The causes of death are tabulated. Twenty-one patients died from carcinoma, a figure which corresponds to the expected number of cancer deaths. Among this group, however, no fewer than eight females and six males died from gastric carcinoma. The expected number of deaths from carcinoma in all sites is 15, from gastric carcinoma only 5, so that the excessive mortality from gastric carcinoma is statistically significant.

It is found that patients suffering from pernicious anaemia do not develop their gastric carcinoma in the fundus and upper part of the body of the stomach, where the pathological changes characteristic of pernicious anaemia are localized. Possibly the explanation is that both pernicious anaemia and gastric carcinoma result from achlorhydria.

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HAEMOLYTIC STREPTOCOCCAL GANGRENE OF BREAST SUCCESSFULLY TREATED WITH STREPTOMYCIN

BY

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Haemolytic streptococcal gangrene was first accurately described by Meleney (1924). In almost all cases there is an initial lesion which may escape the patient's notice. The limbs are affected more commonly than any other part of the body, as they are exposed to injury. The disease may occur in the scrotum (Marcus, 1949) and rarely on the trunk. Its clinical course is characterized by very rapid development. Within twenty-four hours the affected part becomes markedly swollen and shows all the signs of a rapidly spreading inflammation. In a day or two blisters and bullae begin to form and then the skin becomes frankly gangrenous. The condition is due to the haemolytic streptococcus, which can be obtained by culturing the discharge aerobically or anaerobically. Other organisms, such as *Staphylococcus aureus*, *Pseudomonas pyocyanea*, *Bact. coli*, *Proteus vulgaris*, *Streptococcus faecalis*, and diphtheroids may occur as secondary invaders.

Meleney (1924) recommends incision as far as the extension of the subcutaneous necrosis, but not further, as incisions in the zone of cellulitis may be harmful. The gangrenous skin should be excised as soon as the line of demarcation has developed and removal can be adopted without causing much bleeding. Amputation is rarely necessary, as the infection is superficial in most cases and can usually be combated by superficial incisions.

Penicillin and the sulphonamides have proved of value in haemolytic streptococcal infections, and in many cases render incisions unnecessary. The following two cases may be of interest, as these drugs failed to prevent the infection spreading, but when used with streptomycin localization occurred within a few hours.

Case 1

A married woman aged 57 was admitted for investigation for Cushing's syndrome. She had a small infected area on the left breast, for which she was given 100,000 units of penicillin daily. The inflammation extended by 1½ in. (3.8 cm.) in 24 hours and discharged copiously. When seen five days later the skin of the breast, except for the nipple and areola, was gangrenous (Fig. 1). The spreading margin extended upwards towards the clavicle, and was painful and vesiculated. Sulphatriad, 1 g. thrice daily, was given for 48 hours.

FIG. 1.—Case 1. Before streptomycin. The skin of the breast is gangrenous, and the gangrenous process is extending by 1½ in. daily.

Culture on February 16 showed: haemolytic streptococcus sensitive to 1/16 unit of penicillin per ml. and 8 units of streptomycin per ml.; *Staph. aureus* sensitive to 32 units of penicillin per ml. and 2 units of streptomycin per ml. Streptomycin, 0.5 g. six-hourly, was given—total 6 g.

The general condition improved within 12 hours. The tenderness was lessened, the spreading process was arrested, and the gangrenous skin showed a line of demarcation. Culture: haemolytic streptococci sensitive to 1/16 unit of penicillin per ml. and 8 units of streptomycin per ml.; *Staph. aureus* resistant to at least 32 units of penicillin per ml. and sensitive to 4 units of streptomycin per ml.

On February 18 the bacteriological findings and sensitivity to penicillin and streptomycin were unaltered. About three-quarters of the gangrenous skin had separated, and this was easily cut away with scissors, leaving a remarkably clean granulating surface. The remainder of the skin was removed next day without causing much bleeding; the nipple and areola were left intact. A small area below the nipple was affected more deeply than the remainder of the breast and contained a slough about ¼ in. (1.9 cm.) long. Culture from this region grew *Proteus vulgaris*.

On February 23 healing began, and granulations were healthy except for a small area below the nipple. Culture from this region grew *Proteus vulgaris* resistant to at least 32 units of penicillin. On March 23 postage-stamp Thiersch grafts were applied to the granulating surface. By April 1 most of the grafts had taken successfully and healing proceeded rapidly. The raw area had completely epithelized by April 18.

Comment on Case 1

The haemolytic streptococcus isolated was of Lancefield Group A. It was not completely eliminated from the margin of the gangrenous area during the period streptomycin was given. After the gangrenous skin had been removed the organisms were not found in repeated cultures from the margin of the granulating tissue. As the skin was not viable when streptomycin treatment was initiated

it is not surprising that the organisms were not eliminated until the affected area was excised.

Case 2

A married woman aged 64 had a radical mastectomy for carcinoma of the breast. The wound had been sutured without tension. Five days after operation she was toxic and had severe pain in the wound. There was a small area of erythema with a vesicular centre in the outer part of the wound. She was given 500,000 units of penicillin intramuscularly daily and 1 g. of sulphadimidine three times a day.

When seen 14 hours later the temperature was 103° F. (39.4° C.), pulse 180. The outer part of the incision showed a gangrenous area, undermining of the skin, and gross oedema. While being examined the margin was seen extending. The discharge from the wound was copious and foul-smelling. Culture from the margin grew anaerobic haemolytic streptococci sensitive to one unit of streptomycin per ml., *Staph. albus* (coagulase-negative), and an organism of *Bacillus subtilis* group. Streptomycin, 0.5 g. six-hourly, was given—total 6 g. Sulphadimidine was discontinued, as this caused vomiting.

Next day her general condition improved considerably; the tenderness was much less and the spreading margin was arrested. The following day the gangrenous skin showed a line of demarcation and was excised (Fig. 2). Cultures grew

FIG. 2.—Case 2. Two days after receiving streptomycin. The gangrenous skin showed a line of demarcation and was excised. The sutures have been removed and the remainder of the incision has healed. Pain and oedema were markedly decreased.

anaerobic haemolytic streptococci, non-haemolytic streptococci, and an organism of *B. subtilis* group. A week later the wound was dry and healthy. Closure was carried out with interrupted sutures, and a small stab drain was inserted into the dead space below the suture line.

Discussion

Meleney (1933) classified the various types of infectious gangrene of the skin as acute and chronic. The acute forms are represented by gas gangrene and haemolytic streptococcal gangrene; the chronic forms include ecthyma (gangrenous impetigo), anaerobic gangrene, fuso-spirochaetal gangrene, and progressive bacterial synergic gangrene. The last-named condition is due to a symbiotic infection by a non-haemolytic *Staph. aureus* (Brewer and Meleney, 1926; Meleney, 1931, 1933, 1935). There are a few reports of successful treatment of post-operative progressive bacterial synergic gangrene with penicillin (Grimshaw and Stent, 1945; Meleney *et al.*, 1945; Clarke, 1947). In successful cases the inflammation, induration, oedema, and pain around the wound resolve and healing occurs rapidly, or after skin-grafting. Failing a satisfactory response excision

of the wound is necessary before the condition is finally controlled (Meleney *et al.*, 1945).

Haemolytic streptococcal gangrene has been described as phlegmonous or gangrenous erysipelas, but should not be confused with erysipelas, which is also caused by the haemolytic streptococcus. Lymphangitis and lymphadenitis are rare, though phlebitis is fairly common in the former condition. In erysipelas, organisms may be cultivated at and beyond the spreading margin but not in the centre. The reverse is the case in haemolytic streptococcal gangrene. There may be a wide zone of sterile oedema beyond the limits of necrosis.

The synergic effect of penicillin, streptomycin, and the sulphonamides is of value when one drug alone fails to arrest the gangrenous process. This synergic effect has been noted in other infections (Redewill and Potter, 1948; Wells and Marcus, 1949; Bigger and Daly, 1949). The response to this form of treatment in the above two cases was dramatic. Within a few hours there was demonstrable improvement in the local and general condition of the patients. The spreading process was arrested and separation of the gangrenous skin began before completing streptomycin therapy. In both cases incisions as recommended by Meleney (1924) were not necessary.

The morbidity resulting from anaerobic streptococcal gangrene may be decreased by early recognition of the condition and by giving streptomycin before the gangrenous process is extensive. Incisions and skin-grafting will then be unnecessary. It is questionable whether secondary sutures are as valuable as skin-grafting. The undermining of the skin results in a dead space which cannot be easily obliterated by sutures.

Summary

Two cases of streptococcal gangrene of the breast are described. Penicillin and the sulphonamides by themselves failed to prevent the infection spreading, but when used together with streptomycin this was localized within a few hours.

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Normally claims for sickness benefit must be made within three days of the beginning of an illness, but when a person has never claimed sickness benefit before there will be no penalty so long as the claim is made within 21 days of the beginning of the illness. This is the main effect of provisional regulations made by the Minister of National Insurance, Dr. Edith Summerskill, which came into force on July 19. The regulations also enable delay in making a claim to be automatically excused during a period in hospital up to a maximum of three months. There is no change in the general rule that sickness benefit cannot be paid for more than three days before the claim is received at the local National Insurance office unless good cause for the delay is shown. The new regulations, however, allow late claims to be accepted without inquiry into the reason in special circumstances where difficulty has been experienced by insured persons.