tion of the appendix, usually through a diverticulum, but the large quantities of pseudomucin which may be found have led to speculation concerning its origin. There are three possibilities.

1. The serosal cells may be stimulated by the presence of colloid to secrete an identical substance. This seems unlikely. Trotter (1910) stated that the peritoneal lining cells could assume columnar for as but believed that their reaction was of the nature of a foreign-body peritonitis and limited to the formation of enclosing adhesions.

2. The peritoneal pseudomucin may result from its continued discharge from a perforation of the mucocele, but if this were so the complication would be halted by removal of the appendix. It may, however, recur after appendectomy and eventually lead to the death of the patient.

3. The most probable explanation, in both appendiceal and ovarian types, is that mucus-secreting cells escape into the peritoneal cavity and, becoming implanted there, continue to secrete. Such cellular elements are difficult to find histologically in the peritoneal colloid, but the hypothesis is supported by the experiments of Grodinsky and Rubnitz (1941), who injected the contents of mucoceles into the peritoneal cavities of other animals and produced progressive pseudomyxoma peritonei, while if the contents were first passed through a Seitz filter to remove the cells the condition did not develop.

Woodruff and McDonald (1940), in a study of 146 cases, divided appendix mucocele into two groups. In the first the mucosa consists of a single layer of columnar cells. Rupture of such a mucocele leads to a localized type of pseudomyxoma peritonei which does not recur after appendectomy. In the second, smaller group the mucosa is hyperplastic owing to the presence of papillae covered with large columnar cells containing hyperchromatic nuclei. This is regarded as a grade 1 adenocarcinoma, and perforation causes dissemination of malignant cells and a diffuse, progressive peritoneal lesion.

Pseudomyxoma peritonei of appendiceal or ovarian origin differs, therefore, only in degree of malignancy from the coelomic spread of colloid carcinoma of the alimentary tract.

The occurrence of mucocele of the appendix and pseudomucinous ovarian cyst in the same individual has been recorded many times. Bailey (1916) and Ries (1924) described cases with both lesions present simultaneously and discharging colloid into the peritoneal cavity. In Eden's (1912) patient an appendix mucocele was found two years after operation for a ruptured pseudomucinous cyst. The double condition is usually complicated by pseudomyxoma peritonei, and it is likely that one lesion results from transcoelomic implantation of mucus-secreting cells released by perforation of the other, although the reason for selective involvement of these viscera alone is not clear. Willis (1952) considers that the probable sequence is rupture of a primary ovarian cyst which causes colloid and cellular spread in the subserous tissues and thus involves the appendix leading to mucocele. In Case 2, however, the perforated appendix preceded the large ovarian cyst, although a small cyst was noted at the first operation. Hentz (1932) recorded a case with both lesions but without peritoneal colloid, and suggested that cells passed from the ovary to the appendix by lymphatic channels.

Other complications of appendix mucocele are acute inflammation (Case 2), intussusception (Ward-McQuaid, 1949), volvulus (Jones and Carmody, 1936), and occurrence in a hernial sac (Juvara and Borcescu, 1948).

The clinical features of uncomplicated mucocele are vague and symptoms are often absent. There may be a history of recurring pain in the right iliac fossa and a mass may be palpable in the abdomen or the pelvis. Radiology may show calcification of the appendix wall or of its contents, or a soft-tissue shadow displacing the caecum or producing a filling defect may be visible with an opaque meal. Rarely does the mucocele fill with barium.

The treatment is appendectomy; in the female, especially when the mucocele is perforated, the ovaries are examined for concomitant pseudomucinous cyst. Occasionally the dense adhesions of the appendix necessitate resec-

tion of bowel for its removal. When the complication of pseudomyxoma peritonei is present the myxomatous material is removed so far as possible, and post-operative radiotherapy to the abdomen is carried out in an attempt to destroy the disseminated mucus-secreting cells. Drainage of the peritoneal cavity is avoided because of the tendency to secondary infection. A more accurate prognosis may be given in such cases if the appendix mucosa is examined for the presence or absence of papillomatous formations.

Summary

Two cases of mucocele of the appendix are described, one of them associated with pseudomyxoma peritonei and with pseudomucinous cyst of the ovary. The pathogenesis, complications, and clinical features of the condition are discussed.

I am grateful to Mr. W. M. Beattie and Mr. C. H. Walsh for permission to record Case 2; to Dr. J. Carr Brundret for the histological reports; and to Mr. J. Cosbie Ross for advice in the preparation of this paper. I have to thank the central photographic department of the University of Liverpool for the photograph.

REFERENCES

- Bailey, F. W. (1916). *Surg. Gynec. Obstet.*, 23, 219.
 Bunch, G. H. (1945). *Ann. Surg.*, 121, 704.
 Cheng, K. K. (1949). *J. Path. Bact.*, 61, 217.
 Eden, T. W. (1912). *Lancet*, 2, 1498.
 Grodinsky, M., and Rubnitz, A. S. (1941). *Surg. Gynec. Obstet.*, 73, 345.
 Hentz, V. G. (1932). *Ann. Surg.*, 96, 456.
 Jones, T. E., and Carmody, M. G. (1936). *Amer. J. Surg.*, 32, 511.
 Juvara, I., and Borcescu, U. (1948). *British Medical Journal*, 1, 931.
 Muir, J. B. G. (1931). *Lancet*, 1, 131.
 Ries, E. (1924). *Surg. Gynec. Obstet.*, 39, 569.
 Shemilt, P. (1949). *Brit. J. Surg.*, 37, 118.
 Topping, M. H. (1937). Cited by T. R. Waugh and D. Findlay, *Amer. J. Surg.*, 1937, 37, 518.
 Trotter, W. (1910). *British Medical Journal*, 1, 687.
 Vorhaus, M. G. (1930). *J. Amer. med. Ass.*, 94, 165.
 Wangenstein, O. H., et al. (1937). *Ann. Surg.*, 106, 910.
 Ward-McQuaid, J. N. (1949). *Brit. J. Surg.*, 37, 109.
 Wells, A. Q. (1936). *Ibid.*, 24, 766.
 Willis, R. A. (1952). *The Spread of Tumours in the Human Body*, 2nd ed. Butterworth, London.
 Wilson, R. R. (1950). *Brit. J. Surg.*, 38, 65.
 Woodruff, R., and McDonald, J. R. (1940). *Surg. Gynec. Obstet.*, 71, 750.

A CASE OF ULCERATING HODGKIN'S DISEASE

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The ulcerative form of Hodgkin's disease is so rare and so difficult to diagnose that the following case is worthy of record.

Case Report

A woman aged 44 was admitted to St. Luke's Hospital, Bradford, in July, 1948, complaining of a painful swelling on the anterior chest wall, over her sternum, of twelve months' duration. The swelling had gradually become larger, recently fluctuant, and had been aspirated two weeks before admission. She also complained of painful stiffness of the neck for about three years, and aching of both arms for twelve months. The spleen was not palpable and no glands were enlarged. The E.S.R. was 18 mm. in one hour; haemoglobin, 85%; W.B.C., 16,000 per c.mm. (polymorphs 83%, lymphocytes 12%, monocytes 5%); platelets normal. The Wassermann reaction and Kahn test were negative on two occasions. X-ray examination showed erosion of the left sternoclavicular joint and adjacent sternum, with no new bone formation.

The fluctuant swelling was incised, pus and necrotic bone were curetted out, and the wound was closed. The wound healed by first intention. The pus obtained was sterile on culture and no organisms were found in the smear. A provisional diagnosis of a tuberculous lesion was made, and the patient was discharged home four weeks later, to await a bed at a sanatorium.

In March, 1949, she was readmitted from the sanatorium with the abscess from the sternum increasing in size and pointing in two places. Incision with curettage was performed, a large quantity of necrotic debris being evacuated. The appearance favoured the diagnosis of gumma, despite the negative Wassermann reaction and Kahn test. Examination of the pus again showed no tubercle bacilli or other organisms, and section of the curettings of the ulcer wall revealed necrotic tissue. A consultant venereologist diagnosed the ulcer as gummatous in nature despite the absence of other signs of syphilis. He gave a course of bismuth, penicillin, arsenicals, and iodides with no response. She was discharged home in April, and kept under out-patient surveillance.

In July she was readmitted as an emergency case following haemorrhage from the abscess, the cavity being packed to control it. Repeated examination of the pus showed no evidence of tubercle bacilli or actinomycosis. Guinea-pig inoculation was negative. No glands were palpable elsewhere in the body.

In August the swelling over the sternum had developed into a large ulcer, approximately 1 in. (2.5 cm.) in depth and 5 in. (12.5 cm.) in diameter, with an elevated edge and an uneven floor covered with necrotic granulations. A biopsy of the edge of the ulcer was taken, and the section report was as follows: "The histological picture is that of a chronic granulomatous lesion probably tuberculous in origin. The caseous material consists of degenerate cells with mucus and a few pus cells. No tubercle bacilli or other organism seen." The lesion was still thought to be tuberculous in nature.

Until June, 1951, progress was uneventful and the ulcer showed no change. She was then readmitted again for treatment of further haemorrhage from the ulcer. A recent swelling was found to be present below the right clavicle and a few discrete glands were palpable in the neck. This was the first appearance of glandular enlargement. No other glands were palpable and the spleen was not enlarged. A biopsy of one of the cervical glands was carried out, the pathological report on the gland being as follows: "Histological section shows marked fibrosis and complete loss of architecture. There is a proliferation of reticulum cells with several multinucleated cells and many eosinophils. The findings are in keeping with Hodgkin's disease."

In July an abscess was forming over the inner end of the right clavicle (see illustration). The patient was seen by Dr. Chester-Williams and transferred to the Radium Institute for a course of deep x-ray therapy.

In September the course had been completed and she showed a remarkable change; she had gained over 56 lb.

(25.4 kg.) in weight, but her pain was still troublesome. The ulcer had shrunk considerably in size, and in October this improvement had been maintained. X-ray examination of the cervical and dorsal spine showed no abnormality, but both clavicles showed absorption at their medial ends. The mediastinum was within normal limits, but the anterior ends of both first ribs were absorbed and showed no evidence of regeneration. Three months later the ulcer had practically healed.

In April, 1952, there was considerable local improvement, but she had severe pain over the fourth dorsal spine. Some supraclavicular infiltration was present, and her general condition was failing.

In October she had a painful swelling in both posterior triangles of her neck. The lower edge of the ulcer was extending, with a painful swelling over the lower end of the sternum. In November she had further subcutaneous swelling on the right chest wall and some loss of power in the right arm, with considerable induration in the supraclavicular regions.

In April, 1953, she attended for her eighth course of deep x-ray therapy. The ulcer had broken down again and was $1\frac{1}{2}$ by $2\frac{1}{2}$ in. (3.8 by 6.4 cm.) in size. There was a large soft swelling to the right of the ulcer and two smaller swellings on the left side and over the lower end of the sternum. Her general condition was deteriorating, and in the past year she had lost 35 lb. (15.9 kg.) in weight.

Discussion

The first observation of an ulcerative lesion in Hodgkin's disease was reported by Grosz (1906), and in the following 21 years only 26 cases had been recorded. Price (1946) states: "The skin is only rarely involved; and when it is, or when, with equal rarity, the nodes undergo caseation or suppuration, this is due to the secondary infection by pyogenic organisms or by tubercle."

The difficulty of diagnosis is emphasized by a perusal of various case reports (Alderson, 1917; Cole, 1917; Kierland and Montgomery, 1941). Goldman (1940), in an analysis of 212 cases of Hodgkin's disease, did not mention the presence of ulcerating lesions. Senear and Caro (1937) comment that ulceration occurs in three different ways: (1) Ulceration of limited extent developing in a number of small nodules in the skin. (2) Extensive ulceration developing in the skin by extension from underlying involvement of lymph nodes, bones, and other tissues. The case recorded seems to be from this group. (3) Extensive ulceration developing in large infiltrations appearing in the skin without involvement of the underlying structures.

The ulcer may appear before obvious glandular involvement elsewhere, as in the case now recorded, and may cause considerable confusion in differential diagnosis. The differential diagnosis is between gumma, epithelioma, sarcoma, tuberculosis, and mycosis fungoides. The typical ulcerative lesion of Hodgkin's disease has sharply defined rounded borders, but may be irregular, serpiginous, or linear. The edge is elevated and the margins are undermined or sharply punched out to resemble a gumma. Usually, as in this case, the ulcer is deep, with an uneven floor, covered with abundant purulent necrotic material or granulation tissue which bleeds freely when touched. Pain is variable, but in this case was severe. Affection of the neck, thorax, and axillary regions is most common, but the condition can be widespread.

The diagnosis is usually made by biopsy, but the case described illustrates that this is not infallible, and is dependent on demonstration of the characteristic Dorothy Reed or Sternberg cell.

Radiotherapy, as in this case, makes the ulcer melt away (Moriamé, 1949), but recurrence is usual.

Summary

A case of the rare ulcerative type of Hodgkin's disease is described, illustrating the extreme difficulty experienced in diagnosing this atypical form of the disease.

Showing the ulcer over the sternum, with an abscess forming over the right clavicle.

My thanks are due to Mr. A. Naylor for his encouragement and advice, and to Dr. F. E. Chester-Williams for permission to record this case.

REFERENCES

- Alderson, H. E. (1917). *J. cutan. Dis.*, **35**, 481.
 Cole, H. N. (1917). *J. Amer. med. Ass.*, **69**, 341.
 Goldman, L. B. (1940). *Ibid.*, **114**, 1611.
 Groz (1906). *Beltr. path. Anat.*, **39**, 405.
 Kierland, R. R., and Montgomery, H. (1941). *Proc. Mayo Clin.*, **16**, 124.
 Moriamé, G. (1949). *Arch. belges Derm. Syph.*, **5**, 234.
 Price, F. W. (1946). *Textbook of Medicine*, 7th ed., p. 874. Oxford Med. Publ., London.
 Senear, F. E., and Caro, M. R. (1937). *Arch. Derm. Syph.*, Chicago, **35**, 114.

Medical Memorandum

Renal Complications after Using Sulpenin

Combinations of penicillin and sulphonamides have been in clinical use for more than a year. No serious toxic effects have been reported, and the manufacturers know of only a few mild reactions occurring in a small number of instances. The following case report seems to be the first example of a serious toxic effect following the use of "sulpenin."

CASE REPORT

A married woman aged 73 was admitted to hospital on March 7, 1953, with the following history. In the previous ten days she had had "influenza," and mild bronchopneumonia, for which her doctor had prescribed sulpenin, the total amount given before admission being 28 tablets (14 g. sulphonamide). Twenty-four hours before admission she had suddenly developed epigastric pain, which had increased in intensity. It "spread through to the back," but did not radiate to the shoulders. The character of the pain was described as severe, with exacerbations. She had never had anything like this previously. Several times in the previous 24 hours she had vomited a small amount of mucoid fluid. Throughout this period she noticed a diminution in the quantity of urine passed, and what was voided was bloody (she admitted that she had not been drinking very much for the past two days). She had been constipated for five days. In 1916 laparotomy and appendicectomy had been performed, and in 1917 gastric ulcer had been diagnosed radiologically.

On examination she had the appearance of an ill, moderately dehydrated old lady. The tongue was dry and brown. The neck and chest, cardiovascular system, and central nervous system were all normal. Her blood pressure was 160/90 mm. Hg, pulse rate 80, temperature 99° F. (37.2° C.), and respirations 22. In the abdomen there was an upper right paramedian healed scar. Muscular movements were diminished, tenderness was acute in the epigastric area, but not in either loin, bowel sounds were diminished, no mass or abnormal viscus was palpated, and no fluid was detected. Rectal examination was normal. A straight x-ray film of the abdomen did not show air under the diaphragm or any intestinal abnormality. A diagnosis of anuria due to sulphonamide intoxication was made.

On March 8 the cystoscopy findings were: residual urine in the bladder 3½ oz. (100 ml.); some trigonitis; right ureteric orifice oedematous and blocked with bloody material, no efflux being present; left ureteric orifice oedematous without efflux. Attempted catheterization of the right ureter failed. There was a block 1.5 cm. from the vesical opening. A left ureteric catheter passed easily and was left *in situ*.

An indwelling gastric tube was left *in situ* for 24 hours, but yielded practically no material on aspiration. She was given oral fluids, 1 oz. (28 ml.) hourly for 12 hours, after which time the amount was doubled each 12 hours; 500 ml. of M/6 sodium lactate was administered intravenously. After the cystoscopy no urine was passed for 17 hours, at which time spontaneous diuresis took place. (The left ureteric catheter was left *in situ* for 72 hours, but no urine drained through it.) In the next 24 hours she passed 35 oz. (1 litre) of urine. She was discharged on March 13.

Investigations.—March 7: microscopy of urine removed from bladder on cystoscopy revealed it to be acid in reaction, with a microscopic haematuria. No sulphonamide crystals were seen. March 9: urine turbid, red-brown, pH 6.2; deposit abundant red blood cells, with no excess of leucocytes and no crystals seen; alkaline reserve, 40.4 vols. CO₂%. March 11: urine deep red, pH 5.6; still large numbers of red blood cells. On March 13 the report was similar. Intravenous pyelography showed good function on both sides, with normal renal outlines. The concentration of dye excreted was better on the left than on the right.

COMMENT

The simultaneous administration of two antibacterial agents is now an accepted principle of therapeutics. The drugs employed are many, proceeding from mixtures of synthetic agents, such as sulphonamides, to mixtures of sulphonamides with various antibiotics. Sulpenin is one of these; each tablet contains penicillin, 100,000 units, sulphadiazine, 0.25 g., and sulphamerazine, 0.25 g. The dose administered for infection of average severity is two tablets every four hours.

Garrod (1953) outlined the principles and the problems of this kind of therapy. He gives the following indications for its use: prevention of acquired resistance, achievement of synergism, prevention of toxic effects, mixed and double infections, and, rarely, the urgent undiagnosed case. The main difficulty is to avoid the production of resistant strains of infecting organism, but penicillin-sulphonamide mixtures tend to do this much less often than do other combinations.

This case emphasizes the fact that combinations of antibacterial agents do not abolish the capacity of the individual drugs to produce their specific toxic actions on the host. It seems likely that sulphadiazine was probably the responsible fraction, as its solubility in urine of pH 6-6.5 is less than half that of a comparable dose of sulphamerazine at that pH. Recent work has cast some doubt on the routine use of sulphonamide mixtures alone. Weinstein and Murphy (1952) state "that combinations of sulphonamides may have little clinical usefulness in many instances, since they are often not as effective as the single agents which compose them." This raises the question of what sulphonamide is best combined with penicillin. Of the sulphonamide preparations now available, sulphasomidine (6 (*p*-aminobenzene-sulphonamido)-2:4-dimethylpyrimidine), the isomer of sulphadimidine, would seem to be worth combining with penicillin. It has a greater solubility in acid urine than any other sulphonamide, the degree of acetylation is only 10-15%, the blood level remains consistently high, and side-effects are slight.

The clinical picture was not entirely typical in that no signs or symptoms referable to the loins were obtainable; a superficial examination suggested the presence of an intra-abdominal condition. A careful history provided the answer.

In the treatment—carried out along standard lines—it is significant to note that return of renal function occurred first on the non-catheterized side. Although the condition was what is often classified as an obstructive type of anuria, spontaneous diuresis occurred within 24 hours. The left ureteric catheter, *in situ* for 72 hours, did not drain urine in that period. It is possible that traumatic oedema of the ureteric mucosa, already partly damaged by a saturated solution of sulphonamide, was the cause of this depression of function. This experience would tend to support the view of those who recommend, after an initial cystoscopy, the application of the principles of the Bull regime to cases of sulphonamide anuria.

This case was under the care of Mr. Cameron MacLeod, to whom I am indebted for permission to publish.

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REFERENCES

- Garrod, L. P. (1953). *British Medical Journal*, **1**, 953.
 Weinstein, L., and Murphy, E. B. (1952). *Proc. Soc. exp. Biol., N.Y.*, **88**, 519.