tions revealed no abnormality in the levels of his total and differential white count. His serum alkaline phosphatase, serum proteins, albumin/globulin ratio, serum calcium, P.C.V., and E.S.R. were within normal limits. His maximum breathing capacity was 62.5 litres a minute and his vital capacity 1,700 c.cm. A chest x-ray film showed small areas of nodulation scattered fairly uniformly throughout all zones of both lung fields (see Fig.). These nodular

Radiograph showing small areas of nodulation in both lung fields.

shadows were closely packed, and under the hand lens appeared to be of fairly homogeneous density. There was also evidence of a lattice- or matrix-work background on which the nodular deposits were superimposed. In the right upper lobe, apex, and first space there was evidence of a diffuse opacity suspiciously like pulmonary tuberculosis. Radiologically the findings were thought to be those of talc pneumoconiosis probably complicated by apical pulmonary tuberculosis.

Occupational History.—This patient had been employed for 43 years (starting at 14 years of age) in the textile industry. His occupation was that of picker maker. These employees are concerned in making thongs, originally of buffalo hide, but in recent years from any type of leather skin. The picker is employed to drive the shuttle which threads the weft in the weaving loom from side to side. The hide is first steeped in a vat of water for three hours and is then hung up for five minutes to allow the surplus fluid to drain off. It is next placed on old sacking on the floor and dusted liberally with talc (French chalk, hydrated magnesium silicate). The talc is now spread uniformly on the hide by means of a whitewash brush. The hide is then reversed and the process repeated. Later the hide is lifted by two picker makers on to a table, and throughout these operations the atmosphere is cloudy with fine talc dust. Each week about 40 hides, each 12 by 6 ft. (3.6 by 1.8 metres) in size, are treated in this fashion by each picker maker. It was after working 39 years in this process that the patient began to observe the symptoms indicated above.

Discussion

Petrographically, talc consists of straight fibres, curved fibres, and shreds. These fibres measure up to 10 μ in length, though many are only 4 to 5 μ . Radiological evidence of talc plaques varying from single linear strands in the region of the diaphragm to massive deposits, bizarre in shape, extending over a large part of the lung fields, has

been recorded by Siegal *et al.* (1943). There is no certain association between talc pneumoconiosis and pulmonary tuberculosis, though Thorel (1896) and Zanelli (1931) have recorded cases in which these two conditions were probably present.

It is of interest to observe that the allied condition of talc granuloma has been reported, both in the U.S. and in the British literature (Mackey and Gibson, 1948; Walker, 1948; and Smith, 1948), as occurring in abdominal and gynaecological surgery, following the use of talc or French chalk in surgical gloves.

A survey of the literature suggests that this condition is not a pure pulmonary silicosis but is rather a slowly developing fibrogenic disorder; and it has been suggested that it may be allied to asbestosis. In the above reported case, talc pneumoconiosis manifested itself by a very insidiously developing dyspnoea associated with a mildly productive "smoker's cough."

We wish to record our thanks to Dr. K. Perry for his helpful comments on this case.

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FATAL CASE OF ENCEPHALITIS AFTER PHENOLPHTHALEIN INGESTION

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Acute disseminated encephalomyelitis is not an uncommon condition in childhood, and Brewis (1954) was able to collect a series of 93 cases, occurring over an eight-year period, from the children's wards of three hospitals. Those cases which occur as a complication of the acute specific fevers have often been assumed to be due either to a direct invasion of the brain by the virus concerned in the primary infection or to the activation of a virus already present in the nerve tissue. Glanzmann (quoted by Russell Brain, 1940) suggested in 1927 that the mechanism was an allergic process, the nervous tissues having become sensitized to the original virus. Miller (1954), expanding this viewpoint, believes that, although acute disseminated encephalomyelitis has a multiple aetiology, the common factor in all cases is an allergic reaction involving nervous tissues. In the case now reported the ingestion of phenolphthalein, a substance known to be capable of exciting a hypersensitivity reaction in certain individuals, was followed by a fatal encephalomyelitis.

Case Report

A healthy female child aged 2½ years had been given a number of chocolate laxative tablets by an older child. It was not possible, therefore, to determine how much

phenolphthalein was ingested, but it was probably between 10 and 20 gr. (0.65 and 1.3 g.). A few hours later she became fretful, and on the following morning passed several loose stools. Shortly afterwards it was noticed that the right side of the face and the right arm were twitching, and at that stage she was admitted to hospital. Then, although the myoclonic movements were continuous, she appeared to be quite conscious. In spite of sedation with phenobarbitone and amylobarbitone, the movements continued intermittently, at times becoming generalized. She passed from drowsiness to stupor, and after an illness lasting eight days died in coma.

Her temperature on admission was 100° F. (37.8° C.), and throughout she ran a continuous fever, mainly in the range of 101 to 103° F. (38.3 to 39.4° C.). The diarrhoea continued, and as late as the seventh day phenolphthalein could be demonstrated in the urine. Lumbar puncture was carried out on two occasions: the first specimen of cerebrospinal fluid contained 19 red cells and 8 white cells per c.mm. (5 polymorphs and 3 lymphocytes); in the second specimen there were three white cells per c.mm. In neither of these specimens could phenolphthalein be detected. Other investigations included a chest x-ray examination, which was normal; routine testing of several specimens of urine, which were found to be normal; and a blood count which showed 90% haemoglobin, and 22,800 white cells, with a normal differential count.

Salient features of the post-mortem examination were that the brain showed considerable flattening of the convolutions and much oedema. On section, a number of fine petechial haemorrhages were present, but no grosser lesions. On the anterior surface of the heart there were a number of small petechial haemorrhages.

In contrast, the microscopical appearances of the brain were most striking, and were reported on as follows: "Sections from various parts of the cortex and the ventral surface of the pons show similar appearances consisting of cellular infiltration essentially perivascular in type and in some areas of great intensity. The infiltrating cells are mainly lymphocytes or large mononuclears, but some resemble plasma cells, and polymorphs are also present in small numbers. They form an apparently continuous sheath around the perforating vessels and extend through the cortex to the subjacent tissues. In the most severely affected areas infiltration has become practically diffuse, there is evidence of demyelination, with considerable numbers of foamy phagocytes, and the nervous tissue may be completely disorganized. Such changes are to be found in superficial cortical layers in the depths of the sulci and also in the white matter. The meninges show cellular infiltration proportionate to that in the underlying tissues and in some sections are practically normal."

Discussion

The laxative effect of phenolphthalein was discovered by Professor Vamossy in 1902. His observations were published after he had been unsuccessful in attempting to produce toxic manifestations in himself, his associates, and a variety of animals (Vamossy, 1936).

Nevertheless toxic reactions have been reported and have included albuminuria and allergic skin reactions, the latter being summarized and reviewed by Haber (1950). The standard textbooks of paediatrics and pharmacology make only scanty reference to phenolphthalein toxicity, although in Mitchell-Nelson's *Textbook of Paediatrics* (1950) one reads: "High fever, hemiplegia, albuminuria, oliguria, respiratory and cardiac failure, coma and death have been attributed to phenolphthalein poisoning."

The only case in which death was ascribed to phenolphthalein poisoning was reported by Cleaves (1932). He related that a boy of 10 years ate the contents of a box of "ex-lax"; within a few hours there was severe purgation, and by the next day his temperature had reached 106° F. (41.1° C.). Four days later huge weals developed over the abdomen, legs, and arms, disappearing on the following day,

by which time he had become hemiplegic and comatose. Multiple petechiae then appeared on the abdomen and feet, and he died on the tenth day. During the course of this illness his cerebrospinal fluid had shown a sterile lymphocytosis. Post-mortem examination showed haemorrhagic areas throughout the length of the intestine, in the kidneys, and in the liver. Haemorrhagic areas were also present in the brain, and the meninges showed congestion. Microscopical examination of the brain was not carried out.

In the following year, Nelson (1933) described the case of a child aged 3 years who developed a bloody diarrhoea after the ingestion of 19 laxative tablets containing phenolphthalein. Two days later the diarrhoea ceased, but he became semicomatose and developed a bilateral internal squint and meningism. His urine contained albumin and granular casts; six days later it was normal. His cerebrospinal fluid contained 50 lymphocytes per c.mm. Improvement was slow, but eventually it was complete.

In addition to cases in which its ingestion has been followed by toxic effects, many cases have been reported in which relatively enormous amounts of phenolphthalein have been taken with no untoward effects (Blatt, Steigmann, and Dyniewicz, 1943). While it is clear, therefore, that phenolphthalein does not exert a direct toxic action, the well-documented reports of skin reactions indicate that it is capable of producing a hypersensitivity reaction. If such a reaction were to occur in the brain, the lesions would be expected to resemble histologically those which have been produced experimentally in animals by the induction of a hypersensitive state following the injection of brain tissue. Histologically, the appearance in experimentally induced encephalitis bear a close resemblance to those seen in human cases following the inoculation of various biological products, in acute disseminated encephalomyelitis of apparently spontaneous origin, and in the case described above. The relationship of the ingestion of phenolphthalein to the subsequent encephalitis in this case may have been coincidental, but the possibility of its being causal cannot be denied.

Conclusions

Phenolphthalein has no direct toxic action.

It can cause an allergic skin reaction in certain individuals who show an idiosyncrasy towards it.

The histological appearances of the brain in the case reported are closely similar to those seen in experimentally induced encephalitis.

It is possible that in the present case the encephalitic reaction may have been due to a hypersensitivity reaction to phenolphthalein.

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"After 40 years of teaching medicine to graduates and undergraduates I have the unhappy feeling that most of the men whom I have watched as undergraduates, interns, residents, and graduate students, preparing for a specialty, were not interested in becoming learned and widely experienced and wise. They were interested in getting a certificate of three years' attendance that would enable them to take an examination, which, if passed, would give them a listing as a specialist. The less effort used in getting this certificate, the better."—Emeritus Professor WALTER C. ALVAREZ in a letter to *Science* (November 26, p. 896).