

Use of a continuously recording intravascular oxygen electrode in the newborn

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Goddard, P., Keith, I., Marcovitch, H., Robertson, N. R. C., Rolfe, P., and Scopes, J. W. (1974). *Archives of Disease in Childhood*, **49**, 853. **Use of a continuously recording intravascular oxygen electrode in the newborn.** The use of a continuously recording intravascular PO_2 electrode is described. The electrode, based on the Galvanic principle, is built into the tip of a French gauge (FG) 5 umbilical arterial catheter. Its use has considerably improved the management of oxygen therapy in the seriously ill premature newborn infant and has done so with at least a 50% reduction in the amount of blood needed to be removed for gas analysis.

Frequent measurement of arterial oxygen tensions is an essential part of the management of oxygen therapy in low birthweight infants with pulmonary disease, thus avoiding the danger of hypoxia and oxygen toxicity (Robertson *et al.*, 1968; Scopes, 1971; Davies *et al.*, 1972; Banerjee, Girling, and Wigglesworth, 1972). Orthodox monitoring of such babies is to sample umbilical arterial blood from an indwelling catheter at least 4-hourly. The PaO_2 needs to be checked more frequently whenever therapy is changed, and in particular when some form of continuous distending pressure (Gregory *et al.*, 1971; Chernick and Vidyasagar, 1972; Dunn, Speidel, and Storrs, 1973; Fanaroff *et al.*, 1973) is applied to the lungs or positive pressure ventilation is instituted. Though samples of only 200–300 μl are needed, the total blood loss in the course of a few days' illness is considerable.

Veasey *et al.* (1971) described computerized on-line real-time analysis (CABAS), which in the first infant studied resulted in a 3.8 kg baby having 349 arterial samples taken during a 12-day period at a mean interval of 49 minutes. This system has the disadvantages of necessitating frequent restorative blood transfusions and of being extremely costly.

The ideal solution is to have an indwelling arterial PO_2 sensor which is inexpensive and will minimize blood sampling. We have published preliminary data on such a system using a Galvanic electrode (Parker *et al.*, 1971; Goddard *et al.*, 1972), and an indwelling polarographic oxygen electrode has recently been described for use in the newborn (Harris and Nugent, 1973). In the latter system the standard error of PaO_2 from the predicted value was 18.8 torr and problems of drift and nonlinearity at high PaO_2 ranges were noted.

Experience of using our system in newborn babies with the respiratory distress syndrome has satisfied us of the clinical value of knowing the immediate effect on PaO_2 of various manoeuvres—both therapeutic, such as CPAP, or accidental, such as unplanned changes in the oxygen supply.

Cell construction and operation

The cell is basically that designed and described by Parker *et al.* (1971), but a number of modifications have been made to overcome practical difficulties with the original assembly.

The transducer consists of a Galvanic type cell as described by Hersch (1952a, b) surrounded by a thin gas-permeable membrane, similar to that used by Mancy, Okun, and Reilley (1962) and micro-miniaturized so that it can be assembled in the tip of a 5 FG catheter. An oxygen concentration gradient exists across the gas-permeable membrane and the oxygen is then electrolytically

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reduced at the cell cathode to produce a flow of electrons in an external circuit. The reaction of the cell is such that the oxygen tension at the silver surface is maintained at zero and therefore in the presence of different oxygen tensions corresponding currents will be generated by the cell achieving this zero tension. Thus, this current is proportional to the oxygen tension outside the membrane. Lead hydroxide is deposited on the anode as the reduction process proceeds, and it is this formation which eventually brings the cell action to an end.

The form of the transducer employed for this study is shown in Fig. 1. A silver cathode is fixed

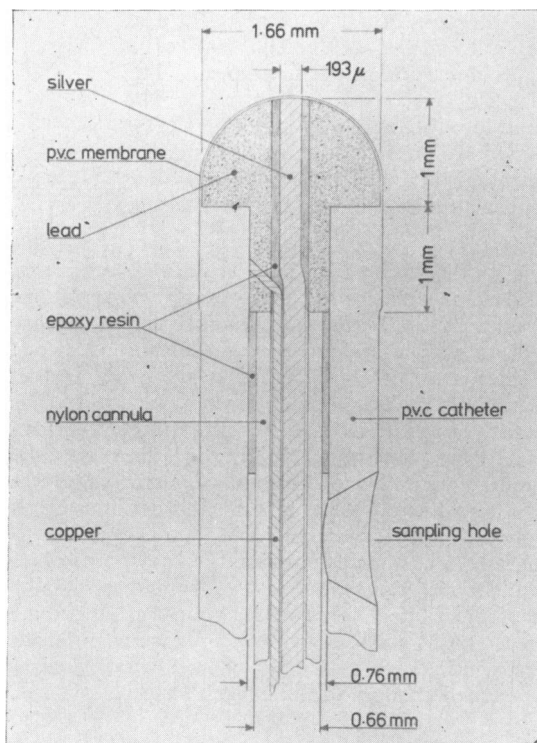


FIG. 1.—Diagram of catheter tip transducer.

coaxially within a domed cylindrical lead anode by means of epoxy resin (Araldite* type AY 105 with HY 972 hardener, Key, Parker, and Davies, 1970) and a copper wire is attached to the lead anode. The silver and copper wires are sheathed within a fine nylon cannula and the whole assembly is then glued to the end of a polyvinyl chloride (PVC) FG5 catheter. This leaves a narrow cylindrical sampling

lumen within the FG5 catheter. The silver and copper wires leave the FG5 catheter near its distal end through a hole in the side wall sealed with epoxy resin and are connected to a miniature electrical plug.

The lead tip is etched with dilute sulphuric acid, washed in distilled water, dried, and then dipped into a saturated solution of potassium chloride. A fine coating of crystals is deposited on the tip as the electrolyte evaporates, but the etching helps to reduce the size of the crystals thus formed. The membrane is formed using a dip-coating method developed by D. Parker (personal communication, 1971). The lead tip and terminal 2 mm of the PVC catheter are lowered into a solution of PVC in cyclohexanone of constant viscosity and temperature and withdrawn at a constant rate in an attempt to produce membranes of constant thickness. The PVC membrane thus formed over the cell is chemically bonded to the supporting catheter, which virtually eliminates any risk of dislodging the membrane. Activation of the cell is achieved by steaming the tip of the transducer for approximately 30 seconds when water vapour diffuses through the membrane and dissolves the potassium chloride. The catheter is packed with its transducer tip immersed in a water jacket, and is gamma sterilized and stored until required. Storing the cell in water allows the cell membrane to absorb as much water as it can and this to some extent stabilizes the subsequent response of the transducers when used in a baby. The cell output current is directly proportional to the partial pressure of oxygen and the transducers produce 0.6–1.8 nA/10 torr O₂ at 37 °C. The output of the transducers varies with the membrane thickness, which we try to keep constant. The transducer output increases 3% for each degree centigrade temperature rise due to the membrane permeability temperature coefficient and this varies for each transducer. No attempt has been made to compensate for it, though investigation is in progress to provide automatic temperature compensation. The output is not affected by change of flow, pressure, or pH in the range found in the neonatal aorta. An increase of 10 torr in P_aO₂ increased the output by 0.9%.

The cell may be considered to be a current generator, having an internal impedance of approximately 40 MΩ, and should therefore be fed into a very low input impedance amplifying system. Electrical safety considerations make it necessary to employ isolated amplifier techniques (Pocock, 1972; Dobbie, 1972). The system developed for use with babies consists of an isolated first stage, feeding a digital display with provision for a pen recorder

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output. A calibration control consisting of a ten-turn dial adjusts the gain of the amplifier, and to simplify setting up the recorder, zero and any arbitrary full-scale reading may be selected with push buttons.

Calibration

Because of the gradual change in sensitivity caused by membrane thickening due to water absorption, and because of the existence of an unpredictable difference in sensitivity in blood and saline, it is essential to calibrate the cell *in vivo*. The transducer is connected to the amplifier before insertion to ensure that it is functioning. Approximately 15 minutes are allowed *in vivo* for stabilization and then a blood sample is drawn through the catheter, the digital display being read at the moment of sampling. The PO_2 of the sample is measured with a standard blood gas analyser. On the basis of this value and the digital display reading, a calibration factor for the cell is determined and this is set directly into the amplifier calibration dial. Subsequent blood samples are taken 4- to 6-hourly and a new calibration factor calculated if necessary.

In vivo experiments

An initial series of experiments was carried out on rabbits anaesthetized with intravenous phenobarbitone 30 mg/kg. The transducer catheter was inserted into one femoral artery such that its tip was located in the abdominal aorta. As earlier transducers had no sampling lumen a catheter was inserted into the opposite femoral artery to allow for continuous monitoring of pulse and blood pressure and for blood sampling. After calibration the animals breathed varying oxygen concentrations via a face mask. Blood samples were taken when the PO_2 readout from the transducer had stabilized. In 3 animals the experiment was terminated after 3 to 6 hours, but a further 3 animals were allowed to recover from the anaesthetic and further readings were taken at intervals during the subsequent 36 hours, after which current output from the transducer began to decline; in one of these there was no necessity for any calibration change throughout the experiment but in the other 2 there was a gradual fall in current output during the first 3 hours of use before stability was achieved.

Fig. 2 shows the cumulated results of these experiments. After the transducer had been calibrated the correlation between PaO_2 values obtained from the withdrawn aortic blood and the reading from the transducers was 0.987 ($P < 0.001$). Blood lead values were measured in 3 animals before

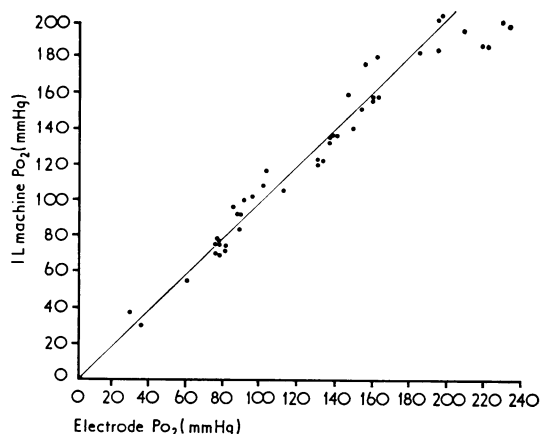


FIG. 2.—Correlation between readout PaO_2 and PaO_2 from a sample of withdrawn blood. 43 readings from 6 rabbits (6–10 readings/animal).

and after insertion of the catheter and no change occurred.

Experience in newborn babies

Transducers have been used in 8 infants: in Case 8 the first catheter did not work and was then replaced by another which did function. Two other babies were catheterized but the procedure was abandoned as blood could never be withdrawn through the sampling lumen. The catheters were inserted into the umbilical artery and positioned with their tip at about the level of the diaphragm. The position was checked radiographically. No more difficulty was experienced than usual with umbilical arterial catheterization, and in fact the slightly increased rigidity of the catheter may have made the procedure somewhat easier.

Methods

The management of the infant was that of routine intensive care. The baby was nursed naked between 36 and 36.5 °C. Blood samples were withdrawn through the catheters 4- to 6-hourly to check the calibration and for blood gas analysis. PaO_2 , pH , and $Paco_2$ were measured on an IL 313 Blood Gas Analyser (Instrumentation Laboratories Inc.). The catheters were constantly perfused with heparinized saline 10 μ m/ml at 0.5 ml/hr with the object of preventing clotting in the sampling lumen. Bicarbonate was given when necessary to maintain pH greater than 7.25. Enough oxygen was given to maintain the babies PaO_2 in the range of 60–80 torr. If more than 60% O_2 was required, constant positive airways pressure (CPAP) was used, given either by endotracheal tube or a head box (Gregory *et al.*, 1971).

TABLE
Clinical details of

Case no.	Weight (g)	Gestational age (wk)	Diagnosis	Outcome
1	2660	40	RDS	Survived
2	1880	33	RDS HDN	Survived
3	1700	32	RDS CPAP IPPV	Survived
4	1040	30	RDS; liver haematoma; subdural haemorrhage; CPAP-IPPV	Died
5	1340	31	RDS CPAP	Survived
6	2170	33	RDS	Survived
7	1150	29	RDS CPAP	Survived
8	1650	29	RDS CPAP	Survived

RDS, respiratory distress syndrome; HDN, haemolytic disease of the newborn; CPAP, continuous positive airways pressure;

Two babies were ventilated because of apnoea. In most cases respirations were recorded simultaneously using either an impedance pneumograph (Air Shields Apnoea Monitor) or a magnetometer (Magnetometer Apnoea Monitor; Rolfe, 1971, 1972). Heart rate was monitored using either Air Shields heart rate meter or a Devices ECG. Blood pressure was recorded in 2 babies via the saline-filled sampling lumen using a Cambridge PT8 transducer which has a low volume displacement allowing comparatively high frequency measurements through small bore catheters. All the data, including PaO_2 , were recorded simultaneously on either a Devices M 19 or M 8 recorder.

Results

The clinical details of the 8 babies in whom the catheters were used are given in the Table. The longest time a catheter worked satisfactorily was for 103 hours. In 5 of the 8 cases the transducer was still working satisfactorily when blockage of the sampling lumen necessitated catheter removal: in Case 1 the catheter was removed while still functioning when the baby had made a rapid recovery from his respiratory distress.

The comparatively long response time of the catheters can be seen, and in the cases where the catheter was tested after removal the response time was even more prolonged. *In vitro* measurements of the 0 to 95% response time were made by subjecting the cells to step changes in PO_2 . This was achieved using a 3-way tap arrangement which

could select pressurized supplies of blood equilibrated at different PO_2 values. Nevertheless, the catheters have proved particularly valuable in certain specific situations.

Effect of CPAP or IPPV. In 5 babies (Cases 3, 4, 5, 7, and 8) it was possible to detect the rapid rise in PaO_2 when CPAP was begun. All these patients had very irregular respirations as shown by the impedance pneumograph before starting CPAP. However, when the PaO_2 began to rise there followed a marked regularization of the respiration rate (Fig. 3). The respiration rate could also increase before the PaO_2 rose (Fig. 4).

Effect of radial artery puncture. In 3 babies (Cases 2, 3, and 6) radial artery punctures were carried out to attempt PaO_2 calibration when the sampling lumen had blocked. On three occasions the PaO_2 fell considerably during the procedure (Fig. 5). On one other occasion the PaO_2 remained steady. 2 babies were receiving oxygen by head box and opening the incubator ports therefore would not lessen the FIO_2 .

Oxygen leak. In one infant (Case 3) a leak developed in the oxygen supply system and the first indication of this was a rapidly falling value on the transducer digital readout. This led to a prompt identification of the leak.

8 catheterized infants

Age catheter inserted (hr)	Duration catheter <i>in situ</i> (hr)	Duration sampling possible (hr)	Response time		Comment on electrode
			Before (sec)	After (sec)	
11	13	13	12		Working satisfactorily when removed
4	29	26	15		Working satisfactorily when removed; blocked
5	18	16	20		Decreasing output at time of removal; blocked
1	27	27			Membrane failure
1	108	103	15	45	Working satisfactorily when removed; blocked
2½	19	7	27	40	Working satisfactorily when removed; blocked
1	24	24	28	43	Electronic failure distal to catheter; (anode connexion broken at catheter/connector junction)
6	26	22½	16	30	Working satisfactorily when removed; blocked

IPPV, intermittent positive pressure ventilator.

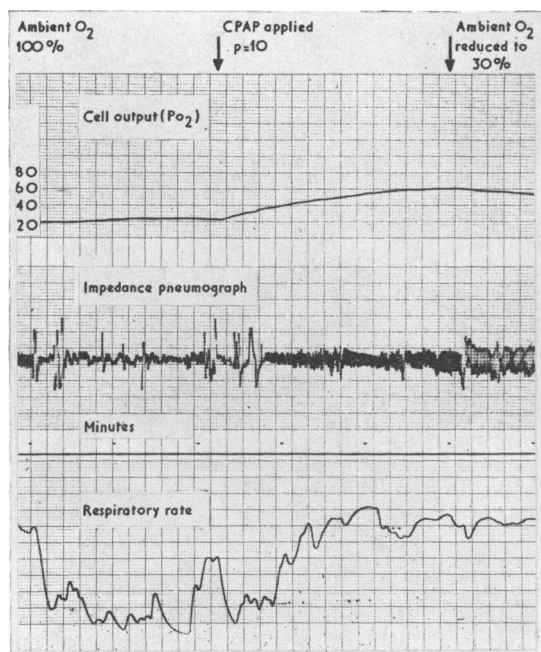


FIG. 3.—Effect of starting distending pressure: improvement in PaO_2 before improvement in respiratory pattern.

Blood pressure monitoring. Using the small displacement transducer it was possible in 2 babies (Cases 5 and 7) to monitor aortic blood pressure through the sampling lumen of the catheter.

Bicarbonate therapy. The effect of infusion was observed in 4 babies (Cases 2, 3, 4, and 8). No significant change in PaO_2 took place.

Exchange transfusion. In 2 infants (Cases 2 and 5) exchange transfusion was carried out through an indwelling umbilical venous catheter. In Case 5 this was carried out to raise haematocrit. With the electrode catheter *in situ*, it was possible in these babies to monitor the PaO_2 during the procedure. No changes occurred in Case 5. In Case 2, however, who was exchanged for rhesus incompatibility, it was noted that the PaO_2 fell 5 to 10 torr with each injection of blood. This might have represented the effect of cold blood on the temperature-sensitive transducer tip rather than a true fall in PaO_2 , since the donor blood was not warmed; however, the temperature at which it was being injected was not known, nor can we estimate the dilution of the bolus injected on the ongoing cardiac output.

Discussion

The use of continuous recording PaO_2 catheters was undoubtedly of great help in the clinical intensive care of these 8 babies. They gave early

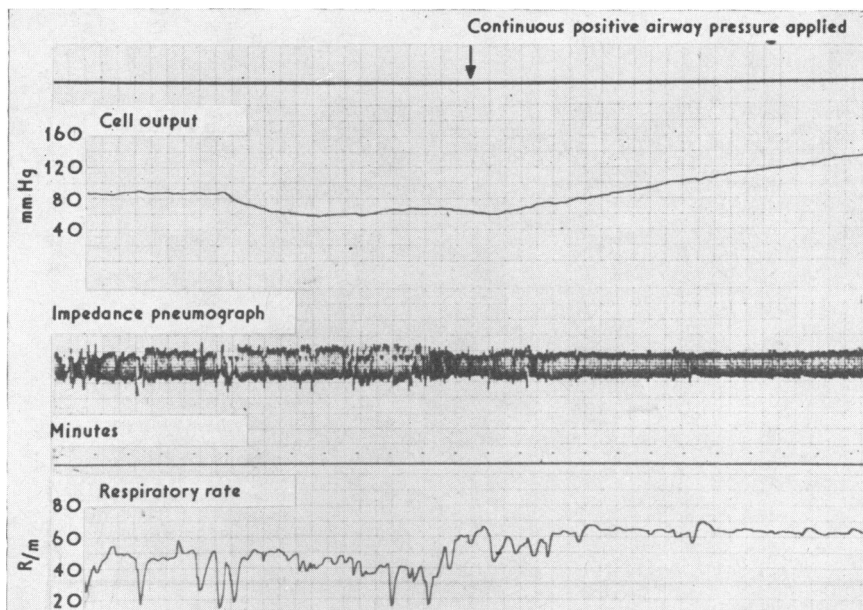


FIG. 4.—Effect of starting distending pressure: improvement on respiratory pattern before rise in PaO_2 .

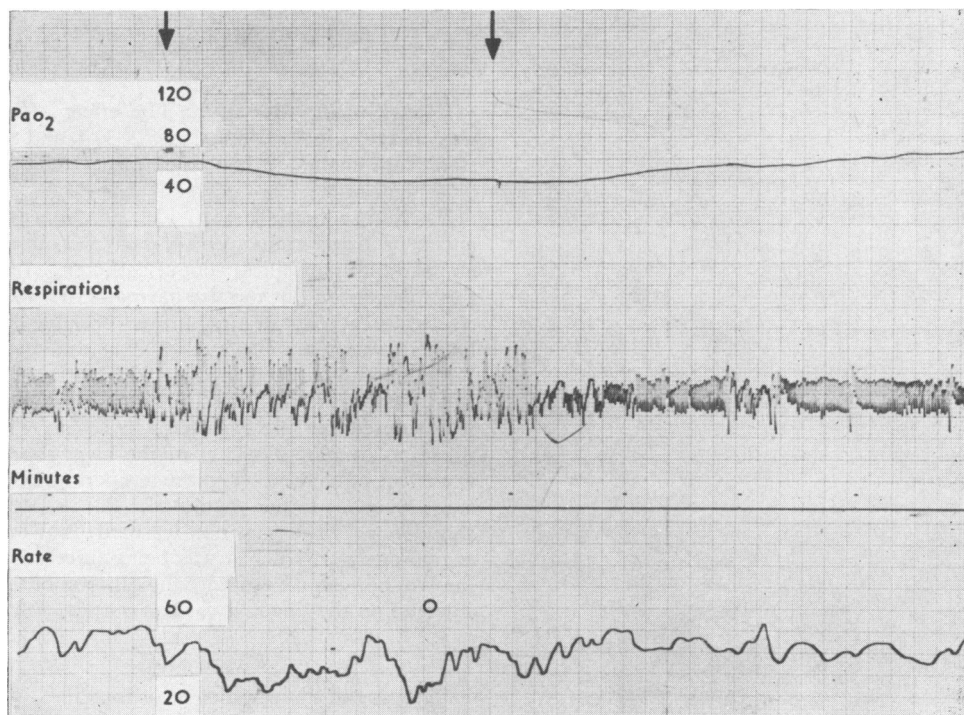


FIG. 5.—Fall in PaO_2 and irregularity of respirations during attempted radial artery stab.

warning of clinical deterioration and provided a continuous guide to the infant's condition at rest and during procedures such as exchange transfusion. They were particularly useful during adjustments in oxygen therapy, when the changes in the transducer readout showed whether the treatment was having the desired effect. We estimated that this led to at least a halving of the number of blood samples withdrawn for conventional blood gas analyses during the acute phase of the illness.

Since the output from the cells varies during the time they are *in situ*, the PaO_2 calibration needs to be checked 4-hourly. In 57 simultaneous blood gas analyses and catheter readouts the difference in PaO_2 was more than 25% on 8 occasions; in 6 this occurred in Case 5, where the transducer was persistently difficult to calibrate. However, in the other cases, particularly during the period when the cell output was stable after the initial calibration, the readout and the PaO_2 of the withdrawn sample was within the limits of error of blood gas analysis systems. We do not feel that the fall in output once the catheter has been *in situ* some time is dangerous since no changes in O_2 therapy based on falling PaO_2 readout are made by the nursing staff without prior consultation with the resident medical staff.

Blood has to be withdrawn for acid-base investigations and biochemical investigations in addition to the periodic calibration check. Thus, a sampling facility is essential and is one of the major problems still to be solved in the design of the transducers. Despite continuous infusions of heparinized saline using a constant infusion pump, 5 out of the 8 babies had to have their catheters removed because the sampling lumen was blocked when the transducer was still working. Attempts to check the PaO_2 by peripheral arterial puncture were not satisfactory since the PaO_2 fell when the baby was handled and a steady state could not be obtained (Fig. 5). These data cast overall doubt on the validity of peripheral arterial punctures for blood gas analysis in any situation in the sick newborn baby. It is certainly well recognized that sick neonates may become cyanosed on handling, though the mechanism of this is not understood.

The catheters we used had response times of 12 to 18 seconds before insertion and 30 to 45 seconds after removal. This increase is due to the hygroscopic properties of the PVC which swells while in contact with plasma water. This not only increased the thickness of the membrane, but also widened the electrolyte layer between the membrane and cathode, further prolonging the response time. Though the lengthy response time does not limit the clinical use of these transducers, it does limit their

research application. Therefore PVC is not the best material for the membrane and we are hoping to use polyethylene in the future, which will give a much faster response time, though the secure attachment of such membranes presents practical problems.

Like Harris and Nugent (1973), we feel that this system is at present suitable only for special care baby units where staffing and facilities are sufficient to allow personnel to become proficient in the use of these transducers. However, their development must provide more satisfactory monitoring of oxygen therapy than is at present available.

We thank Professor J. P. M. Tizard for his help in preparing this paper; the Sir William Coxen Fund for providing facilities; the Department of Medical Physics, Royal Postgraduate Medical School, Hammersmith Hospital, for provision of facilities for developing the transducer; and Misses M. E. Castle and P. Townshend and the nursing staff of the premature baby units in Hammersmith and Oxford for looking after the babies.

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Corrigendum

On page 473 of the June issue in 'Matched development of a pair of monozygous twins of grossly different size at birth' by J. M. H. Buckler and A. Robinson, *Archives*, 1974, **49**, 472, under 'Initial progress', the second paragraph should read:

'Over the course of the first year, the smaller twin caught up her larger sister rapidly. At 14 weeks the weights of twins A and B were 5.78 and 4.54 kg, and at 11½ months 7.94 and 7.63 kg, respectively.'