III. Nine-tenths of the strains were penicillin-resistant and one-fifth tetracycline-resistant.

In infections contracted outside hospitals the mortality rate was 28%. In 44 cases the origin was unknown. In a third of the cases the infections originated from boils. One-third of the strains belonged to group I. 69% of the strains were penicillin-resistant. Only 6% of the strains were tetracycline-resistant.

The properties of the infecting strains were correlated to the mortality rate. No correlation was found concerning the production of alpha-toxin, hyaluronidase, or the phage-type.

Infections due to drug-resistant strains gave a higher mortality rate than those due to sensitive ones, and infections caused by egg-yolk-negative strains gave a higher mortality rate than those caused by egg-yolk-positive ones.

The levels of antibodies in serum against alpha-toxin and hyaluronidase showed no correlation to clinical features, mortality rate, or the *in vitro* production of these two substances.

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