haemoglobinuria did not seriously affect renal function. Marked pigmentation of the skin occurred, but liver function was relatively little affected. A transient decolorization of the irides was observed to accompany the intoxication.

We would like to thank Dr. W. G. Dangerfield for much helpful advice and Dr. D. G. Ferriman, under whose care the patient was admitted.

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Triple Primary Carcinomata of Rectum, Breast, and Transverse Colon Associated with Dermatomyositis

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Brit. med. J., 1965, **2**, 80–83

Over the years cases of multiple malignancies have been reported from clinical and necropsy material by various authors, including Wooley (1903), Warren and Gates (1932), Warren and Ehrenreich (1944), Bacon (1945), Slaughter (1946), Wynder et al. (1956), Dibble and Chambers (1960), and Werthamer et al. (1961); and a study of these cases shows that they fall into four groups. In the great majority two or more primary tumours have appeared in the same organ, such as the large bowel, the skin, or the mouth. Occasionally, multiple tumours have occurred in paired viscera or in viscera of the same system—for example, the renal pelvis and ureter—and, finally, to a much less extent multiple primary malignant tumours have occurred in unrelated organs, as in the case reported here.

In a comprehensive review of the literature Warren and Gates (1932) collected 37 cases which had been reported with three malignant tumours, but the only reference to a patient with two primary carcinomata of the large bowel and a primary carcinoma of the breast was that of Lane (1909). Since then no similar case has been reported, but cases with triple primary malignancies of the breast, large bowel, and an additional viscus have been recorded by Warren and Ehrenreich (1944), who described triple primary carcinomata in a man of 75 affecting the breast, rectum, and prostate, and by Cahan (1955), who described the case of a woman with triple primary carcinomata of the breast, sigmoid colon, and lung.

In 10 to 20% of adults suffering from dermatomyositis there is an associated malignant tumour (Williams, 1959), but a review of the literature has not revealed any report of a case associated with multiple primary malignant tumours.

Case Report

A married woman aged 54 was first seen on 2 January 1963 complaining of red swollen nail-folds which had been present for

three months. Her occupation entailed much wet work, and the disorder had been regarded as chronic paronychia and treated accordingly. She said she was otherwise well, but specific questioning revealed that she had noticed a mild degree of stiffness in her fingers and intermittent redness and swelling of her eyelids for a period of two months. There had also been a recent episode in which she developed redness on her upper chest after exposure to the sun, and this persisted for much longer than she would normally have expected with sunburn. There was no history of dysphagia or other symptoms suggestive of muscle weakness.

Examination revealed a blue discoloration and slight thickening of the nail-folds. There were also some very small ill-defined blue areas on the dorsa of the hands and below the eyes. There was no evidence of muscle wasting or tenderness. Laboratory investigations revealed a mild neutropenia. Haematocrit estimation was 41.5% and white blood cell count 5,100/c.mm. (neutrophils 48%, eosinophils 4%, basophils 1%, lymphocytes 44%, monocytes 3%). Platelets were plentiful, the E.S.R. was 7 mm. per hour (Westergren), and the S.G.O.T. 20 units.

A diagnosis of dermatomyositis was made, and the patient was admitted to Sydney Hospital on 14 February. In view of her age the possibility of occult malignancy was considered. Just prior to admission she had developed aching in her back. Further questioning revealed that she had noticed occasional slight bleeding per rectum. Her general physical examination revealed nothing of any note, but the left breast was found to contain a thickening in its upper and outer quadrant. There was dimpling of the overlying skin, but no discrete mass was palpable. In the left axilla two enlarged hard lymph nodes were attached to the deeper structures. No lymph node was palpable in the right axilla or neck.

On proctosigmoidoscopy a typically malignant ulcer was found with its lower edge 15 cm. from the anus. Biopsy of this edge showed "infiltrating adenocarcinoma." Small first-degree haemorrhoids were also present.

At this time she had a leucopenia, her white blood cell count being 3,600/c.mm. (neutrophils 62%, eosinophils 2%, lymphocytes 27%, monocytes 9%); E.S.R. was 8 mm. per hour, and S.G.O.T. 17 units. Serum proteins, electrophoretogram, serum electrolytes, blood urea, and liver-function tests were within normal limits. X-ray examination of the chest showed nothing abnormal.

On 18 March a radical anterior resection of the upper rectum and lower sigmoid colon was performed (E.W.). No intra-abdominal metastasis or second colonic tumour was detected during

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this operation. At the same time the two palpable lymph nodes were removed from the left axilla.

The pathologist (Dr. P. Bale) reported on the excised specimens as follows:

"The specimens consist of:

"(a) A 30-cm. length of large bowel with attached mesocolon. Four centimetres from one end there is a slightly constricting and ulcerating lesion, almost completely encircling the lumen but allowing the passage of a small finger. The lesion extends along a 3.5-cm. length of the intestine and can be seen to infiltrate out through the muscularis to the adventitia. The mesentery contains 15 lymph nodes, all small, but some are rather firm. Microscopical examination: adenocarcinoma (Fig. 1) infiltrating to the adventitia and surrounding fat. No metastasis was present in the 15 lymph nodes from the mesentery.

FIG. 1.—Adenocarcinoma of upper third of rectum.

"(b) A mass of fatty tissue from the axilla, 5 by 3 by 2 cm., containing two lymph nodes, the largest of which measures 2.3 by 1 by 1 cm.

"These lymph nodes contain metastases which are composed of somewhat more uniform cuboidal cells than those in the rectal tumour (Fig. 2). The possibility of a separate neoplasm in the breast cannot be excluded."

Post-operative recovery was uneventful, and she was discharged home on 8 April. Within the next few weeks a course of radiotherapy was given to the left breast and to the left supraclavicular, axillary, and internal mammary regions.

FIG. 2.—Axillary lymph node containing metastatic mammary adenocarcinoma.

A few weeks after the operation the swelling and discoloration of the fingers, the rash on the skin, and the periorbital oedema all gradually disappeared; but the aching persisted in the muscles of the back of the neck.

Also within a few weeks of this operation a chronic posterior anal fissure developed, and on 18 July an internal anal sphincterotomy was performed (M. K.). The base of the fissure and the surrounding tissues did not show any macroscopic evidence of malignant involvement such as sometimes occurs when a carcinoma of the colon or rectum and an anal fissure coexist (Killingback *et al.*, 1965); but a metastasis due to implantation was not to be expected, for the fissure was not present when the carcinoma of the rectosigmoid was resected and that of the transverse colon was probably not then in existence.

On 6 March 1964 she fell and fractured the greater tuberosity of the right humerus. At this time the haemoglobin level was 8.9 g./100 ml., the leucocyte count was 3,200/c.mm., and the blood film indicated a slight iron deficiency. The cause of the anaemia was not immediately apparent, but it was corrected by blood transfusion. The ominous possibility that the anaemia was due to bony metastases was considered, especially as x-ray examination revealed some rarefaction around the fracture, suggesting that it had occurred through a metastasis. A course of radiotherapy was given to the upper end of the right humerus, and union subsequently occurred.

On 28 April she was again admitted to Sydney Hospital. Episodes of colicky abdominal pain and distension had been present for the previous month, and during this time the reddish-blue discoloration had reappeared around the finger-nails. At laparotomy on 30 April a carcinoma of the transverse colon was resected (M. K.). This lesion had the macroscopic criteria of a typical primary colonic tumour, and there was no evidence of any metastasis within the abdomen.

The report of the pathologist (Dr. E. Hirst) on the specimen was:

"The specimen consisted of a segment of transverse colon which measured 25 cm. in the fixed state, and this had greater omentum and transverse mesocolon attached. The greater omentum was looped upon itself with its distal extremity attached in the region of an area of constriction of the bowel lumen which was situated 10 cm. from the distal end of the specimen. At this site there was an elevated border. In the region of this lesion, and below, there was evidence of bleeding into the bowel lumen. Proximally the bowel was dilated and the muscular wall was hypertrophied.

"Microscopical examination: adenocarcinoma (Fig. 3). Seven lymph nodes are negative."

After this operation the discoloration of the fingers again disappeared within a few weeks and she remained reasonably well at first, but gross lymphoedema of the left arm has since developed. There is at present no definite mass to be felt in the left breast, but this has become indurated throughout owing to the radiotherapy. Since the left axillary lymph nodes were excised, none

FIG. 3.—Adenocarcinoma of transverse colon.

has been palpable in either axilla. Her bowels are now functioning regularly, and sigmoidoscopic examinations have shown no abnormality.¹

Discussion

The presence of multiple primary malignant tumours in the patient poses the problem: Is one of the tumours a metastasis of the other? In this case the histological appearances of the tumours of the colon and rectosigmoid and of the metastases in the axilla were quite different, and there was nothing to support a suggestion that one of the tumours was the primary growth and the others were metastases. Usually, multiple diagnoses are to be avoided if all the lesions may be covered by a simple diagnosis, but the possibility of a single diagnosis does not pertain here. The carcinoma of the rectosigmoid would not have produced metastases in the transverse colon, breast, and axilla while its regional lymph nodes and the liver apparently remained uninvolved; nor would a carcinoma of the breast produce two metastases in the large bowel and in the associated axilla without other evidence of its spread within the abdominal cavity. Both tumours in the large bowel were typically primary lesions, and, as already mentioned, the histological appearances of the three tumours were quite distinct.

The identification of multiple primary malignant tumours was discussed by Billroth as early as 1889, but his criteria were very strict and are no longer followed. They were: "(1) each tumour must be histologically different, (2) each tumour must arise from a different area, and (3) each tumour must produce metastases similar to its primary growth."

Similar views were expressed by Wallace (1957), but cases without metastases would be excluded, and at the present time the criteria of Warren and Gates (1932) are more generally accepted. These are: "(1) each tumour must be malignant, (2) each tumour must be adequately separated from its neighbour, and (3) neither must be a metastasis." The case described here fulfils the criteria of Warren and Gates.

There has also been considerable discussion in the literature on the occurrence of multiple tumours purely due to chance, on the familial incidence of multiple tumours compared with that of single ones, on the increased risk of developing another primary tumour in the presence of one tumour, and on the frequency of congenital abnormalities in cases of multiple primary tumours. Opinions vary greatly on these points, and widely differing conclusions based on clinical, experimental, pathological, or necropsy material have been propounded by such authors as Warren and Gates (1932), Hurt and Broders (1933), Lund (1933), Bugher (1934), Eisenstaedt (1938), Kirshbaum and Shively (1938), Stalker *et al.* (1939), Ewing (1940), Peller (1941), Hellendall (1943), Warren and Ehrenreich (1944), Watson (1953), Epstein and Shaw (1958), Fried (1958), and Dibble and Chambers (1960). A comprehensive review of these opinions is given by the last-mentioned authors.

However, despite the fact that the figures in the majority of these papers suggest that multiple primary malignant tumours do occur more frequently than would be expected by chance alone, it cannot be denied that a single primary malignant tumour is so common that the possibility in any individual case that a second or even a third malignant tumour will appear at the same time, or later, purely by chance is not negligible. This problem will therefore not be discussed on the basis of this single case.

The prognosis must be poor in this patient, for that of a stage III carcinoma of the breast has added to it the prognosis of double carcinomata of the large bowel, which, as Gabriel (1963) pointed out, is worse than that of a single carcinoma of the large bowel.

On two occasions, while primary tumours developed, dermatomyositis appeared and then it settled down after removal of the tumours. After the last operation there has been no further recurrence of the dermatomyositis, but it has been anticipated since the gross lymphoedema of the arm became apparent.

The association of dermatomyositis with internal malignancy is now well established. Since this was first noted by Stertz (1916) there have been many subsequent reports to indicate that the relationship is more than coincidental. There is some diversity of opinion regarding the proportion of patients with dermatomyositis who have an associated neoplasm. Williams (1959) reviewed the literature and found reports of malignancy in 92 (15%) of 590 cases, a figure which is in accord with the personal series of Dowling (1955) and of Sneddon (1963). A study of the recorded cases reveals certain well-defined facets of this association. Although dermatomyositis occurs in children, it is not seen with neoplasm in this age group. It is also apparent that this peculiar symptom-complex precedes the associated tumour in a majority of the properly documented cases reported. Stomach, breast, lung, and ovary are the organs most frequently involved.

During the course of this patient's illness her married daughter developed chronic myeloid leukaemia, which adds further interest to this remarkable sequence of events. No inference is drawn from this, and it is likely that it is a coincidental happening. However, the possibility that malignant disease and leukaemia might be linked has been considered by many authorities, and there are a number of cases of familial leukaemia on record. Kolmeier and Bayrd (1963) have reported a case and reviewed the literature.

Lymphoid leukaemia has been observed six times more often than the myeloid type in the familial cases reported.

Videbaek (1947) analysed the family histories of 209 patients with leukaemia and a corresponding number of controls, and claimed that the chance of a relative of such a patient developing leukaemia was 1 in 250 compared with 1 in 4,000 of the controls. In addition, he found that the incidence of malignant disease was 50% higher in the relatives of patients with leukaemia than in those of his control population. However, these figures have been criticized by a number of authorities, including Morganti and Cresseri (1954).

Summary

A case of dermatomyositis associated with triple multiple primary malignant tumours is discussed. Although at least 10% of patients with dermatomyositis have an associated malignancy, there does not appear to be any previous report of a case associated with multiple primary malignancies.

The course of dermatomyositis in this patient conformed to the common pattern of behaviour in that it appeared before her malignant tumours were detected. It improved after treatment of her breast and rectosigmoid carcinomata, and subsequently reappeared *pari passu* with the symptoms of her colonic lesion. Resection of this third carcinoma brought about a further regression in the dermatomyositis.

The importance of a persistent rash on light-exposed areas in a patient past middle age cannot be emphasized too strongly. It has often preceded the onset of classical dermatomyositis. Such an episode was an important clue in this patient's history. It is also interesting that she presented with minimal cutaneous signs, and at no time has she shown evidence of gross myositis.

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¹ After submitting this paper for publication, death occurred on 16 April 1965. Prior to that, widespread metastases had developed but there was no reappearance of the dermatomyositis.

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Case of Myxoedema with a Huge Pericardial Effusion and Cardiac Tamponade

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Brit. med. J., 1965, **2**, 83–85

It has been known for many years that hypothyroidism affects the heart according to its degree of severity. When it is mild or of recent origin a sinus bradycardia may be the only finding, but in severe or long-standing cases the heart may be grossly enlarged, and congestive failure, a pericardial effusion, and electrocardiographic changes may be present, giving rise to the condition of "myxoedema heart." The clinical findings are variable and the underlying pathological changes ill-defined because myxoedema of sufficient duration or severity to present with predominant cardiac manifestations usually occurs in the middle-aged or elderly—mainly women—who often have hypertensive or ischaemic heart disease as well. Thus there is doubt whether myxoedema *per se* can cause heart failure (Hamolsky *et al.*, 1963; McBrien and Hindle, 1963), but there is no doubt that gross enlargement of the heart may be found, and in some cases this is certainly due to a pericardial effusion.

The object of this communication is to record a case of severe myxoedema in which a huge pericardial effusion produced cardiac tamponade, and to comment upon certain features in the light of what is known about myxoedema heart and the aetiology of the associated pericardial effusion.

FIG. 1.—Photograph of patient, October 1963.

FIG. 6.—Photograph of patient, October 1964.

Case Report

A spinster aged 57 was admitted to hospital on 17 October 1963. Her main complaints were of gain in weight to 13 st. 5½ lb. (85 kg.), swelling of the legs, and constipation.

She had attended as an out-patient in December 1949, when her weight was 11 st. 3 lb. (71.2 kg.), and complained of colicky lower abdominal pain and increasing constipation. Apart from a rectum loaded with faeces, nothing abnormal was found. A barium enema revealed a colon of large calibre with poor evacuation, but it was not a true megacolon. Liquid paraffin and enemata as required were advised. She was not seen again until her admission to hospital, when she was evidently grossly myxoedematous. She then revealed that she had taken thyroid extract from infancy until 1952, when she had stopped it. This explained why hypothyroidism did not show at her out-patient attendance in 1949. Inquiry at the Victoria Hospital for Children, where she had been taken in infancy and where thyroid therapy had been started, was unavailing, as their old records had been destroyed during the war of 1939–45.

On examination she was bloated, plethoric, and evidently myxoedematous (Fig. 1). Her voice was gruff, her skin was dry, and her legs were swollen with pitting oedema to the thighs. Jugular veins were distended beyond the angles of the jaw without visible pulsation. Pulse was 100, regular; blood-pressure 230/145, settling to 160/130 a few hours later. Apex beat was impalpable; heart sounds were faint but normal. Coarse rales were heard at both lung bases. Tendon reflexes were active, but the ankle-jerks were notably pendular. X-ray examination of the chest showed an enormous heart shadow, virtually filling the left lower hemi-thorax (Fig. 2).

By the next day (18 October) the pulse had fallen to 90 but showed a paradox effect, her blood-pressure readings being 165/115 during expiration and 155/120 on inspiration. A pericardial effusion with tamponade was diagnosed. The urinary output remained low and her weight increased despite relief dyspnoea by bed rest. An E.C.G. showed electrical alternans and low voltages, with flat or inverted T waves and slight S-T depression over the left ventricle (Fig. 3). Thyroid uptake of ¹³¹I was 8%

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