the calf muscles. Tenotomy of the tendo Achillis was described by Boyd *et al.* (1949), and Boyd and Bloor (1960) assessed the long-term results. They regarded it as being of value in selected cases, and in a series of 62 cases of unilateral tenotomies, found that 14 patients obtained complete relief of symptoms, 14 had initial relief but deteriorated subsequently, and 34 obtained no relief from the operation. The higher success rate of selective nerve crush, which, unlike tenotomy, usually does not produce a limp, suggests that it is to be preferred in treatment. At the start of the present series, one of us (W. R.) performed eight tenotomies and eight nerve-crush operations. These were reviewed after a year. Of the selective nerve-crush patients, seven were working and none had a limp; and of the tenotomies, one was working and all had a limp.

Learmonth and Slessor (1952) described the operation to divide the nerves to the gastrocnemius and the upper nerve to the soleus, but thought that it was advisable to give anticoagulants to forestall the possibility of venous thrombosis due to inactivation of the muscle pump. They first used denervation towards the end of the second world war as the result of an observation (also made by Boyd in the Middle East) that claudication might not follow wounds of the popliteal artery requiring ligation if (1) the nerve branches to the gastrocnemius were involved, or (2) if the medial popliteal nerve trunk was involved, and power was not regained in the gastrocnemius and soleus. About 1947 they had an arteriosclerotic patient in whom claudication did not occur after resection of a popliteal aneurysm which included the nerves and blood-vessels to the gastrocnemius. They also had a patient with a fixed ankle-joint due to calcification of the anterior calf muscles who did not have claudication. Learmonth (personal communication, 1962) considers it is possible to determine which patient may be helped by nerve section by trying the effect on walking of a check-iron to keep the ankle fixed.

Marston and Cockett (1962) published a short-term follow-up of 15 cases in which they performed total denervation of the gastrocnemius and soleus, with sympathectomy in nine of these. Good results for this procedure are claimed but, in contrast to our experience with selective nerve crush, they had a high incidence of complications (two developed deep-vein thrombosis, and three had skin necrosis at the site of operation).

One very striking feature of the present series is that none of the 65 treated patients subsequently developed gangrene. We believe that this was due to the selection of patients whose feet were warm and viable, and is an indication of the efficacy of phenol block in ensuring an adequate development of the collateral circulation.

The results in some patients of the present series have been disappointing. Late failure due to further occlusion in either leg and a reduced expectation of life are a natural consequence of the underlying disease. The other principal cause of failure was early regeneration of the nerve supply to the gastrocnemius and soleus.

Summary

An account is presented of an operation for treatment of intermittent claudication which produced good results in 85% of unilateral cases, although 35% later deteriorated owing to further occlusion.

Operation is indicated where severe claudication is confined to the calf muscles of one leg and interferes with the patient's working capacity.

Operation is contraindicated in patients with serious cardiac insufficiency or where the viability of the leg is in doubt.

Bilateral operation should seldom be undertaken.

We wish to record our thanks to Mrs. M. Baird for her valued secretarial services, essential to the preparation of this paper, and for her efficiency in tracing so many patients.

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AGROSAN POISONING IN MAN

BY

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Poisoning through the medium of food has been known for centuries. Acute food poisoning has always been a hazard, sometimes in the form of botulism and lathyrism as well as poisoning with heavy metals, especially arsenic. We are also familiar with chronic and insidious poisoning by means of arsenic in food. But, of recent years, outbreaks of chronic food poisoning with organic chemicals have taken a considerable toll of human life in different parts of the world. Of particular concern have been the loss of human life and the suffering caused by adulteration of oil or ghee used for cooking purposes, as happened in Morocco (Smith and Spalding, 1959; Moroccan Situation, 1959) and in Karachi in 1961, or by the mercurial poisoning of wheat in Iraq in 1956 and 1960 (Jalili and Abbasi, 1961).

In this paper cases of agrosan poisoning due to eating seed wheat treated with "agrosan GN" (a mixture of phenyl mercury acetate and ethyl mercury chloride) are reported. The series includes several fatal cases.

Epidemiology

The outbreak began in the middle of February, 1961, and food poisoning was first suspected during early March, in three patients admitted to the Government Lady Reading Hospital at Peshawar. It continued till about the middle of March and affected about 100 people. Several families were afflicted by similar symptoms in Nizampur Area, Tehsil Nowshera, and District Peshawar, and still more cases followed in the nearby villages. Some of these cases died at home, others were admitted to local hospitals or treated as out-patients. At the end of March, 1961, and beginning of April, 1961, some of these families from Nizampur, Badabher, Ziarat Kaka Sahib, Landi Arbab, Village Kahi, and Akora Khattak were admitted to the Government Lady Reading Hospital, Peshawar, and the following account is based on the data collected from them, their relatives, and well-wishers. In all, 34 patients were admitted: 2 men, 7 women, 14 boys of 15 years old and under, and 11 girls in the same age group.

Four of these patients died in hospital and five seriously ill patients were taken away by their relatives. They also may have died soon after. Permission could be obtained for one necropsy only. Among the remaining 25 patients 14 were mild cases, 7 moderately severe, and 4 seriously affected ones.

It is thought that the reason why the seed wheat was bought for food in the first place was that wheat was scarce in January and February. Moreover it was of higher quality and some of the wealthier families bought it for that reason.

Long before the patients came to hospital most of their families had suspected that this mysterious disease was due to eating the suspected wheat. Without exception all who ate it were affected, and any member who did not escaped the illness. Some of the families washed the wheat thoroughly before they ate it, and they too showed no symptoms whatsoever. Some had given the suspected wheat to birds and dogs as an experiment and found that all were seriously affected.

The Agricultural Department, Peshawar, confirmed that the seed wheat, treated with an organic mercurial compound, agrosan GN, was intended for planting purposes only during the harvesting season of September, 1960, to January, 1961, and was distributed through depots in Nizampur and other affected areas. Samples of the suspected wheat flour were collected from two different families and sent to the Chemical Examiner, West Pakistan, who confirmed the presence in it of a mercurial poison. He also examined the viscera, obtained at necropsy, of a patient from Nizampur and again reported that mercurial poison was present.

Signs and Symptoms

In a typical case the symptoms started with malaise, lethargy, tiredness, and lack of interest in work and at home. In a few days these symptoms were followed by a burning sensation in the mouth and stomach, nausea and vomiting, occasional fever, excessive thirst, and loss of appetite. Simultaneously the patient experienced weakness in the limbs, difficulty in walking, slow cerebration, confusion, flight of ideas or thought block, slurred speech, and sometimes difficulty in swallowing. At a later stage there was inability to stand, walk, or even sit, greater disability in speech and swallowing, mild to severe visual impairment, followed by extreme confusion, spontaneous crying, sucking and chewing movements, coma, spasticity, and death. This picture usually developed in one to three weeks from the onset of the illness. Clinical features included moderate to severe anaemia, wasting and emaciation of the extremities, stomatitis, and hypertrophy of the gums. Mental activity and cerebration were slow, and lethargy was a prominent feature. In others spasticity of the limbs, dysarthria, a positive Babinski's reflex, increased tendon jerks, spontaneous crying, and involuntary sucking and chewing movements dominated the clinical picture. Visual impairment, when present, was permanent, and the fundi, in a few cases, showed optic atrophy. Five out of the 34 patients complained of paraesthesia and pain in the extremities, whereas marked calf muscle tenderness was the main feature in three of them. No other sensory loss was detected.

The following is an analysis of the early symptoms, established symptoms, and signs found in these 34 patients.

Early Symptoms	No.
Nausea, vomiting	16
Polydipsia	11
Lethargy	10
Weakness	10
Fever	9
Burning sensation in mouth, stomach	6
Epigastric discomfort, pain	5
Salivation	4
Constipation	3
Not thriving	2
Slow cerebration	1
Irritability	1
Frequency of micturition	1
Anorexia	1
Taste in mouth	1

Established Symptoms	No.
Weakness in limbs	30
Fever	26
Vomiting, nausea	24
Lethargy	19
Inability to walk, sit, or stand	16
Apathy	15
Abdominal pain, epigastric discomfort	15
Constipation	15
Polydipsia	13
Irritability	13
Diarrhoea	12
Slurring speech	12
Anorexia	10
Burning or raw sensation in mouth, stomach	9
Visual disturbances	9
Difficulty in swallowing	8
Pains in limbs	5
Paraesthesia	5
Salivation	4
Taste in mouth	3
Frequency of micturition	3
Not thriving	2
Incontinence of urine	1

Signs	No.
Anaemia	29
Wasting, emaciation	15
Speech defects	13
Positive Babinski's sign	13
Hypertrophy of gums	11
Spontaneous crying	11
Slow cerebration	10
Diminished power in limbs	9
Spasticity in limbs	7
Increased tendon jerks	7
Stomatitis	5
Involuntary chewing, sucking movements	5
Optic atrophy	4
Tenderness in limbs	3
Delirium	2
Convulsions	1

Case Histories

Case 1.—A married woman, aged 35, from Landi Arbab. She was admitted on April 27, 1961, with a history of polydipsia, occasional fever, nausea, and retching after meals for one month. Ten days later weakness in the limbs and pains all over the body developed. She was moderately anaemic (Hb 8 g./100 ml.), lethargic, and depressed. There was no evidence of stomatitis, excessive salivation, or gum hypertrophy. Physical examination did not reveal any gross abnormality. There was moderate albuminuria. She was treated with B.A.L., a compound preparation of the B group vitamins, and iron, and was discharged home symptom-free on May 17, 1961. She was one of a family of eight who had eaten the wheat for three weeks before symptoms appeared.

Case 2.—A youth, aged 15 years, from Badaber was admitted on April 25, 1961. He gave a history of epigastric discomfort, vomiting, and anorexia for a few days about two months before admission. He also complained of frequency of micturition for two months, occasional fever for one and a half months, and weakness in the limbs for a fortnight. He was unable to walk, and had had blurred vision and slurred speech for one day, along with formication for the previous few days. All the members of his family had become ill after eating the suspected wheat for three weeks. He was apathetic, confused, and his thought processes were slow; his speech, too, was slow and slurred. His lips were dry and scaly, and his gums hypertrophied. He had slight visual impairment. There was marked muscular weakness and wasting in the limbs, and a transitory extensor plantar response. There was moderate albuminuria. He was emaciated and anaemic (Hb 8.5 g./100 ml.).

He was treated with B.A.L., vitamins, iron, and antibiotics. When he was discharged on May 26, 1961, his speech, mental state, cerebration, appetite, and vision had improved. There was no more nausea or vomiting, and he was left with only slight epigastric discomfort.

Case 3.—A 10-year-old girl from Landi Arbab complained of easy fatigability and lethargy three weeks after consuming the suspected wheat. Weakness gradually increased so much so that she could neither sit nor stand. For the first few days she had nausea and vomiting followed by polydipsia and occasional fever. She complained of blurring of vision three weeks after the initial symptoms and was blind a fortnight later when she was admitted on April 25, 1961. She was emaciated, anaemic (Hb 8 g./100 ml.), apathetic, and irritable, and her speech was slurred. Her gums were hypertrophied. There was wasting and weakness of the limbs, which were rigid but occasionally became completely flaccid. There was extensor plantar response. She had episodes of spontaneous crying and had complete visual loss with optic atrophy. She was treated with B.A.L., vitamins, iron, "largactil" (chlorpromazine hydrochloride) and symptomatic therapy. The restlessness, irritability, rigidity, and spontaneous crying had improved by June 13, 1961, when she was discharged home. There was no visual improvement.

Case 4.—(Necropsy performed.) A married woman, aged 45, was admitted on March 30, 1961, with a history of a burning sensation in the stomach, epigastric discomfort, and excessive salivation after eating the suspected wheat for three weeks. This was followed by abdominal pain, vomiting, diarrhoea, anorexia, and weakness of the limbs. These symptoms were present for two weeks before admission. She was depressed, apathetic, irritable, and rather slow to respond. She could walk with support. Her temperature was 101° F. (38.3° C.). Liver and spleen were just palpable. Her condition gradually deteriorated. The fever persisted in spite of antibiotics. Vomiting and diarrhoea became intractable. She became confused, later on collapsed, and lapsed into acute adrenal crisis and died. At no time were there any specific findings related to the central nervous system, and the cerebrospinal fluid did not reveal any abnormality. Urine contained slight traces of albumin, E.S.R. was 40 mm. in the first hour, and Hb 8 g./100 ml. Blood sugar and urea levels were within normal limits. Treatment consisted of intravenous glucose and saline, largactil, B.A.L., antibiotics, blood transfusion and cortisone, noradrenaline, intravenous drip, and "methedrine" (methylamphetamine hydrochloride).

It was noted at necropsy that she was an emaciated middle-aged woman. There was a purpuric rash over the body, and there were two large sloughing, necrotic areas of ulceration, each measuring 5 by 3 cm., near the cardio-oesophageal area in the fundus of the stomach. Numerous other superficial ulcers were present all along the lesser curvature. The mucosa of the jejunum and ileum was focally congested. On microscopic examination the liver showed marked fatty infiltration in the periportal and other zones of the liver lobule, giving a "signet-ring" appearance to the cells. Milder vacuolation of foamy appearance was noted in the middle and central zones.

The kidneys were large and strikingly pale, each weighing 248 g., and the distinction between the cortex and medulla was diminished. There was marked fatty change in the epithelial cells lining the proximal tubular convolutions. Epithelial cells were desquamated. Protein casts were present in the distal and collecting tubules. Glomeruli were bloodless and showed increased cellularity, which was due to endothelial and mesenglial proliferation. There were a few foci of mild chronic pyelonephritis. The two adrenals together weighed 11.5 g., and the cortex showed marked lipid depletion and cellular shrinkage. The spleen was enlarged and diffluent, weighing 404 g. There was abundant haemosiderin in the reticuloendothelial cells. There were many polymorphs, monocytes, lymphocytes, and plasma cells in the pulp. No abnormality was found in the meninges, cerebrum, cerebellum, or spinal cord.

These findings are consistent with a diagnosis of chronic mercurial poisoning, the organs chiefly affected being the gastrointestinal tract and the kidneys.

Discussion

As far as the aetiology of these illnesses was concerned there were only two possibilities that could be considered. The first was that the illness might have an infective origin. Initially, a lot of confusion was created by the possibility that a virus infection was responsible, for this type of infection is sporadically prevalent in this area. Such a virus infection affected young children and presented a picture mimicking this outbreak. Diagnosis was made more difficult by the admission of three children with such an illness (other members of their family escaped infection) under my care during early April, 1961. But the theory of a virus aetiology had to be abandoned because of the overwhelming evidence supporting the second possibility—that poisoned wheat had been eaten.

Agrosan GN is a mixture of phenyl mercury acetate and ethyl mercury chloride, and is employed by the Department of Agriculture, Government of West Pakistan, as an agent against seed- and soil-borne diseases. It contains 1% organically combined mercury. It is a local irritant and is capable of producing blisters on the skin, especially in the presence of perspiration. Its dust can produce severe irritation of the respiratory tract, and the manufacturers advise that mask, gown, and gloves should be worn while handling it. The effect of mercurial compounds on the gastrointestinal tract is well known, and, being locally irritative, agrosan produces congestion and ulceration of the mucosa of mouth, oesophagus, stomach, and intestine. Some of the mercury is excreted by the colon and may be responsible for the lesions there. Its irritant effect accounts for the clinical features of taste in the mouth, excessive salivation, a burning sensation in the mouth and stomach, stomatitis, epigastric pain and discomfort, abdominal colic, diarrhoea, and constipation (the latter being due to reflex spasm of the intestines), excessive thirst (due to congestion of the mucosa), a dysentery-like syndrome, and anorexia. Hypertrophy of the gums is a recognized feature of chronic mercurial poisoning. Albuminuria and frequency of micturition are explained on the basis of damage to the kidney—witness the strikingly pale kidney of the one case that came to necropsy.

Fever, lethargy, wasting, and emaciation are the general effects of chronic metallic poisoning in the body through metabolic enzymic blockage. Emaciation is further augmented by lack of nutrition, due to anorexia, nausea and vomiting, ulceration, and congestion in the gastrointestinal tract, as well as to the depressed effect on body metabolism brought about by mercurial poisoning. Difficulty in swallowing can be due to three factors: ulceration in the mouth, pharynx, and oesophagus; mercurial neuropathy; and the patient's confused state of mind.

Severe mental symptoms, known as erethism, and manifesting themselves as excessive sensibility to stimulation, are also a well-known disease entity and are seen especially in the mirror industry. These symptoms are probably due to the effect of mercury on the cerebrum, especially the frontal lobes. Slow cerebration, apathy, irritability, thought block, flight of ideas, hallucinations, delirium, confusion, loss of memory, and

spontaneous crying are features that may not be produced by specific microscopic changes in the cerebrum but may be the outcome of metabolic disturbances in the brain.

Speech disturbances consist either of dysarthria, manifested as slurring speech, or aphasia, and are the result of cortical damage. Spasticity, positive Babinski's sign, and increased tendon jerks may be the outcome of a motor cortical lesion or a pyramidal lesion, or both combined—the latter being the most probable explanation in these cases. Sucking and chewing movements could be due to cortical involvement.

Peripheral nerve involvement is an important feature of chronic and insidious mercurial poisoning as evidenced by paraesthesiae, pains, and tenderness in the limbs.

The optic nerve is the only cranial nerve to be involved, and that to a variable degree. Apart from the slight blurring of vision that may be present in the early stages the optic changes are permanent. Agrosan can thus produce visual impairment, blindness, and optic changes, presumably because of its content of ethyl mercury chloride. In this respect it resembles the alkyl mercury compound "granosan M," as reported from Iraq by Jalili and Abbasi (1961). Granosan M is ethyl mercury *p*-toluene sulphonanilide. In my series there were nine such cases, four of which showed optic atrophy. Contrary to Jalili and Abbasi's experience, however, the visual damage shown by my cases has been permanent.

Muscular weakness is the outcome of peripheral nerve involvement as well as being the direct effect of the poisoning of the muscles. Alkyl mercury compounds are also known to cause degeneration of the cerebellum and so may be responsible for ataxia in some of these cases.

The mode of onset, symptomatology, and progress of some of my cases closely resembled those of the cases reported from Iraq—such as involvement of the nervous system, ataxia, mental symptoms, and muscular weakness. But pruritus, a common feature in the Iraq cases, was absent in my cases. The comparison of the two series shows that the clinical features were very similar.

All the patients in my series except three were treated with B.A.L., and of those who were treated all except three made an appreciable recovery. The condition of the three who were not given B.A.L. deteriorated. Hence B.A.L. deserves a trial as an antidote to agrosan poisoning.

My experience with B.A.L. is rather different from that of Jalili and Abbasi in Iraq. They have, however, reported that B.A.L. had a dramatic effect in at least two cases. This discrepancy may be due to the very advanced nature of the cases in the Iraq series with their severe involvement of the nervous system, whereas my cases were of all grades of severity. However, it is more probably due to the presence of ethyl mercuric chloride apart from the phenyl acetate in agrosan GN.

The severity of the disease varied with the patient's age, the number of days for which the wheat was eaten, the patient's appetite, previous health, and the speed with which the illness was treated.

Jalili and Abbasi suggested that measures should be taken to prevent such outbreaks, either by colouring the seed-dressing or by giving it an unpleasant taste or odour. With this suggestion I entirely agree.

Summary

An outbreak of poisoning in West Pakistan due to the consumption of seed wheat dressed with an organic mercurial compound, agrosan GN, is described. Agrosan GN is a mixture of phenyl mercury acetate and ethyl mercury chloride.

Thirty-four patients were admitted to hospital, where four of them died; five seriously ill patients were removed by relatives and may also have died. The illness among the remaining 25 patients was mild in 14, moderately severe in seven, and severe in four.

In a typical case the earliest symptoms were malaise and lethargy, followed in a few days by nausea and vomiting, excessive thirst, increasing weakness, and burning in the mouth and stomach. The patient would be irritable, have difficulty in walking, his speech would be slurred, and he would be confused. In the more severe cases this condition would progress to an inability to stand, greater disability in speech and swallowing, blindness, and extreme confusion, progressing to coma, spasticity, and death.

It was only possible to perform one necropsy, but the findings were consistent with chronic mercurial poisoning. Treatment with B.A.L. is discussed, the author concluding that it is an effective antidote.

The author believes that colouring seed grain treated with mercurial compounds or giving it an unpleasant smell or taste would help to prevent such outbreaks occurring in future.

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The Minister of Health, Mr. Enoch Powell, opened Hitchin Health Centre and Junior Training Centre on May 17. Among the services to be provided at the clinic are dental services for children. Referring to the benefits of fluoridation, Mr. Powell said: ". . . I am aware that there are cranks who are trying to hold up fluoridation by scaremongering and misrepresentation. It is hard to speak of these people in moderate language. They themselves drink water which contains numerous chemicals artificially added. They themselves drink water which already contains fluoride, sometimes at appreciable levels. Yet, for the sake of a private fad or personal quirk, they are satisfied to see whole generations of children grow up suffering avoidable pain and ill-health. . . I am glad to know that in Hertfordshire no fewer than 27 out of the 29 county districts that have considered fluoridation want the county to go ahead with it; and I am sure that the Hertfordshire County Council, with their encouragement, will not deny to Hertfordshire children the benefits which children in some fortunate parts of the country have always enjoyed and which can now be available to all."