A one of seven had an antitoxin titre of 0.1 unit or more per ml. before the tablets were given, and six of seven had 0.1 unit or more after the tablets were given. In group B 2 of 15 had 0.1 unit or more of antitoxin per ml. before the tablets were given and 11 of 15 had 0.1 unit or more per ml. after the tablets were given. In the two groups together, titres of 0.1 unit per ml. or more were observed in 3 of 22 sera before the tablets were given and in 17 of 22 afterwards.

In the group with a negative or indefinite history of

TABLE III.—Antitoxin Titres in Persons with No* Previous History of Immunization

	<0.001	≥0.001 <0.01	≥0.01 <0.1	≥0.1 <1.0	≥1.0 <10.0	≥10	Total
Pre-immunization	8	1	4	5	3	3	18
Post-immunization	1	3	4	5	3	3	18

* In some there was an indefinite history of immunization.

previous immunization (Table III) 5 of 18 sera contained 0.1 unit or more of antitoxin per ml. before the tablets were given and 11 of 18 afterwards.

It is doubtful whether the results in Table III indicate that the lozenges would be effective in primary immunization. The volunteers concerned probably had either been previously immunized or been in contact with natural infection, and the increases in titre were the result of the response to a reinforcing dose.

The individual titres before and after the administration of the lozenges are shown in the Graph for the 22 volunteers with a previous history of immunization. Only one of eight subjects with less than 0.001 unit of antitoxin per ml. before the lozenges were given

Antitoxin titres in 22 persons with a previous history of immunization (groups A and B together).

remained in this category afterwards. Of the others only two—one whose serum contained between 0.1 and 1 unit of antitoxin and the other whose serum contained between 1 and 10 units before the lozenges were given—failed to show a tenfold or greater increase in the antitoxin level after receiving the lozenges. Six showed tenfold increases, eight 100-fold increases, and five 1,000-fold increases.

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DISCUSSION

These preliminary results indicate that diphtheria toxoid can be absorbed through the buccal mucous membrane in quantities sufficient to stimulate a substantial antitoxin response in persons previously immunized. The increases observed are similar to those obtained by Edsall *et al.* (1954) after two injections each of 1 Lf of alum-absorbed toxoid given three weeks apart to young adults, but they are less than those obtained by the same workers when they gave a third dose, also of 1 Lf. However, of the 22 previously immunized subjects it is probable that only one would have been Schick-positive after the lozenges. The method is thought to be promising enough to warrant further large-scale studies, and these are now in progress in children aged 10–12 years in whom reinforcing immunization by the oral route would be of considerable practical value.

SUMMARY

In a preliminary study two lozenges each containing 1,500 Lf of purified diphtheria toxoid and 1,500 units of hyaluronidase were given a week apart to 40 adult volunteers to suck. An increase in antitoxin titre was observed in blood samples taken two weeks after the lozenges were administered. The results justify further study of the lozenges as a means of producing satisfactory antitoxin responses to reinforcing immunization in children primarily immunized by parenteral injections.

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Medical Memoranda

Finger-tip Necrosis in the Newly Born : a Hazard of Wearing Mittens

In recent years a disquieting number of therapeutic mishaps and nursing accidents involving neonates have come to light. Another form of avoidable injury results from the common practice of applying mittens† to the hands of newly born infants.

CASE 1

A prematurely born infant of 28 weeks' gestation and birth weight 2 lb. 13 oz. (1,275 g.) was admitted to the Royal Alexandra Hospital for Sick Children, Brighton, aged

†The mitten customarily used for neonates is a bag made of cotton material with a seam at the top and down one side. This accommodates the whole hand and the covering is secured at the infant's wrist with tapes or a drawstring.

4 days, because of hyperbilirubinaemia. Exchange transfusion was just avoided. Five and a half weeks later the baby was removed from an incubator and clothed for the first time. At this point cotton mittens were applied.

A few days later, after a feed which was taken well, the mittens were removed as a part of a change of clothing. On taking off the left one a piece of cotton from the interior of the top seam was found tightly wound round the middle finger in the region of the proximal interphalangeal joint and the distal part of the finger was black. After removing the offending thread the circulation slowly improved, but the next day the finger presented the ugly appearance shown in Fig. 1. In spite of prophylactic tetracycline the haemorrhagic bleb on the back of the finger became infected. Three weeks later a remarkable degree of recovery had occurred, but the whole finger was still swollen and there was obviously some loss of terminal pulp tissue. The nail had separated and there was a yellow crust in its place.

At the age of 15 months the nail was normal but the finger-tip was tapered owing to loss of pulp tissue. Although movements at the terminal joint were good, full extension of the distal phalanx was not possible.

CASE 2

The incident in this case actually occurred a year before the one just described but only came to light subsequently.

The accident happened at home after the mother's discharge from one of our maternity units. A 3-weeks-old baby (the mother's first, for which she had been waiting 14 years) was wearing home-made nylon-and-wool knitted mittens. On the day of the mishap the mother was in the process of removing the right mitten at bath-time when she noticed it could not be completely removed because a thread from the inner seam was tightly encircling the index finger at the distal interphalangeal joint and had to be cut loose. The terminal part of the digit was purple-black. As soon as the thread was cut the circulation improved. However, the nail separated in a few days and it was soon apparent that the finger-tip was gangrenous. Thereafter recovery was slow, and it was necessary for the baby to attend the orthopaedic clinic for three months' treatment. Fig. 2 shows the appearance of the finger at the age of 1 year. The distal portion is foreshortened and bulbous in shape and there is a flexion deformity similar to that in Case 1.

COMMENT

The mechanism whereby an internal thread from a mitten becomes wound round a finger is not difficult to

understand. A similar thing may happen occasionally to a toe of a child or adult if there is a loose thread inside the top of a sock. In the case of a baby, flexion and extension movements of the fingers inside the spacious bag will encourage coiling of a piece of cotton round the digit with increasing constriction. It is remarkable that this process and the ischaemic complications which follow should cause neither pain nor discomfort.

Nowadays mittens are rarely used in our hospitals. If a baby is scratching its face or sucking its fingers and making them sore then swaddling with a shawl for a few days seems to be a reasonable and safe alternative measure for dealing with such situations. For those who cannot be persuaded to abandon the use of mittens in the light of these two accidents, the only advice that can be offered is that the coverings should have a firm French seam and they should be examined carefully for internal threads before each application.

I thank Mr. Austin Brown for permission to publish details of Case 2; and Mr. S. T. Higgins for his help with the photographs.

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Pyridoxine-responsive Anaemia

Hypochromic anaemia is usually the result of iron deficiency. It may, however, occur despite the presence of normal or increased amounts of iron. Thalassaemia is the most familiar example of such a refractory hypochromic anaemia. Harris *et al.* (1956) described the first case of a naturally occurring iron-refractory hypochromic anaemia which responded to the administration of pyridoxine. Nine further cases have been recorded (Maier, 1957; Foy and Kondi, 1958; Gehrmann, 1958; Bishop and Bethell, 1959; Verloop and Rademaker, 1960; Erslev *et al.*, 1960; Jones and Hutt, 1961; Dawson *et al.*, 1961). It has been suggested that the reported cases of pyridoxine-responsive anaemia show too much variation for them to be regarded as a homogeneous syndrome at present (Jones and Hutt, 1961). The following observations on a patient with an iron-refractory hypochromic anaemia which responded completely to treatment with pyridoxine are perhaps pertinent.

CASE REPORT

A man aged 61 presented in November, 1957, with symptoms of anaemia. Apart from pallor there were no physical signs of disease and he was found to have a hypochromic anaemia with a haemoglobin of 3.1 g./100 ml. The leucocytes and platelets were normal. A fractional test meal revealed complete achlorhydria, and tests of hepatic function were normal. No evidence of gastro-intestinal haemorrhage could be discovered and radiological examination of the small and large bowel was normal. There was no response to treatment with oral or parenteral iron and 6 pints (3.4 litres) of blood was transfused.

In March, 1958, he was severely anaemic again and required blood transfusion. The serum iron at this time was normal (110 µg./100 ml.). Isotope studies performed within three weeks of blood transfusion revealed a normal plasma iron turnover, and 80% of the ⁵⁵Fe had reappeared in the red cells by the ninth day. The survival of the patient's red cells labelled with ⁵¹Cr was slightly reduced, the time taken for half disappearance being 21 days. He was given a further course of parenteral iron, but a recurrence of anaemia required blood transfusion in May and August.

FIG. 1

FIG. 2

FIG. 1.—Case 1. Discoloured appearance of middle finger of left hand on day after accident. Note haemorrhagic bleb over back of middle portion of digit. FIG. 2.—Case 2. Appearance of index finger of right hand one year after accident. Note bulbous tip and flexion deformity at distal joint.