vacuolation. The Purkinje cells were severely damaged and the endothelial lining of some of the cerebral blood vessels was swollen and had separated from the surrounding tissues.

Neither ethylene chlorohydrin, nor chloracetic acid were found in the necropsy findings of the blood and tissues.

Discussion

No descriptions are available of the effects in humans after drinking ethylene chlorohydrin, but extrapolating from the data obtained with rats it is likely that 1 or 2 ml. would be lethal for this exploring toddler.

Ethylene chlorohydrin is also toxic by inhalation and by absorption through the unbroken skin. Browning (1965) has reviewed the 8 reports where the chemical entered the body through these routes in industrial accidents. Carpenter, Smyth, and Pozzani (1949) found experimentally that exposure to 32 p.p.m. of ethylene chlorohydrin in air for 4 hours killed half their rats, while 9 cases of illness caused by breathing low concentrations of the substance over a long period were described by Goldblatt and Chiesman (1944). These patients complained chiefly of nausea, vomiting, and abdominal pain. Because amateur photographers might work in ill-ventilated rooms they might encounter toxic concentrations of this volatile poison. In the fatal inhalation cases symptoms appeared only insidiously, while the rats left by Ambrose (1950) in lethal concentrations of the gas died 1–2 hours after the completion of their experimental exposure but appeared well up to the time of their deaths.

Some of the industrial deaths reviewed by Browning (1965) and the 5 cases of illness described by Bleckat and Strube (1968) were caused by the chemical contaminating the unbroken skin. Similarly, Ambrose (1950) showed that small amounts of the poison applied to the intact epidermis of laboratory animals can be fatal.

Thus, the studies of the industrial accidents and the experiments on animals have shown that inhalation of the gas and skin contact with this chemical should be avoided. Ethylene chlorohydrin is also extremely poisonous when taken by mouth, and, therefore, to avoid domestic accidents, especially to children, a less toxic agent should be found as a simple film cement.

Summary

A 23-month-old boy drank 1–2 ml. of ethylene chlorohydrin and died. The clinical course of his illness and the necropsy findings are described. The dangers of the chemical are discussed, and it is recommended that less toxic products should be sought as film-base solvents for amateur use.

D. Summerfield, Esq., H.M. Coroner, Manchester, kindly gave permission to publish this case. Mr. A. Hoole of the Forensic Science Laboratory, Preston, performed the toxicological analyses, and Mr. A. R. Pippard of Johnsons of Hendon, Ltd., helped with information about Cinecol.

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Cryptorchidism, Chest Deformities, and other Congenital Anomalies in Three Brothers

A family is described in which all male offspring displayed an identical clinical picture which included cryptorchidism, chest deformities, and pulmonary anomalies, abnormal shape of skull, hypoplasia of fatty and muscle tissue, and severe mental retardation.

Family Investigation

Details of the family tree are given in Fig. 1. There is no consanguinity. None of the other relatives showed any congenital anomalies of the kind described here. All living members of the family have been examined.

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Fig. 1.—Pedigree.
The mother, as well as one of the girls, had a continuous simian line in the palm of the left hand. The eldest girl had a history of a small ventricular septum defect during infancy and early childhood, but at the time of the family investigation no signs of congenital heart disease were found. The son of the eldest daughter was apparently normal. The twin sister of Case 2 died in a hospital when 12 days old, birthweight 3300 g. On clinical grounds congenital heart disease was suspected, but no necropsy was performed.

**Case 1.** At the time of investigation of the family this boy was already dead, hence only retrospective information was available. He was born at home after a normal 40 weeks' gestation and spontaneous delivery. The neonatal period was uneventful. After some months, abnormalities of the shape of the chest, as well as mental and motor deterioration became evident. The clinical findings are given in the Table. The boy was admitted to hospital twice because of bronchopneumonia, and died in the second episode, aged 8 months. Necropsy was not allowed.

**Case 2.** He was born after a normal 40 weeks' gestation and uneventful delivery in January 1959, birthweight about 2000 g. This boy was the first-born of binovular twins and was nursed in an incubator until he weighed about 3000 g. When about 6 months old the parents noticed the same abnormal features as Case 1 had exhibited. Weight gain and development were retarded, and he had hypotonia, mental retardation, and an abnormally shaped chest. At the age of 8 months he was admitted to hospital for investigation: no diagnosis was made. Subsequently he suffered from repeated lower respiratory tract infections and atelectasis of the left lung. The left bronchial system appeared to be hypoplastic, bronchoscopy showing collapse of the left main bronchus during inspiration. In 1967 a haematemesis occurred, probably as a result of a hiatus hernia, together with cardio-oesophageal reflux and an ulcer of the oesophageal mucosa.

After Case 3 died, this boy was once again investigated. He was now 10½ years, with a height of 124 cm. (below the 3rd centile); the weight was 15·4 kg. (far below the 3rd centile). The head circumference was unduly large, 54 cm., and the span (124 cm.) was appropriate to the height. The IQ (WISC test) was 46. His emotional development was that of a 4-year-old boy. Motor development was seriously retarded; he was able to lie and roll on to the other side. Supported by an orthopaedic corset, he could sit in a wheelchair and move about, but could not walk without help. The most striking physical features were the much flattened left part of the chest, with the sternum shifted to the right. The spine was kyphoscoliotic. Muscle and fat tissue were underdeveloped. There was cryptorchidism and hypospadias. Further findings on physical examination are shown in the Table. Laboratory investigations which included urinary excretion of 17 ketosteroids, amino acid paper chromatography of urine, and plasma protein-bound iodine, were normal. At the age of

### TABLE

**Results of Physical Examination**

<table>
<thead>
<tr>
<th>Feature</th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dolichocephaly</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Convergent squint</td>
<td>+†</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>High-arched palate</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Ears of unequal size and of ear-lobes</td>
<td>+‡</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Irregular dentition</td>
<td></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>High-pitched squeaky voice</td>
<td></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Chest and spinal deformations, scapulae alata</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Elongated narrow left main bronchus</td>
<td></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Recurrent atelectasis of left lung</td>
<td>Frequent pneumonia, died of pneumonia</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Arachnoidally</td>
<td></td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Contracture of knees</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drop foot</td>
<td>+†</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Hypotonia</td>
<td></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Generalized muscle hypoplasia</td>
<td></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Absence of subcutaneous fatty tissue</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Cryptorchidiam</td>
<td></td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Hypospadias</td>
<td></td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Severe mental retardation</td>
<td></td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>

*Family paediatrician's observation.
†Mother's description.
‡As shown on photographs.

FIG. 2.—Case 3. Note the flattening of the left part of the chest and the hypoplastic musculature.
10 11/12 years the bone age was 9 years. There was a simian line in the palm of the right hand. The chromosomes showed a normal pattern, after examining a total of 100 cells and 6 karyotypes.

Case 3. He was born in April 1964 after a normal 40 weeks' gestation and spontaneous delivery. When 4 months old it was noticed that growth and development were retarded, and that chest deformities and contractures of the lower extremities were appearing. The clinical picture was identical to that of Case 2 (see Table and Fig. 2). At 4½ years he was admitted to hospital with pneumonia; at that time his weight was only 9 kg., head circumference 53 cm. He died suddenly a few hours after admission.

Necropsy. External findings are summarized in the Table. There was hardly any subcutaneous fatty tissue. The entire musculature was pale and atrophic. The wall of the left main bronchus was thinner than that of the right main bronchus. On microscopical examination the cartilagenous rings were not continuous. There were no cardiovascular abnormalities. The penis was normal, but the scrotum 'empty'; examination of the abdominal cavity failed to show testes; it was concluded that there was testicular agenesis. The prostate and the ejaculatory ducts were normal. Examination of the brain was not allowed. Bronchiolitis was the probable cause of death.

Discussion

The main characteristics of the clinical picture in the three brothers were: serious chest deformities with pulmonary disorders; agenesis of the testes; grossly depressed weight gain; hypoplasia of the musculature and absence of subcutaneous fatty tissue; severe mental retardation; and dolichocephaly.

Since three sibs were affected, the condition is probably inherited either as an autosomal or a sex-linked recessive. The cause of death in the twin sister is uncertain, so we cannot distinguish between these two possibilities. As far as we know this complex of symptoms has not been described. In 1912 Benjamin described a syndrome with clinical features of anaemia, skeletal and muscular underdevelopment, anomalies of the ear, hypoplasia of the genitals, and cardiac disorders. As none of our patients were anaemic and as chest deformities, so outstanding in our patients, were not mentioned by Benjamin, we do not think our patients had the same syndrome.

Summary

A family is described in which all male offspring (3 brothers) displayed the same multiple congenital anomalies. The syndrome consisted of severe chest deformities with pulmonary anomalies; agene-

sia of the testes; hypoplasia of the musculature and absence of subcutaneous fatty tissue; and dolichocephaly with severe mental retardation. No chromosomal abnormality was found.

Reference


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Plasma Cortisol Levels in the Neonatal Period

At birth the concentrations of 17-hydroxycorticosteroids (17-OHCS) in the cord blood reflect the maternal levels and are also related to the degree of stress occurring at birth (Migeon, 1959). Babies born by caesarian section usually have low levels, less than 10 μg./100 ml., whereas in these born vaginally the level is usually greater than 10 μg./100 ml. (Gemzell, 1954; Migeon, Keller, and Holmstrom, 1955). The cord plasma values are in most cases lower than the corresponding maternal values. It has been shown that there is a gradual fall in the plasma 17-OHCS level after birth (Bayliss et al., 1955; Klein, Fortunato, and Papadatos, 1954), and at the end of the first week of life the plasma levels in normal full-term babies are similar to those of the normal adult (Gray, Greenaway, and Holness, 1961).

Various methods have been used in the past to measure plasma 17-OHCS but the majority of these methods are not specific for cortisol. Interference from cortisone, corticosterone, and inactive breakdown products such as tetrahydrocortisone may occur using methods based on the 'Porter Silber' reaction (Porter and Silber, 1950) or a fluorimetric technique (Mattingly et al., 1964). In 1963, a complicated technique was described which utilized the steroid-binding properties of a specific protein, transcortin, the cortisol binding globulin (CBG) in a competitive protein-binding 'radio-assay' using C14-cortisol (Murphy, Engelberg, and Pattee, 1963). Subsequently the method was modified by the use of tritiated cortisol (Murphy, 1967) which greatly increased the sensitivity of the method and allowed