had no adverse effect. Ampoules containing 1 c.cm. of semen were therefore vitrified at $-196^{\circ}\text{C}.$ or $-79^{\circ}\text{C}.$ and maintained at the latter temperature for 2 days and 8 days. In each case thawing out showed that an abundance of spermatozoa had survived. A long-term experiment has now been set up, but in view of the work of Jahnel and of Shettles it is fairly certain that under optimum conditions large numbers of human spermatozoa will survive prolonged vitrification.

A much more important and doubtful point is whether vitrification affects the power of the spermatozoon to fertilize and activate the egg and induce normal embryonic development. In the experiments on fowl spermatozoa, quoted above, normal development was not induced after freezing for 1 hour at $-79^{\circ}\text{C}.$, but the partial dehydration before vitrification may have affected their genetic properties. The question is of great interest. Artificial insemination of humans will no doubt become increasingly common, and the elaboration of a method permitting of prolonged storage and transport of the semen without affecting the genetic properties of the spermatozoa would open up remarkable possibilities. It is not obvious how the problem of genetic modification is to be investigated with human material, and it is unfortunate that the spermatozoa of laboratory mammals, including those of the Rhesus monkey, are killed by vitrification under any conditions so far investigated.

Summary

A large proportion of human spermatozoa survive for long periods in semen frozen in bulk at $-196^{\circ}\text{C}.$ or $-79^{\circ}\text{C}.$

Spermatozoa do not survive when minute amounts of semen are frozen as films or in fine capillary tubes.

The rate of freezing and thawing is not the primary factor in the survival of human spermatozoa exposed to low temperatures.

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HAEMOLYTIC STREPTOCOCCAL THROAT INFECTIONS: THEIR COMPLICATIONS AND SEQUELS

WITH SPECIAL REFERENCE TO PENICILLIN TREATMENT

BY

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The British garrison in a small Italian harbour town has recently had a very high incidence of carriers of haemolytic streptococci. No systematic survey had been attempted, but a throat swab from any unselected person not showing in the culture at least a few colonies of haemolytic streptococci was an unusual occurrence. Accordingly the number of admissions for haemolytic streptococcal tonsillitis was considerable—79 cases, including 11 peritonsillar abscesses, in 6 months. A few complications such as pneumonia and scarlet fever also occurred. Along with the streptococcal infection ran a high incidence of erythema nodosum and acute rheumatism—some of the cases developing under our very eyes.

The material may be divided in two groups: the first covers the period Nov., 1944, to Jan., 1945, and comprises 34 cases of tonsillitis, including two peritonsillar abscesses, 3 cases of pneumonia, 1 of scarlet fever, 4 of erythema nodosum, and 6 of acute rheumatism; the second group of patients, treated in Feb.–April, 1945, consists of 43 cases of tonsillitis—including 9 peritonsillar abscesses, 7 cases of erythema nodosum, and 11 cases of acute rheumatism.

Acute Tonsillitis

No special attention at first had been paid to the mild cases. If the temperature did not rise above 102° for more than two days no treatment was given. The throat swabs remained positive in almost every case. An attempt to sterilize the throats

in a number of cases through frequent spraying with sulphathiazole powder or calcium penicillin powder failed completely. Cases with pyrexia in the first group were given 20 to 30 g. of sulphathiazole, but the results were no better. Six of the 32 cases returned with a recurrence of their symptoms.

Encouraged by the favourable results achieved by MacGregor and Long (1944) with penicillin pastilles, we introduced them as a routine treatment at the end of January. In preparing the pastilles we followed the technique described by these authors, and gave 10 pastilles daily, 1½-hourly, until the throat became clear. A throat swab was taken on admission, and treatment started at once. Anything between 18 and 46 pastilles was given. On completion of treatment a throat swab was taken again, and the patient was discharged from hospital if it was sterile. No recurrence of symptoms and no complications occurred in this group. The clinical and bacteriological results are summarized in Table I.

TABLE I.—*Haemolytic Streptococcal Tonsillitis*

	Mild Cases (Temperature not above 102° for more than Two Days)				Moderate and Severe Cases (Temperature above 102° for Two or More Days)			
	No Treatment	Sulphathiazole Spray 4-hourly	Calcium Penicillin Spray 4-hourly	Penicillin Pastilles	Sulphathiazole 20–30 g.	Sulphathiazole 20–30 g. and Calc. Penicillin Spray	Sulphathiazole 20–30 g. and Penicillin Pastilles	Penicillin Pastilles only
No. of cases	6	6	6	18	7	7	8	8
Clinical cure in days	4–11	5–10	6–11	3–5	5–21	6–22	3–7	2–9
Average	(7)	(6)	(8)	(3½)	(14)	(13)	(5)	(6)
Days in hospital	7–14	7–16	8–14	5–10	8–33	8–30	5–10	4–14
Average	(10)	(11)	(11)	(8)	(17)	(16)	(8)	(8)
No. of patients with positive cultures before discharge	5	6	5	0	5	7	0	1

No claim of a permanent sterilization can be made. In two cases of chronic tonsillitis throat swabs remained positive after 88 and 126 pastilles.

Peritonsillar Abscesses

The two patients with peritonsillar abscesses in the first group were given 30 g. of sulphathiazole and inhalations. One recovered in 12 days, but his general condition did not allow discharge from hospital until the 28th day. Repeated throat swabs showed pure growths of haemolytic streptococci. The second was very seriously ill for 3 days and a tracheotomy was considered; he recovered slowly, and left hospital after 26 days. The throat swab before discharge still showed a good growth of haemolytic streptococci.

The results in the nine cases of the second group are summarized in Table II.

TABLE II.—*Cases of Haemolytic Streptococcal Peritonsillar Abscesses Treated with Penicillin Pastilles*

Patient No.	No. of Penicillin Pastilles Given	Subjective Relief (Days)	Clinical Cure (Days)	Discharge from Hospital After (Days)	Throat Swab on Discharge
1	22	1	3	8	Sterile
2	18	1	2	8	"
3	40	2	4	9	"
4	28	2	3	10	A "few colonies of haemolytic streptococci"
5	32	1	3	8	Sterile
6	36	1	4	7	"
7	20	1	2	6	"
8	38	2	4	11	"
9	42	1	4	9	"

Erythema Nodosum

The four cases of erythema nodosum in the first group occurred in Jan., 1945, all in patients with mild haemolytic streptococcal tonsillitis—two untreated and two treated with sulphathiazole spray. In one of each group acute rheumatism followed. The rash faded after 8 to 11 days, during which period throat swabs constantly showed a growth of haemolytic streptococci. The erythrocyte sedimentation rate

was, and remained, high in the two cases followed by acute rheumatism, and became gradually normal within three weeks in the other two. Five more cases of untreated haemolytic streptococcal tonsillitis developed erythema nodosum at the end of Jan., 1945, when treatment with penicillin pastilles was introduced; they had been given the pastilles as soon as the rash became evident. Two more cases were admitted with a history of erythema nodosum of 1 to 2 days' duration; they also were given penicillin pastilles. In one of them acute rheumatism followed very soon. In all those instances in which penicillin pastilles were given the rash faded and disappeared in 1 to 3 days, and the erythrocyte sedimentation rate dropped from values ranging between 23 and 54 mm. per hour to less than 10 mm. per hour on the fifth day at the latest, with the exception of the one followed by rheumatic fever. All throat swabs became negative within 4 days. All the 11 cases of erythema nodosum had a thorough clinical and radiological examination to exclude tuberculosis.

On two occasions "erythema nodosum" appeared in patients with lobar pneumonia under sulphathiazole treatment. The E.S.R. was 10 and 14 mm. per hour. Sulphathiazole was discontinued, and the rash disappeared within 24 hours. Not a single patient suffering from haemolytic streptococcal tonsillitis and treated with penicillin pastilles developed erythema nodosum.

Acute Rheumatism

Six of our tonsillitis cases of the first group developed rheumatic fever while in hospital; two of them—as mentioned—have also had erythema nodosum. * None of the patients treated with penicillin pastilles showed any signs of acute rheumatism. From those admitted with already evident symptoms, 6 were fresh cases and 4 relapses. All but one gave a history of recent tonsillitis, and all throat swabs showed a growth of haemolytic streptococci.

The first six patients were treated with intramuscular penicillin injections. In all but one case pyrexia did not last for more than two days, and the E.S.R. returned to normal at the 14th day at the latest. The swelling remained confined to the primarily affected joints, and subsided in 3 to 10 days. Only one had a clinical course which, though mild, could not be regarded as affected by treatment. Of the patients who were admitted with already developed rheumatic symptoms, 3 fresh and 2 relapsing cases were given penicillin treatment; the rest had the customary doses of sodium salicylate. Two of the primary and one of the relapsing penicillin-treated cases showed the course described above. All the others presented the well-known clinical picture of this disease.

The maximum amount of penicillin given was half a million units. It is noteworthy that three of those patients whose course of illness seemed to have been affected by the penicillin treatment liked the tiresome three-hourly injections immensely and begged us not to discontinue them.

Comment

The superiority of penicillin to sulphonamides in treatment of haemolytic streptococcal infections had been sufficiently stressed by the American National Research Council (1943) and Herrel (1944). The results achieved by Plummer *et al.* (1945) in throat infections with systemic penicillin treatment are better than ours—"Improvement in 8 to 12 hours, fever normal in 24 hours, and all throat swabs negative in 48 hours"—but relapses and complications were frequent unless the treatment was carried through for six days. MacGregor and Long (1944) had good results with penicillin pastilles, but found the treatment of carriers disappointing. The longer duration of illness in our patients as compared with those of Plummer *et al.* may be considered partly counterbalanced by the absence of recurrences and complications and the cheapness and simplicity of the treatment. Our results with peritonsillar abscesses can safely be described as striking; on several occasions the abscesses "melted away."

The relatively frequent occurrence of erythema nodosum is of some theoretical interest. Though there is a tendency to minimize the importance of the "rheumatic" origin as compared with the tuberculous, experimental work has shown that streptococcal nucleoprotein can cause the typical eruptions (Collis, 1932; Coburn and Moore, 1936). Lymphopathia

venerea and sulphonamides may also cause "erythema nodosum." It seems feasible that just as discontinuation of sulphonamides is followed by disappearance of the eruption, so sterilization of the throat with penicillin pastilles may abort or even prevent the development of erythema nodosum.

Though acute rheumatism may follow different infections (Copeman, 1944), the connexion with haemolytic streptococci is certainly common, as shown only lately for the Canadian Army (Feasby, 1944). We are unable to explain by coincidence alone the benign course of several of our cases treated with penicillin. This is in contradiction to the conclusions of Watson *et al.* (1944), Herrel and Kennedy (1944), and Foster *et al.* (1944); the last-named author believes even in a deleterious effect of penicillin. The number of cases reported by these authors seems to us too small for a definite conclusion.

Summary

Acute haemolytic streptococcal tonsillitis and peritonsillar abscess respond well to treatment with penicillin pastilles.

Erythema nodosum following haemolytic streptococcal tonsillitis may be aborted, and possibly prevented, by penicillin pastilles.

Some cases of rheumatic fever seem to respond to systemic penicillin treatment.

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TWO UNUSUAL STRESS FRACTURES

BY

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AND

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Stress fracture, as represented by spontaneous fracture of a metatarsal, usually the second, was common enough during the war of 1914–18, but stress fractures of other bones were not recognized as such at that time, and very little was heard on the subject until Roberts and Vogt, in 1939, published 12 cases of "pseudo-fracture of the tibia." Since then stress fracture—to use the most popular name—has been recognized in a variety of sites. That it is a true spontaneous fracture and not a "pseudo" was first demonstrated in one of Hartley's (1942) cases, although fracture with displacement did occur in one case of Roberts and Vogt's, but there trauma could not be altogether excluded. Now stress fractures have been reported as occurring in metatarsals, fibula, tibia, femur—shaft and neck—pubis, vertebrae, and first rib.

In two of the early series of cases published, where the bone involved was the tibia, the average age of the patients was just over 10 years. In all series those affected are almost entirely adolescent or in the early twenties and involved in strenuous exertion; though in 1940 Jackson Burrows reported a case of spontaneous fracture of the lower third of the fibula in a lady of 61 years who had been leading an energetic life. It is this almost invariable history of early age and strenuous exertion in cases of stress fracture which has prompted us to describe in detail the following two cases.

Case I

Miss C., aged 64, housekeeper. She was first seen by one of us on Oct. 6, 1944, when she complained of pain in the upper third of the right tibia of one month's duration. There was no history of injury; her work was not hard and her duties had not varied for a number of years. The pain was described as gnawing in character, and, strangely enough, was most severe at night, being