Discussion

The genetics of harelip in the mouse have not as yet been satisfactorily elucidated. The most significant theoretical concept is that of Grüneberg (1943), who suggested that the Strong A line may be homozygous for a harelip gene, or more probably a small number of cumulative genes, with a series of minus modifiers exerting a protective action and, in most cases, cancelling out the effect of the gene or genes. That such modification might be due to environmental factors was the opinion of Reed (1936), who attributed the variation in incidence of harelip in the house mouse to the interplay of environmental and genetic effects, the environmental factors being five times as influential as the genetic.

The influence of maternal factors on the incidence of harelip in mice was shown by Steiniger (1939), who was able to increase the incidence of harelip in a susceptible strain by the administration to the dam of "preloban," a preparation which contains all the known anterior pituitary hormones, during the first half of pregnancy. Since anterior pituitary hormones increase, and thyroxine decreases, the influence of the gene or genes for harelip, it would seem that the hormonal balance of the mother is of considerable significance for the proper development of the lip in the foetal mouse. Unfortunately the part played by the maternal organs and placenta in the endocrine control of the foetus is as yet only imperfectly understood, but such information as is available suggests that, at the critical period of development of the lip, the foetal mouse is entirely dependent for thyroxine and insulin upon the endocrine system of the mother. Therefore, though it is not possible to detect the precise mechanism by which thyroxine exerts its protective action against the deleterious effects of the harelip gene or genes, it is clear that, if it acts by influencing the production of hormones by the thyroid gland or islets of Langerhans, it must do so by influencing these structures in the mother rather than in the foetus. If, on the other hand, the activity of the thyroxine is directly on the developing foetal tissues, it may be that it exerts its protective effects by an influence on the carbohydrate metabolism of the cell.

It is interesting to note that Eggenberger (1928) observed that many congenital malformations are more common in cretins than in the population at large. There are a number of congenital conditions, of which cretinism is but one example, in the production of which the interplay of genetic and environmental factors appears to be involved. It may be that in the elucidation of the aetiology of these conditions, which can be explained only partially on a genetic basis, attention should be paid to what is perhaps the most significant environmental factor to which the developing foetus is exposed, the influence of the endocrine system of its mother.

Summary

A significant decrease in the incidence of harelip in the Strong A line of mice was produced by administering 0.1 mg. of thyroxine to the dam on the 11th and 12th day of pregnancy.

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THE POLYMASK AS A MEANS OF ADMINISTERING OXYGEN

BY

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The polymask is often used to administer oxygen to patients, and in the General Infirmary at Leeds (1,000 beds) 2,160 polymasks were used last year on medical and surgical cases.

The polymask is a bag made of soft "polythene" sheeting, with an inner smaller bag at the top. Oxygen is fed into the larger bag through a narrow plastic tube, then into the smaller compartment through two holes, each $\frac{1}{4}$ in. (12.5 mm.) in diameter. Two smaller holes, piercing both the inner compartment and the outer bag and situated near the patient's nostrils, are designed for the emergence of carbon dioxide. A bare wire runs round half the top of the bag and is moulded over the patient's nose and cheeks; the portion of the bag beneath the chin is quite loose and no attempt at close fitting is made. Thread elastic passes round the head and fixes the bag in position.

The polymask has been tested for the accumulation of carbon dioxide, and this was found not to occur to any significant degree (Ogilvie, 1956). However, its efficacy as a means of delivering oxygen to the wearer was in doubt after observing it in use. It seemed that one or both of two occurrences could be responsible for the patient's inspiring room air through the holes designed for expiration even when the oxygen was entering the mask at 8 litres a minute.

Firstly, owing to the lightness and softness of a bag which is of relatively large dimensions (8 by 8 in.—20 by 20 cm.) and the presence at its base of a tube of extremely narrow bore to which is attached, through a tapered connexion, a much heavier connecting tube from the oxygen cylinder, kinking of the bag above the entry tube can occur, with the production of deep creases in it (Fig. 1). This usually causes the second occurrence, which is that the two holes into the inner compartment either collapse on themselves or get so displaced that they come to lie beneath the chin, with

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FIG. 1.—The polymask in the "usual" position. The patient has moved the head about, with the following results: (1) The bag above the entry tube is kinked and deep creases have appeared in it; (2) the two holes for the oxygen inflow to the smaller bag have slipped beneath the chin and oxygen is flowing down the neck; (3) the bag can be seen to be indrawn as the patient inspires room air through the expiratory holes; and (4) though the oxygen flow was 8 l./min., the gas available inside the mask contained only 25% oxygen on this occasion.

FIG. 2.—The patient, wearing the polymask and sitting upright, has turned the head and produced the same state of affairs as in Fig. 1.

the consequence that the oxygen which passes through them flows out of the lower part of the bag, and escapes uselessly down the neck.

This kinking and creasing of the bag can very easily occur with a restless patient, still only semi-conscious after an anaesthetic, but it can also occur in a patient who is sitting upright and moving the head a little (Fig. 2).

The present investigation was therefore undertaken, and was concerned with measuring the amount of oxygen made available to the person wearing the polymask.

The Method

The mask was carefully moulded to the face and the wearer was first of all arranged in the "ideal" position, which entailed lying still on the back, with the tube connecting the bag to the oxygen cylinder pinned to the sheet with a safety-pin (Fig. 3). In this way the weight of the tube was prevented from pulling on the polymask, and as the head was kept still no creases appeared in the bag, which became filled with oxygen. The oxygen was run in at 2, 4, 6, and 8 litres a minute.

Then the mask was again carefully applied, but the connecting tube was not pinned to the sheet and the wearer moved the head from side to side for five minutes. This is referred to in the results as the "usual" position. The oxygen was administered at the same rates of flow as in the ideal position.

Two patients in the ward were also tested. The nursing staff had previously been requested to ascertain that the inflow of oxygen was as near as possible to the "ideal."

Tests were performed on the wearer in the ideal position and in the usual position at each of the different rates of flow enumerated above—that is, at 2, 4, 6, and 8 l./min.

The tests consisted of drawing into an evacuated tonometer the gas inside the mask at the region of the top lip, the end of the tonometer being introduced

FIG. 3.—Polymask in the "ideal" position, which requires constant supervision. The patient is still, and the weight of the connecting tube is taken from the thin bag by being fixed to the sheet. The oxygen flow is 8 l./min. and the inspired air available to the patient contains nearly 80% oxygen.

through one of the expiratory holes. All gas samples were taken on inspiration and were analysed on a Haldane gas analyser.

Results

In none of the samples analysed was the carbon-dioxide content greater than 1%. The results obtained for oxygen percentages in the ideal and the usual positions are given in Table I. The results obtained from the patients are shown in Table II. It will be remembered that room air contains 20% oxygen.

TABLE I

Rate of Flow from O ₂ Cylinder	Percentage of Oxygen Available to Patient	
	Ideal Position	Usual Position
8 l./min.	77	33
6 " " " " " " "	70.5	21.6
4 " " " " " " "	44	21.4
2 " " " " " " "	46	22

TABLE II

Patient No.	O ₂ Flow	O ₂ Percentage in Mask
1.	7 l./min.	25
" " 2.	8 " "	30

Discussion

Under ideal conditions the polymask delivers to the region of the patient's top lip an atmosphere containing 77% oxygen when the flow from the cylinder is 8 litres a minute, while at 2 litres a minute the atmosphere is still enriched to 46% oxygen. These ideal conditions require that the weight of the delivery tube is removed from the polymask, that this remains well ventilated, and that the patient keeps still. If any of these criteria are not carried out, kinking and creasing of the bag occurs and the holes for the passage of oxygen into the inner compartment slip beneath the chin and the oxygen is directed down the neck. The patient then inspires room air through the holes designed for expiration.

At 8 litres a minute and in the usual position, it is still possible for a patient to have an oxygen-rich inspire (33%–30%), and this is probably due to the force of the oxygen flow. It is, however, extremely wasteful, and this is an important consideration, especially in domiciliary practice. Even at 8 litres a minute, however, it is possible to inspire room air if the two holes into the inner compartment have slipped beneath the chin. As these are invisible from the outside it is impossible, even with supervision, to ensure against this.

Conclusion

The delivery of oxygen to a patient through the polymask is unpredictable whatever the rate of flow of oxygen from the cylinder, but the higher the rate of flow the more chance there is of an oxygen-rich atmosphere being available to the patient.

From the evidence of gas analyses, the mask is inefficient and the wearer is more likely to breathe room air than an oxygen-rich atmosphere.

There is no undue accumulation of carbon dioxide.

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Medical Memoranda

An Overdose of "Plaquenil"

In view of the widespread use of the hydroxy derivative of the antimalarial compound chloroquine (plaquenil) in rheumatoid arthritis and other "collagen diseases," the following history may be of interest.

CASE REPORT

At 9.30 p.m. on July 4, 1959, a keeper roused a sleeping man from a park bench. The man spoke in an odd way and had vomited and defaecated in his clothing. The police arrived and elicited an admission that he had swallowed 36 tablets, and he was admitted to St. David's Hospital, Cardiff, at 10.30 p.m. He was conscious but drowsy, he readily co-operated in a slow way, his speech was slurred, and his extremities were cold and clammy. Respiration was irregular, deep or sighing, and 14 a minute. There were no physical signs of abnormality in the lungs. The pulse was regular at 68 a minute but of poor volume, and the blood-pressure was dangerously low (40/? mm. Hg). The pupils were dilated and reacted sluggishly to light; the other reflexes were present.

In view of the peripheral circulatory failure, an intravenous injection of amphetamine sulphate (10 mg.) was given at once. Blood samples were withdrawn a few minutes later, and the plasma level of plaquenil proved to be 6.1 mg./l. The response to stimulation was dramatic, and with the aid of 1.5 l. of glucose-saline to correct slight dehydration and alkalosis (Na 137, K 22, Cl 94, bicarbonate 32 mEq/l. on admission) and inhalation of oxygen for one hour, he recovered quickly. At that time x-ray films showed clear lung fields and a normal cardiac outline. The E.C.G. showed a sinus tachycardia at 112 a minute, prolongation of the P-R interval, and ST depression with left axis deviation. Apart from initial oliguria with a trace of albumin, there was no renal damage. The output was restored quickly and 1.8 l. of urine was passed in 24 hours—a deficit of 1.5 l. on the intake. An initial rise in temperature to 100° F. (37.8° C.) was countered with penicillin, 500,000 units, and streptomycin, 0.5 g., twice a day for two days, and vanished shortly after the infusion ceased. Two days later the plasma level of plaquenil was 2.7 mg./l.; Hb, 12.9 g./100 ml.; W.B.C., 7,800; E.C.G., normal; pulse rate, 74; blood-pressure, 120/80; respirations 20 a minute. The liver and renal function tests were normal, there was no evidence of corneal or other ophthalmic abnormality, and he was discharged. The crisis was a result of guilty feelings consequent upon ruinous gambling.

I am indebted to Dr. J. R. Gwilt, of Winthrop Laboratories Ltd., for analysis of plaquenil in the plasma samples, which were stored at -8° C. for 24 days.

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"Smuggling across the Malacca Strait from Sumatra to Malaya is one of the oldest activities in this part of the world. . . . Cigarettes and drugs are among the most popular items for the smugglers, but the Federation's Customs officers have recently come across an unexpected item in the traffic—lepers. . . . Lepers are unable to get efficient treatment in Sumatra, but there are now 50 Indonesian patients, all of whom have entered Malaya illegally, in the Sungei Buloh Leper Settlement near Kuala Lumpur, and the cost of their treatment adds considerably to the worries of this excellent institution. There seems to be no doubt that a well-organized band of smugglers brings them across the Strait to a small island near Port Swettenham and then smuggles them ashore." (*Manchester Guardian*, April 4.)