could usually be isolated so long as they were present, presumably from viable spores or hyphal fragments within the "residuum cone." No evidence was seen of acquisition of resistance by the fungus to griseofulvin, but there is no evidence that this might not occur when the drug is used in prophylaxis at a low dosage.

Conclusions

Our investigations showed that the fungus had been present in the school for probably not less than four years before the investigations began. It seems certain that we were dealing with a build-up of infection over a number of years rather than an outbreak. Large quantities of viable fungus were demonstrated in non-living sites, and it is believed that these extrahuman sources were important in transmission of the organism, in addition to direct transfer. The methods of control adopted were only partially successful, since a scalp infection was found six months after all known cases were cured. In this child five previous clinical examinations had failed to reveal a lesion. The prophylactic dose of griseofulvin did not apparently control the fungus in this case.

Perhaps the greatest single factor which has prevented complete elimination of the pathogen is the inability to detect infection, particularly that of the scalp. In our opinion it is almost impossible to detect what is virtually a carrier phase, and we found it necessary to have recourse to indirect examination—that is, the use of mycological techniques—to detect the organism on non-living sites such as hairbrushes, combs, and pillows. Probably complete elimination of the fungus could be achieved only by administering the full therapeutic dosage of griseofulvin to all children, combining this with regular clinical and mycological examinations and efforts to eradicate all extraneous infection.

Without griseofulvin there is little doubt that infection could not be eliminated from the school. The combined use of griseofulvin, topical treatment, and the removal of extraneous infection should ensure ultimate success.

Summary

Twenty children at a residential school were found to be infected with *T. sulphureum*. Eradication was attempted by therapeutic and prophylactic use of griseofulvin and by sterilization of all sites shown to harbour the fungus. Follow-up of all children at six months showed that with the exception of one child all were free from infection. At this time the fungus could still be recovered from a few non-living sites. Failure to eliminate all infection is attributed to the difficulty of clinical detection.

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ADDENDUM.—Since this article was submitted for publication an additional scalp infection has been found, bringing the total number of infected children to 21. This child owned the hairbrush described in the text, on which infection was repeatedly demonstrated, but on whose person no traces of infection could be revealed when examined clinically on 10 previous occasions. Two or three isolated broken hairs were found, and one of these gave rise to *T. sulphureum*; apparently only one hair was infected. Results now show that when the fungus was isolated on

three or more occasions from the effects of any one child, that child was invariably found to be infected. A measure of the value of indirect examination in infections of the scalp can be gained by the discovery of infected hairs on seven children after the presence of the fungus was revealed by mycological sampling of their hairbrushes, combs, or bedding.

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CONTROL OF DEGREE OF OXYGENATION DURING TOTAL BODY PERFUSION

BY

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Davies and Brink (1942) described the use of the platinum electrode for the polarographic measurement of partial pressure of oxygen (pO_2), ascribing its first use to Danneel and Nanst in 1897. Clark *et al.* (1953) described a modified electrode which has been used by us since January, 1959, for the continuous monitoring of oxygen content of blood, leaving a Kay-Cross spinning-disk-type pump oxygenator. The electrode has been used in experimental animal work by Clark *et al.* (1958) and Rennie, Reeves, and Pappenheimer (1958), and in clinical and experimental investigations by Montgomery and Horwitz (1950), Nahas, Morgan, and Wood (1952), Severinghaus and Bradley (1958), Urbach and Noell (1958), and Johansen and Krog (1959).

It is our policy to attempt to maintain physiological conditions during total body perfusion: the patient's temperature at, or as near as possible to, 37° C., and the venous blood oxygen saturation near 70%. To do this latter the flow is selected after consideration of the patient's surface area and age, and the pathology of the heart lesion. In this present group of cases the flow has varied between 1.8 and 3.4 l./min./sq.m., with a mean of 2.4 l./min./sq.m. The partial pressure of oxygen in blood leaving the oxygenator is maintained between 100 and 140 mm. Hg (giving a theoretical value of haemoglobin oxygen saturation of 98%) by alteration of the rate of revolution of the spinning disks.

The polarograph electrode assembly (Fig. 1) consists of a shiny platinum button and a silver-silver chloride indifferent electrode bathed in a saturated solution of potassium chloride, all enclosed in a lucite cylinder closed at the top by a nylon cap and at the bottom by a membrane of polyethylene 0.001 in. thick. The membrane is freely permeable to oxygen but prevents contamination of the platinum surface by blood.

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FIG. 1.—Diagram of the Clark electrode.

Oxygen is reduced at the platinum cathode (held at -0.6v in respect to the silver anode), causing the flow of a small current which can be measured by a sensitive galvanometer. The following equation represents the reaction:

Sproule *et al.* (1957) have investigated the electrode and conclude that, within the physiological range its response to changes in partial pressure of oxygen is linear, that its temperature coefficient is linear, and that it is not sensitive to changes in pH , CO_2 concentration, or haematocrit. However, there are variations in the slope of the response curve from sample to sample, and because of this it is necessary to calibrate the instrument in the specimen of blood to be analysed.

The electrode is sterilized in formalin vapour before use, and is placed, enclosed in a suitable rubber stopper, in a port at the outflow end of the oxygenator (Fig. 2). The machine is primed with heparinized blood, the volume generally being between 3 and 4.5 l., and the

FIG. 2.—View of the arterial end of the Kay-Cross oxygenator with the Clark electrode in position. Also shown are the thermistor in the corresponding back port, the galvanometer, and the gas-flow meters for regulating the supply of carbogen and air to the oxygenator.

polarograph is then calibrated. Calibration is performed by allowing the slowly recirculating blood to equilibrate—recognized by a steady state of the galvanometer—firstly with air ($\text{pO}_2 = 140 \text{ mm. Hg}$) and then with carbogen ($95\% \text{ O}_2 + 5\% \text{ CO}_2$) ($\text{pO}_2 = 680 \text{ mm. Hg}$), the corresponding galvanometer readings being noted.

If necessary they are adjusted to the same temperature by adding or subtracting $0.17 \mu\text{A}$ for each 1°C . temperature change, and then plotted on squared graph paper (Fig. 3). From this graph the galvanometer readings necessary to maintain a range of pO_2 100–140 mm. Hg are obtained, and during perfusion the pO_2 of the oxygenated blood can be immediately determined. The errors introduced by this method of calibration are small, as the priming volume is about equal to the patient's blood volume and the unexplained variations in slope tend to be minimized by the heterogeneity of the priming blood.

FIG. 3.—The calibration chart for the polarograph with the air and the carbogen points marked.

During perfusion, blood samples have been taken simultaneously from both arterial and venous lines and analysed for oxygen content and oxygen-carrying capacity (method of Van Slyke and Neill: Peters and Van Slyke, 1932), for haemoglobin content, and for pH and CO_2 content. In Fig. 4 are plotted the resultant arterial saturations against the graphically determined pO_2 .

During the course of perfusion it is necessary to alter the disk-revolution rate quite often in order to maintain the desired range of pO_2 . These changes are due to variations in both the quantity and the oxygen content of the venous blood returning to the oxygenator and of the cardiectomy return blood. In addition, we have found a variability in the amount and quality of the circulating haemoglobin. The measured haemoglobin oxygen-carrying capacity (method of Van Slyke and

FIG. 4.—Plotting of arterial saturations against graphically determined partial pressure of oxygen (pO_2) of the last 26 perfusions. (Note (i) the range of the saturations; (ii) the apparent shift of the dissociation curve to the right.)

Neill) has been shown to be less than that calculated by the factor 1.34 c.cm. O₂/1 g. Hb, suggesting that the haemoglobin dissociation curve has been shifted "to the right." This is in direct contrast to the work of Valtis and Kennedy (1954), who demonstrated a shift to the left in stored blood, and of Van Slyke *et al.* (1946), who showed that "inactive" haemoglobin in freshly drawn blood disappeared after standing at room temperature for two hours.

Variables such as these cannot be predicted before the start of perfusion, and, once perfusion has begun, cannot be readily influenced. They are among the important limiting factors of the effectiveness of the perfusion.

While not firmly established, evidence is accumulating that high partial pressures of oxygen in arterial blood exert a deleterious effect on the function of cerebral tissues and to a less extent on other tissues. Dickens (1946) and Mann and Quastel (1946) have demonstrated a toxic effect on cerebral aerobic glycogen metabolism; Donald (1947) and Lambertsen *et al.* (1953a) showed a deterioration of cerebral function; and Lambertsen *et al.* (1953b) and Clark *et al.* (1953) showed an effect on cerebral blood-flow. Kirklin (1958) has indicated that this is the cause of otherwise unexplained post-perfusion deaths. All the evidence is derived from experiments in which a higher partial pressure of oxygen has been used than can be obtained in our machine, but Rennie and Pappenheimer (1958) have shown that, despite very high ambient pressures, the alveolar pO₂ always exceeds that of arterial blood.

In addition, there are the theoretical considerations of micro-bubble formation—discussed by Gibbon (1959)—and interference with carbon-dioxide transport (Peters and Van Slyke, 1931). We have found, too, that with disk speeds in excess of 130 there is a tendency for the blood to foam in the oxygenator and for small bubbles to appear in the blood leaving the oxygenator.

The undesirability of a low content of arterial blood oxygen, though not well documented, is generally accepted, leading, amongst other things, to a decrease in circulating blood pH and an increase in blood acidemia (Biddulph *et al.*, 1958; Huckabee, 1958; and Magovern *et al.*, 1959). Tobian, Martin, and Eilers (1959) have shown that one of the effects of decreasing pH is to decrease the pressor action of noradrenaline.

If it is agreed that control of the degree of blood oxygenation leaving an artificial heart-lung machine is necessary, then we are sure that the polarographic method is the method of choice—the advantages being low cost, accuracy, and simplicity.

It has been suggested that oximetry could be used. In the range of haemoglobin oxygen saturation levels with which we are concerned, the oximeter is inaccurate owing to the flattening of the haemoglobin dissociation curve; it gives no information about pO₂ level above those necessary to cause 100% haemoglobin oxygen saturation (Nahas *et al.* (1952) has shown this to occur at 400 mm. Hg pO₂); it is expensive and cannot be readily adapted for continuous monitoring.

Summary and Conclusions

The reasons for the introduction of a monitoring device of the level of blood oxygen content leaving the heart-lung machine are discussed, the literature is briefly reviewed, the method of use of the Clark oxygen electrode is described, and some results are presented.

We would stress that the polarograph electrode circuit is simple and very reliable, the electrode is easily and

quickly calibrated, and the pump operator can at all times determine if the oxygenator is acting as an adequate respirator.

The platinum oxygen electrode is as supplied by Yellow Spring Instruments Co. Inc., Yellow Springs, Ohio. The galvanometer is a Pye Scalamp Type 7904/3, and the associated circuit was made from standard radio components in our electronics workshop.

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AETIOLOGY OF CONGENITAL TALIPES

BY

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The frequent occurrence of malformations in association with congenital talipes is well known. Attention has often been drawn to this fact. One of the more comprehensive reviews of the subject is by Ehrenfried (1912), who reviewed 232 cases of congenital talipes, with an incidence of associated anomalies of 13.4%. The anomalies included such conditions as congenital dislocation of the hip, mental deficiency, club-hand, cleft palate, amniotic bands, congenital herniae, and scoliosis. He ascribed the cause to heredity in those cases with a strong family history (about 10%), faulty nutrition of the zygote due to chorionic abnormalities, and mechanical distortion of the foetus.

Waller (1923) reviewed 735 cases of talipes and found a 4% incidence of associated anomalies. He reported that anomalies occurred twice as frequently in associa-