

### Summary

A case of poisoning as a result of the ingestion of an alcoholic podophyllum extract is described.

The resulting toxic effects comprised an initial severe disturbance of consciousness followed by a state of confusion, and a fairly severe type of peripheral neuropathy.

A substantial amount of recovery of function had occurred at the end of six months after ingestion of the podophyllin, but a residual neurological deficit was still evident at the end of 16 months.

The mode of action and probable effects of the podophyllum extract are discussed briefly.

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## ANKYLOSING SPONDYLITIS AND CHRONIC INFLAMMATORY LESIONS OF THE INTESTINES

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This paper describes six cases in which ankylosing spondylitis was associated with chronic non-specific inflammatory lesions of the intestines. Four of these cases had chronic ulcerative colitis, one had Crohn's disease, and one had ulcerative colitis and Crohn's disease. The aetiology of ulcerative colitis and Crohn's disease is uncertain. Although it seems unlikely that they represent different manifestations of the same diseases, nevertheless there appears to be enough similarity between them to make differentiation difficult at times (Butler, 1953; Crohn, Garlock, and Yarnis, 1947), and we may be justified in considering them together. The diagnosis of Crohn's disease was made at operation in both our cases, while radiology with a barium-filled colon was relied on for the diagnosis of ulcerative colitis.

The English literature has few references to the association of ankylosing spondylitis and ulcerative colitis. West (1949) makes no mention of the two conditions in his discussions of the aetiology of ankylosing spondylitis, and Hart (1955), reviewing 184 cases of ankylosing spondylitis, does not mention ulcerative colitis or Crohn's disease (although he refers to other diseases of the intestines). However, Romanus (1953) describes three

cases of ulcerative colitis associated with ankylosing spondylitis, and, indeed, French authors have always believed that ankylosing spondylitis might be related to disorders of the intestines. Forestier (1939) stated that the primary focus in ankylosing spondylitis lay in the genito-urinary system or in the lower bowel. Further, dysentery and post-dysentery syndromes have always, since Reiter's (1916) original description, been recognized as aetiological factors in Reiter's syndrome, and it is recognized that involvement of the sacro-iliac joints may be a part of this syndrome (Marche, 1950; Ford, 1953). We have been unable to find any reference to the association of ankylosing spondylitis and Crohn's disease.

### Case Reports

**Case 1.**—A man aged 42 was first admitted to the London Hospital in 1938 with an acute attack of diarrhoea and blood in his stools. Sigmoidoscopy revealed changes typical of ulcerative colitis. Following treatment he was much improved. Since that time he has been readmitted five times for recurrences of ulcerative colitis, and on the last occasion a barium enema showed changes of advanced ulcerative colitis throughout the whole of the large intestine, and possibly some involvement of the small gut. Three years after the diagnosis of ulcerative colitis was made he complained of pain in the lumbar region lasting for three months. In 1945 he had a recurrence of low back pain, associated with aching pain and stiffness in his neck. At that time he began to develop a stoop. The ulcerative colitis was still active. Examination showed an upper dorsal kyphosis and rigidity throughout the spine. Chest expansion was limited to  $\frac{1}{2}$  in. (1.3 cm.). The right temporo-mandibular joint was also affected. X-ray examination showed obliteration of the sacro-iliac joints and calcification of the anterior longitudinal ligaments. These changes were regarded as typical of ankylosing spondylitis. Radiotherapy was given, but had to be discontinued as severe diarrhoea developed after a few treatments. In 1949 the symptoms of ankylosing spondylitis became more severe, and he was given a course of radiotherapy, with marked relief.

**Case 2.**—A man aged 50 began in 1949 to have diarrhoea with blood in his stools. This improved with treatment, and for several years he had little trouble. In 1954 he complained of pain in the right knee, followed by pain in the back. Examination showed rigidity of the thoracic and lumbar spines, and limitation of movement of the cervical spine. There was an effusion in the right knee. X-ray examination showed typical changes of ankylosing spondylitis, with obliteration of the sacro-iliac joints and calcification of the spinal ligaments. Erythrocyte sedimentation rate was 20 mm. in one hour. He was treated by physical methods, with improvement. One month before this was written he had a further relapse of diarrhoea, with blood, and a barium enema showed a loss of haustration involving the descending and pelvic colon. For some years this man had had diffuse psoriasis.

**Case 3.**—A man aged 48 complained in 1937 of diarrhoea and bloody stools. He was admitted to hospital, and ulcerative colitis was diagnosed. In 1942, while in hospital with a further attack, he first noted stiffness of his spine. Since then he has had intermittent attacks of ulcerative colitis. He also found that his neck was bending forward, and that he was unable to look up. In 1949 a diagnosis of ankylosing spondylitis was made. He was treated with deep x-ray therapy. Following this he developed his first attack of iridocyclitis, affecting the left eye. In 1950 he experienced a severe attack, affecting the right eye. X-ray examination revealed obliteration of both sacro-iliac joints, typical of ankylosing spondylitis.

**Case 4.**—A married woman aged 49 developed umbilical pain and vomiting eight years ago. She attended the London Hospital for investigation. A barium-meal examination revealed a filling defect in the colon. Laparotomy was performed, and a right hemicolectomy, with removal of 3 ft.

(90 cm.) of terminal ileum, and end-to-end ileocolostomy were carried out. Histological examination of the specimen showed the changes of Crohn's disease. After the operation she first complained of low back pain, which continued and became more severe. The following year x-ray examination revealed sclerosis around both sacro-iliac joints, typical of ankylosing spondylitis. Radiotherapy gave some improvement. More recent x-ray films show irregularity of the margins of both sacro-iliac joints, with increased sclerosis. They also show the presence of sclerosis around the symphysis pubis, with irregularity of the bony margins and squaring of the vertebral bodies. Six years ago she was investigated for persistent diarrhoea, but the results were negative. They were suggestive, however, of early ulcerative colitis. Two years ago she was readmitted, with diarrhoea, blood in the stools, marked weight loss, and pyrexia. Sigmoidoscopy showed typical changes of ulcerative colitis in the rectal mucosa, and a barium enema revealed changes of advanced ulcerative colitis throughout the large gut.

**Case 5.**—A man aged 49 first suffered from blood-stained diarrhoea in 1943. After one attack he was free of symptoms until 1951, when he had a recurrence of symptoms. Radiological examination with barium showed typical ulcerative colitis, the smooth appearance involving the whole colon. Two years later he began to suffer from pain and stiffness of the back and pains in the limbs. On examination nine months later (January, 1954) the movements of the cervical and thoracic spines were greatly limited. The lumbar spine was also limited in its movements, but it was not rigid. Chest movement was limited. X-ray examination of the lumbar spine and sacro-iliac joints showed nothing abnormal, but calcification of the interspinous ligaments in the cervical and lower dorsal region, and bony bridging between vertebrae L 1 and 2 were present. The erythrocyte sedimentation rate was 62 mm. in one hour. A course of deep x-ray therapy improved the mobility of the spine, and the patient has remained symptom-free for the past two years.

**Case 6.**—A man aged 42 first complained of diarrhoea and vomiting 16 years ago, when in the Army. The following year an appendicectomy was performed, but two weeks later an abscess developed in the right groin, with slight flexion contracture of the right hip. At first a diagnosis of a tuberculous hip-joint was made. He was admitted to an orthopaedic hospital, and, as his vomiting continued, a barium-meal examination was performed; this showed the appearances of Crohn's disease. Following this, three operations were performed on his gut. The exact nature of these is uncertain. Seven years ago he first noticed that his neck and back were becoming stiff. Later the same year a diagnosis of ankylosing spondylitis was made. X-ray films showed typical changes of ankylosing spondylitis in the sacro-iliac joints. Deep x-ray therapy brought marked improvement.

### Discussion

The course of events in these six cases was very similar. The onset of backache followed the beginning of bowel symptoms, usually in a few years, but the diagnosis of ankylosing spondylitis was delayed for several more years. In Case 4 the spondylitis followed the development of Crohn's disease but preceded the demonstration of involvement of the colon. Five of these cases were classical ankylosing spondylitis. In Case 6 only the sacro-iliac joints showed radiological abnormality. Case 4 had erosions of the sacro-iliac joints and the symphysis pubis, while Cases 1, 2, and 3 had involvement of the sacro-iliac joints, with uniform calcification of spinal ligaments. Case 5 was atypical in that the cervical spine and lower dorsal spine were mainly affected, the sacro-iliac joints being spared. This, however, is recognized as occurring in 14% of cases of ankylosing spondylitis (Oppenheimer, 1943). Case 3 also suffered from psoriasis, which has been associated with ankylosing spondylitis (Fletcher and Rose, 1955).

In all these cases, however, the main emphasis of the arthritis centred on the spine, and, although other joints

were involved, these appeared to be secondary phenomena. This feature differentiates this group of cases from that in which the peripheral joints are involved in ulcerative colitis. The peripheral type of arthritis is well recognized, and has been reported in from 4 to 8% of cases (Kirsner, Palmer, Maimon, and Ricketts, 1948). It occurs in severe late cases of ulcerative colitis, although it may occur early in right-sided colitis (Butler, 1952). It involves one or more of the larger joints, and waxes and wanes with exacerbations of the colitis. There are no reports of changes in the spine in these cases, and spinal involvement has been absent in those cases which we have had the opportunity of examining.

It seems unlikely that the cases reported here represent chance associations of intestinal disease with ankylosing spondylitis. The four cases of ulcerative colitis occurred among 399 cases of ankylosing spondylitis admitted to the London Hospital for the period 1937-55, an incidence of 1%. West (1949) states that the incidence of ankylosing spondylitis in the general population is 1 in 2,000, so that the association seems to be more than one of chance. From a review of the literature also there seems to be an association between intestinal disorders and spinal disease. The association of bacillary dysentery with Reiter's syndrome, in which sacro-iliac involvement is sometimes a feature, has already been mentioned. In brucellosis infections, where the portal of entry is the intestinal tract, there is also a predilection for the spine. As a rule, according to Benassi (1952), the pathological changes in this condition are those of a low-grade localized osteomyelitis in which hypertrophy of bone is well marked (as distinct from the osteoporosis of tuberculosis), so that in a late stage two adjoining vertebrae become invested with hypertrophic bone. In some cases the sacro-iliac joints are affected, but here again the changes are usually unilateral and represent a low-grade osteomyelitis (Steinberg, 1948). Nevertheless, it seems that typical ankylosing spondylitis occurs in some cases; for Goldfain (1943) reported five cases of ankylosing spondylitis with positive serological tests for brucellosis, and Steinberg (1948) reported one case, although he believed that brucellosis was not a factor in ankylosing spondylitis.

Typhoid fever has similar effects. Generally the process is a low-grade osteomyelitis, affecting the intervertebral disk region (Silver, 1907) in the lower dorsal and lumbar vertebrae, producing irregular density of adjacent vertebrae and ossification of perispinal ligaments. The prognosis is good (Swart, 1938). Sometimes, however, ankylosing spondylitis occurs, and Romanus (1953) reported one such case.

Oppenheimer (1938) has described a type of hypertrophic spondylo-arthritis which he differentiates from osteoarthritis and from ankylosing spondylitis, and which he believes was related to amoebic dysentery, as 13 out of 14 patients had *Entamoeba histolytica* in their stools. However, he did not publish x-ray films to allow an opinion on whether the condition simulated brucellosis and typhoid fever.

It seems that ankylosing spondylitis may represent a non-specific reaction to diseases of the intestinal tract. Brucellosis and typhoid fever as a rule produce a low-grade osteomyelitis. Bacillary dysentery is associated with Reiter's syndrome, and ulcerative colitis with a type of arthritis confined to one or two large joints, but all of these conditions and Crohn's disease are sometimes associated with typical ankylosing spondylitis.

The reason for the association of spinal disorders and diseases of the intestines has been suggested by Romanus (1953). He believes that the connexion is via the system of veins which has been demonstrated by Batson (1942). These connect the pelvic veins to the vertebral veins. Batson was interested in the spread of secondary carcinoma of the prostate, but Romanus considers that infection from the prostatic bed may spread in this way. The rectal veins form part of the pelvic system. However, it is less easy to account for the association of Crohn's disease with ankylosing spondylitis in this way, and, indeed, until the aetiology of ulcerative colitis and of ankylosing spondylitis is known, it seems premature to speculate about the channels of spread.

### Summary and Conclusions

Of the six cases described, four had ulcerative colitis and ankylosing spondylitis, one had Crohn's disease and ankylosing spondylitis, and one had ulcerative colitis, Crohn's disease, and ankylosing spondylitis.

It is believed that these associations are more than those of chance.

There seems to be a definite relationship between diseases of the intestines and spinal disorders.

Ankylosing spondylitis can be a non-specific reaction to diseases of the intestinal tract.

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## MICROSPORUM CANIS—AN INTENSIVE OUTBREAK ×

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Cases of ringworm diagnosed at the Royal Victoria Hospital, Belfast, and the Royal Belfast Hospital for Sick Children are notified to the medical officer of health of the area in which the patient resides. On January 15, 1957, one such notification reported *Microsporum canis* infection in three adults, two dogs, and a Persian kitten—this comprising all the individuals living in one household. The diagnosis had been confirmed by examination of the animals under Wood's light (ultra-violet light screened with nickel oxide glass), when the typical bright pale-green fluorescence was obtained. The kitten was noted to be most heavily infected, and, as it had been acquired on December 17, 1956, it was believed to be the source of the infection. It had been obtained from a local breeder of Persian cats.

All 12 of the animals in the breeder's cattery were examined under Wood's light, and two tom-cats showed typical fluorescence. Confirmation of the diagnosis was obtained by sending affected hairs to the laboratory, where *M. canis* was cultured.

Two litters had been born in September, and the first two kittens were sold in October, but the breeder then

noticed bald patches on the face of the remaining kittens and deferred selling them until this condition improved. Further sales took place from November 25 to December 17, 1956, and, in all, 10 kittens had been sold in the period October 24 to December 17.

### Summary of Contacts

Kitten	Date of Purchase	Human Contacts		Animal Contacts in Home	
		Infected	Not Infected	Infected	Not Infected
No. 1	24/10/56	2 children (1 M, 1 F), 1 adult (F)	1 adult (M)	0	0
„ 2	25/10/56	2 children (1 M, 1 F), 1 adult (F)	1 adult (M)	0	0
„ 3	11/12/56	2 children (2 F)	2 adults (1 M, 1 F)	0	0
„ 4	12/12/56	1 child (F), 1 adult (F)	1 adult (M)	0	0
„ 5	13/12/56	1 adult (F)	1 adult (M)	0	0
„ 6	13/12/56	4 children (4 F)	2 adults (1 F, 1 M)	0	0
„ 7*	13/12/56	3 adults (1 M, 2 F)		2 dogs	0
„ 8	17/12/56	1 adult (F)	1 child (F), 1 adult (M)	1 cat	0
„ 9†	17/12/56	3 children (2 M, 1 F)	10 adults (5 M, 5 F)	3 cats	3 cats
Total		22 (5 M, 17 F)	20 (12 M, 8 F)	6	3

\* This kitten was responsible for the infections which started the investigation.

† This kitten had passed through four households before it was finally located.

The addresses to which the kittens had been sold were obtained and visited (see Table). We were, however, unable to complete the investigations in respect of a kitten sold on November 25.

Of persons exposed to infection from the kittens 14 of 15 children (93%) and 8 of 27 adults (30%) are known to have been infected.

The common sites for lesions were the face, neck, forearm, and backs of hands. In only two cases were the scalp and the hair affected. The most extensive infection was in a girl of 8, whose neck, face, trunk, and scalp were involved.

The sex distribution of the cases was predominantly female (17 F., 5 M.), perhaps because many of the kittens were bought as pets for girls. Only one adult male was affected.

### Investigation in Retrospect

The breeder recalled that all kittens born after the purchase of a tom-cat from Leeds in February, 1955, had soon shown patchy alopecia of the face. The tom-cat itself had suffered from a skin condition on arrival, and, although the breeder and her two children developed ringworm within three weeks after its arrival, no one had thought of blaming the newly acquired tom-cat. Three kittens born on the breeder's premises before the arrival of the Leeds tom-cat were traced and no cases of ringworm were reported from these three households.

All the kittens born between February, 1955, and September, 1956, could not be traced, but visits to six households receiving kittens during this period revealed that three of these kittens had given rise to four cases of ringworm; the other three kittens produced no cases, but there were no children in these last households.

It was confirmed that *M. canis* infections have been endemic among cats in Leeds in recent years (La Touche, personal communication).

Examination under Wood's light of cats belonging to neighbours of the breeder and of several pedigree Persian cats elsewhere showed no infection. The case against the tom-cat was considered proved.