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Corynebacterium haemolyticum infections in Cambridgeshire

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SUMMARY

In the Cambridge area, 143 patients infected with *Corynebacterium haemolyticum* were found during the period May 1967 to December 1974. The pharynx was the commonest site of infection and 100 of the 137 pharyngeal infections were in patients aged between 15 and 25 years. Such patients usually had a sore throat; about half of them also had a maculopapular rash. The organism and the clinical features which we have come to regard as typical of this infection are briefly described.

INTRODUCTION

Corynebacterium haemolyticum was first described by MacLean, Liebow & Rosenberg (1946). They collected 150 strains of the organism from throat infections in American servicemen and from skin lesions in South Pacific Islanders during World War II. Subsequently Gärtner & Knothe (1960) isolated 10 strains in Germany and Hermann (1961) 8 in U.S.A. Czeckoslovakian workers have since recognized many infections (Patočka, Mára, Souček & Součková, 1962).

In the United Kingdom, Richardson & Smith (1968) isolated one strain from bovine semen and Roberts (1969) one from an ovine pneumonia. Ryan (1972) reported that he had recognized three strains from human infections in Exeter. A strain of *C. haemolyticum*, NCTC 9998, was isolated by J. D. Abbott, P.H.L.S. Manchester, in 1957.

The 143 strains reported in this paper were isolated in Cambridge during the period May 1967 to December 1974. A preliminary report of our work has already appeared (Fell, Nagington, Naylor & Olds, 1973).

MATERIALS AND METHODS

Swabs submitted by general medical practitioners were plated on 5% horse blood agar layered on a digest agar base. After overnight incubation the plates were examined with a hand lens. When the presence of *C. haemolyticum* was suspected the plates were reincubated for a further day to check for the characteristic 48 h colonies.

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Table 1. Corynebacterium haemolyticum: *age and sex of patients with pharyngeal infections*

	Age							
	0–< 5	5–< 10	10–< 15	15–< 20	20–< 25	25–< 30	⩾ 30	Total
Male	1	3	2	13	25	5	4	53
Female	0	8	5	46	16	5	4	84
Total	1	11	7	59	41	10	8	137

Hartley's tryptic digest broth was used as the base for digest agar and for blood agar. Occasionally Columbia (Oxoid) base was used instead of the digest agar underlay.

Other procedures were as described by Cruickshank, Duguid, Marmion & Swain (1975).

RESULTS

First patient

A 25-year-old research biochemist developed a rash on his feet which spread to his legs and arms. He had the sensation of a lump in the throat, but he did not otherwise feel ill, nor was he pyrexial. He went to his doctor on the third day of his illness. Scarlet fever was diagnosed, a throat swab was taken, and a 7-day course of penicillin was prescribed. The rash faded in 3 days and was followed by desquamation. The swab was plated on horse blood agar, and an almost pure growth of *C. haemolyticum* resulted.

Throat infections

The age and sex distributions of the 137 patients with symptoms of upper respiratory tract infection are shown in Table 1. Of these, 100 were between the ages of 15 and 25 years. There was usually some degree of sore throat, although this was of variable severity: sometimes it was minimal as in the first patient; at other times it was more like that of an acute streptococcal tonsillitis. It was often mentioned by clinicians that the appearance of the throat was worse than the symptoms would suggest.

There was a skin rash in 65 patients; in 34 of them the rash was the first or predominant symptom. It was typically erythematous, maculopapular and irritant, and was usually peripheral in distribution. In some patients it was described as scarlatiniform or rubelliform.

In 35 patients enlargement of the cervical lymph nodes was noted and in 11 it was specifically stated that they were not enlarged. A nose swab was taken from 47 patients at the same time as a throat swab; only two of the nasal cultures yielded *C. haemolyticum*. The organism was isolated from the excised tonsils of one patient.

Almost without exception, the symptoms and signs abated on administration of a chemotherapeutic agent which was usually penicillin. Milder infections cleared without treatment. Three patients had persistent symptoms; their throat cultures yielded *C. haemolyticum* at intervals varying from 2–4 weeks after first isolation,

despite a course of oral antibiotics (penicillin in two cases; erythromycin followed by penicillin in one). Six patients had a recurrence of their symptoms at various intervals after the first isolation of the organism. *C. haemolyticum* was cultured during these recurrences, although it had not been found immediately after treatment with penicillin. One patient promptly relapsed after finishing a course of penicillin; his culture was still positive.

The organism was found only in association with current or recent symptoms.

Infection of sites other than the throat

The six patients who had infections of sites other than the throat were all male; all had negative nose and throat cultures, and none had a rash. The lesions, with the age of the patient in parentheses, were: septic toe (14 years), recurrent paronychia (15), septic finger (35), varicose ulcer (57), acute paronychia (71), trophic ulcer in a diabetic (84). Thus, the age and sex distributions characteristic of throat infections did not apply to infections of other sites.

In three of these six patients and in nine of the patients with throat infections, the culture also yielded a haemolytic streptococcus of Lancefield group A, C or G; in each instance *C. haemolyticum* was the predominant organism.

Source of infection

Usually this was not known. In five instances, *C. haemolyticum* was isolated from typical throat infections which developed in close household contacts of a patient. No patient had a history of close association with farm animals.

Bacteriology

After overnight incubation of horse blood agar plates, colonies of *C. haemolyticum* were circular, 0·5 mm in diameter, low-convex, with a finely matt surface and an entire edge, grey, opaque, friable, undifferentiated and *non-haemolytic*.

After incubation for 48 h (Plate 1A) the colony was usually 1–1·5 mm in diameter, and had a narrow zone of complete haemolysis. Occasionally the colonies had a rough surface and an irregular edge (Plate 1B). Sometimes there was a central surface pit and concentric contour lines. The most remarkable and constant feature of the 48 h colony was a central opaque dot; if the colony was lightly scraped aside (arrow), the central dot was left behind and the colony had etched the medium; this was very helpful in finding colonies in mixed cultures. The uniformity of the colonial appearance of any one plate culture was a striking feature.

On microscopic examination the organisms were gram-positive rods without clubbing or barring. They varied in length. Individual bacteria remained in contact at angles to each other, and large, raft-like clusters were common. Rods with a short branch were often observed. Metachromatic granules were not seen in smears stained by Albert's method or by Loeffler's methylene blue.

The biochemical reactions of our strains are summarized in Table 2. The few strains we tested by the disk-diffusion method were sensitive to penicillin, erythromycin and tetracycline.

Table 2. *Cultural and biochemical properties of* Corynebacterium haemolyticum

Shape	Rods	Mannitol	–
Gram reaction	+	Mannose	–
Motility	–	Fructose	+ (late)
Growth in air	+	Xylose	–
Growth anaerobically	+	Galactose	–
Catalase	–	Arabinose	–
Loeffler's medium	No liquefaction	Inositol	–
Hoyle's tellurite medium	No growth	Glycerol	–
Glucose	+	Salicin	–
Lactose	+	Gelatin	–
Maltose	+	Nitrate	–
Sucrose	–	Urea	–
Trehalose	–	Indole	–
Starch	+	H_2S	–

Intramuscular or subcutaneous inoculation of cultures into guinea-pigs induced local necrotic lesions but no evidence of toxaemia. Intraperitoneal inoculation of mice with undiluted 24 h serum broth culture usually killed the animals within 4 days. *C. haemolyticum* was recovered from the local lesions of the guinea-pigs; it was grown from the peritoneal fluid of the dead mice and sometimes from their heart blood as well.

Differentiation from glandular fever

Eighteen patients with *C. haemolyticum* infection of the pharynx were diagnosed clinically as suffering from glandular fever. The general practitioner submitted sera for a Paul Bunnell test from 16 of these, four of which gave a positive result.

The laboratory sometimes requested serum after *C. haemolyticum* infection had been diagnosed. Of 23 sera so obtained, all were Paul Bunnell negative.

In addition, the VDRL test for syphilis was applied to 31 sera of *C. haemolyticum* patients, all with negative results.

DISCUSSION

In our experience, infection with *C. haemolyticum* is not uncommon when it is regularly looked for in cultures from patients with sore throat. Successful recognition of the organism depends on being familiar with the colonial appearance on the particular blood agar in regular use in the laboratory.

The numbers of isolations from pharyngeal infections for the years 1967–74 were 1, 2, 6, 15, 26, 23, 40 and 24 respectively. The increase from 1967 to 1971 may represent our increased interest and familiarity with the organism. On the other hand, there may have been a real increase in the number of infections because the first isolation in 1967 was made by one of us who had been examining throat swab cultures for the previous 5 years without recognizing a strain of *C. haemolyticum*.

Some workers may have failed to recognize the organism because some properties described by MacLean *et al.* (1946) for their South Pacific strains, and the properties described in textbooks of bacteriology (Cowan & Steel, 1974; Wilson & Miles, 1975) differ from those of our strains. There are several important discre-

pancies: our strains were uniformly catalase-negative; they only liquefied gelatin after 2 weeks if at all; like those of Patočka *et al.* (1962) they failed to ferment sucrose; they were only very slightly haemolytic on horse blood agar after 24 h incubation. The specific name *haemolyticum* is misleading for most laboratory workers, since it refers to the organism's action on human blood (MacLean *et al.* 1946). The properties of the National Collection of Type Cultures strain, NCTC 8452, correspond with those of our strains.

Although we were aided in the identification of our early strains by an information sorter (Olds, 1970), most of the features that we have since found useful in recognizing *C. haemolyticum* were lucidly described by MacLean *et al.* (1946).

Many authors have called this organism *C. pyogenes* var. *hominis* since Barksdale, Li, Cummins & Harris (1957) reported that mutants resembling *C. haemolyticum* were found in cultures of *C. pyogenes*. It seems clear that, whatever the evolutionary origin of *C. haemolyticum* may be, it is behaving as an epidemiological entity in the Cambridge area; it is not evolving from *C. pyogenes* before each isolation since none of our cases was associated with farm animals, and family infections have occurred. In contrast, the rare human infections with *C. pyogenes* which we have encountered have had a close association with farm animals.

A number of observations indicate a pathogenic role for *C. haemolyticum*: the clinical features exhibited by most of our patients were constant; *C. haemolyticum* was generally the dominant organism in throat cultures during the patient's illness and disappeared on recovery; other recognized pathogens were in most instances not found.

It seems possible that the incidence of *C. haemolyticum* infections is relatively greater in the Cambridge area than in other parts of the United Kingdom. If so it may be pertinent that this university town has a large population in the age group in which *C. haemolyticum* infections are most frequent.

On the other hand, *C. haemolyticum* may be common but unrecognized in other parts of the U.K. That it has been present since 1957 is suggested by the entry in the catalogue of the National Collection of Type Cultures for NCTC 9998 – 'from P.H.L.S. Manchester in 1957 (Tonsillitis)'.

We would not have recognized so many infections with *C. haemolyticum* in the Cambridge area except for the close cooperation of the Cambridge Public Health Laboratory with many General Practitioners, whose interest and help we gratefully acknowledge.

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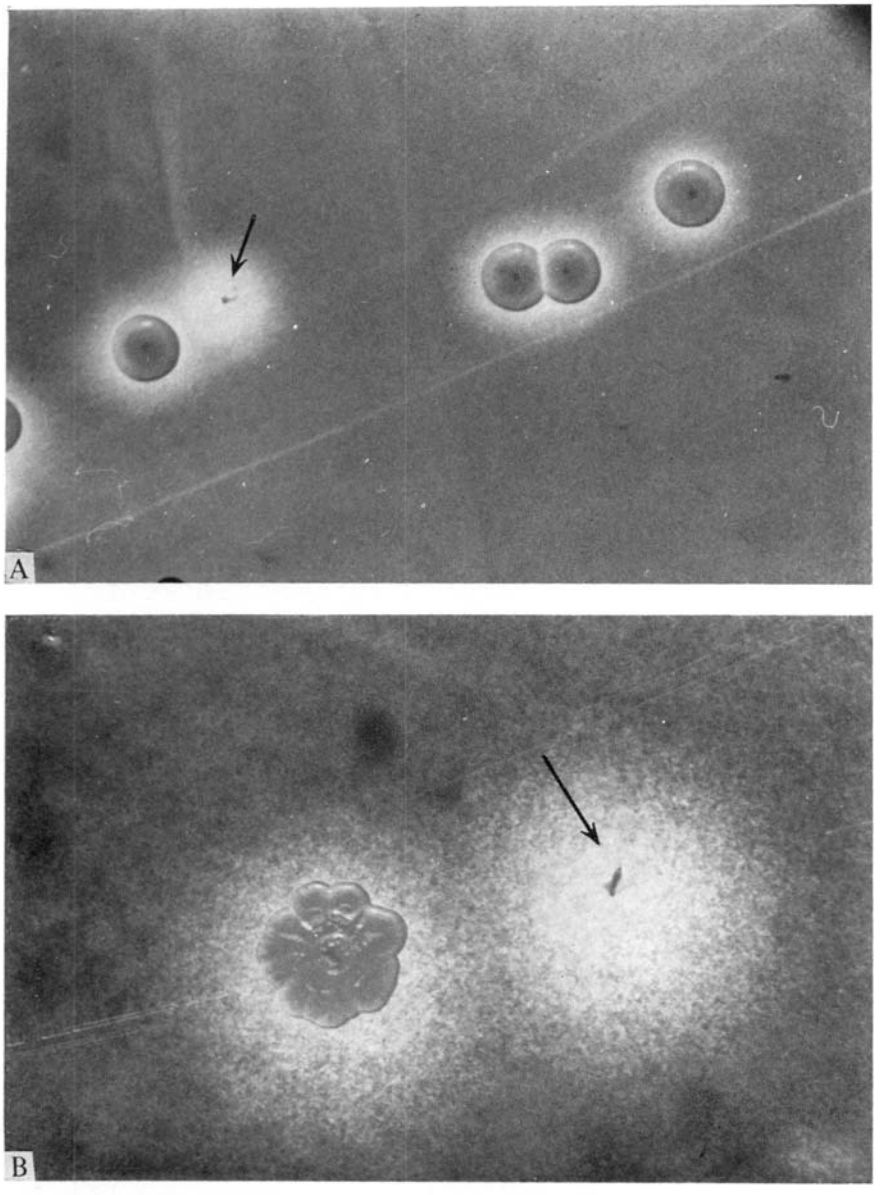
EXPLANATION OF PLATE

A. *Corynebacterium haemolyticum*, smooth colony. Horse blood agar: 48 h at 37 °C, × 10.

B. *Corynebacterium haemolyticum*, rough colony. Horse blood agar: 48 h at 37 °C, × 10.

Arrows indicate the central opaque dot remaining in the medium after the colony has been scraped aside.



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