THE SURGERY OF PREMATURE INFANTS*

BY

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The spectacular advances in neonatal surgery during the last 20 years have solved many problems which in the past seemed unsurmountable. The advances have, however, raised many problems, amongst which perhaps the most important are those associated with the surgery of premature infants. This paper is presented in the hope of throwing some light upon the many difficulties which beset the surgeon operating upon these tiny infants. It is not suggested that we have solved these problems; we have not. Our operative mortality is very high indeed. We hope, however, that this description of our material and our difficulties will stimulate others to improve the present-day methods so that in the future the surgery of premature infants will be as safe as the surgery of full-term infants is today.

At the present time an operation for a single congenital malformation demanding urgent treatment in a full-term infant is relatively safe. It is true that when studying the reports of large series operated upon in various Anglo-Saxon and European centres we find that the operative mortality for newborn infants is not inconsiderable; this is due to two main reasons, prematurity and multiple malformations. We believe that the operative mortality for infants suffering from multiple severe malformations will remain very high. Moreover, even if these infants survive, they do not usually grow up to become healthy children, but are frequently more or less crippled for life. Prematurity is quite different. If the premature infant survives operation he is likely to develop as well or nearly as well as a full-term child operated upon for the same condition. It is today well known that even grossly premature infants may develop into psychologically and physically normal adults. Hess (1953), who followed up premature infants over several decades, found that 370 infants with birth weights of under 1,250 g. (2 lb. 11 oz.) who were discharged from his unit could be traced. Only 5% of them had died. Of the others, 85% were of average or above average physical development and 90% were of average or

above average mental development. There is therefore little doubt that it is worth while to undertake operations in order to save the lives of premature infants.

Incidence

Is the question of prematurity in neonatal surgery of practical importance? How often is it encountered? The literature seems to indicate that operations on premature infants are rare. Surgeons record one or two cases as curiosities and only one extensive series of operations on premature infants has been published. This is the remarkable series reported from the Boston Children's Hospital. In this world centre of paediatric surgery, 159 premature infants were operated upon over a period of 16 years, i.e., an average of about 10 premature infants every year. If these figures represent the true incidence of prematurity in neonatal surgery, then the problem is not worth much consideration.

We were therefore surprised to find an extraordinarily high incidence of prematurity amongst the infants operated upon in our neonatal surgical unit at Alder Hey Children's Hospital (Table 1).

TABLE 1
NUMBER OF NEWBORN INFANTS OPERATED DURING
THE LAST FOUR YEARS

	Number of Cases	Deaths	% Mortality
Total	405	101	24.7
Premature infants	122 (42.3% of all cases)	52	42.3
Full-term infants	283	49	17.3

During the last four years we have operated upon 405 infants with 101 deaths, a mortality of 24.7%. One hundred and twenty-two (30%) of these infants were premature. If these are excluded the operative mortality falls to 17.3%. On the other hand, there were 52 deaths amongst the 122 premature infants, an operative mortality of 42.3%, and infants suffering from pyloric stenosis were included in this figure.

The high proportion of premature infants in our cases is easily explained. Practically all infants born

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TABLE 2

OPERATIVE MORTALITY RATE ACCORDING TO WEIGHT COMPARED WITH FIGURES FOR MORTALITY IN PREMATURE INFANTS IN BIRMINGHAM

Weight (g.)	No. of Cases	No. of Deaths	%Mortality	%Mortality (Birmingham)
1,000 and under (2 lb. 3 oz. and under)	2	2	100	95.1
1,001 to 1,500 (2 lb. 4 oz. to 3 lb. 4 oz.)	13	7	53.8	61.5
1,501 to 2,000 (3 lb. 5 oz. to 4 lb. 6 oz.)	38	25	65.7	19.3
Total under 2,000 g.	53	34	64.1	
2,001 to 2,500 (4 lb. 7 oz. to 5 lb. 8 oz.)	69	18	26.1	5.2

with urgent surgical abnormalities in the Liverpool region are transferred to our unit. Supervision of newborn infants by paediatricians, and their diagnosis and transfer is now so well organized that every infant, however small, ill or deformed, finds its way to the centre. If, as it is hoped, more neonatal surgical centres are founded in the various regions of this country, it will soon become apparent that prematurity is a much greater problem amongst surgical cases in newborn babies than was previously supposed.

Classification According to Weight of Infant

According to the classification of the international committee meeting at Geneva in 1937, a premature baby is defined as an infant weighing 2,500g. ($5\frac{1}{2}$ lb.) or less at birth and we have used the same criterion. If we divide our small series according to the infant's weight and compare them with 'normal' premature infants who have not been operated upon, we obtain the figures given in Table 2. For comparison we have used the figures given for the City of Birmingham by Crosse (1952). It will be seen that except in the 1,000 to 1,500 g. group, where because of our small numbers we obtain a freak result with an inordinately low mortality, the surgical mortality is considerably higher than that of the normal control. It will be further seen that there is a very definite division of the premature infants surgically treated into two groups. Those above 2,000 g. (4 lb. 7 oz.) have an operative mortality of 26%, *i.e.*, nearly the same as our full-term infants. Of the 53 infants of less than 2,000 g. in weight, 34 died, a mortality of 64%. This statistical survey confirms our clinical experience that the larger premature infants do very well indeed; it is the small ones below $4\frac{1}{2}$ lb. in weight which need so much care and supervision. Below 3 lb. in weight the chances of recovery after operation become very small indeed, which is not surprising when it is remembered that about 80% of normal infants in this weight group will die. All the same we had some spectacular recoveries in this group which show that one should never despair when operating upon newborn infants.

Twenty-two infants in this series had multiple severe malformations and only four of these infants survived operation. Multiple malformations in combination with prematurity appears therefore to be very dangerous indeed.

Classification According to Surgical Conditions

The various conditions can be seen in Table 3. A few points merit discussion. Oesophageal atresia (22 premature infants) holds pride of place. When discussing this condition, the effect of prematurity on surgical results becomes apparent. The overall mortality in the 49 cases of oesophageal atresia

TABLE 3
PREMATURE INFANTS CLASSIFIED ACCORDING TO PATHOLOGY

Condition	Numbers	Deaths	% Mortality
Oesophageal atresia	22 (5)	13	59
Pyloric stenosis	20	2	10
Duodenal atresia	12 (3)	5	41.7
Anal atresia	12 (3)	5	42
Malrotation of midgut	9	2	22.2
Exomphalos	9 (5)	7	77.7
Peritonitis	9 (3)	5	55.5
Meconium ileus	7	7	100
Intrathoracic malformations	4 (2)	2	50
Genito-urinary malformations	4	2	50
C.N.S. malformations	4	—	—
Irreducible hernia	3	—	—
Intestinal atresia	3 (1)	2	66.6
Other conditions	4	—	—

Number in brackets = cases with multiple malformations.

which were operated upon during the last four years was 48%, which incidentally is similar to the operative mortality of between 48 and 53% in the half-dozen large series published during the last three years. For full-term infants without associated severe malformations our operative mortality is 23%, but in premature infants it rises to 59%.

The large number of infants with pyloric stenosis is surprising. Only grossly premature infants suffering from this condition are admitted to our unit. Meconium ileus and prematurity seems to be a specially fatal combination; all our seven cases and all Gross's (1953) six cases died. I have been able to find only the record of one premature infant who

survived operation for meconium ileus in the literature (Borenstine and Printz, 1953).

Causes of Death

Necropsy was performed on 51 of the 52 premature infants who died. The main necropsy findings are shown in Table 4. Chest conditions are

TABLE 4
CAUSES OF DEATH

Condition	No
Chest conditions (bronchopneumonia, atelectasis, hypotrophic lungs)	14
Haemorrhagic diathesis	9
Cardiac failure (congenital malformation of heart)	7
Massive venous thrombosis (inferior vena cava, renal veins)	2
Genito-urinary complications (pyelonephritis, absent kidneys)	2
Anastomotic leaks (peritonitis, mediastinitis)	10
Septicaemia (secondary to umbilical sepsis, phlebitis, meningitis)	5
Kernikterus	1
Aspiration pneumonia	1
Total 51 necropsies	

most common (mainly bronchopneumonia and atelectasis, but some cases with absent or hypoplastic lungs). All seven cases of meconium ileus died of bronchopneumonia. There was one death from aspiration pneumonia, which is shown separately, as it is a preventable cause of death. There were 10 anastomotic leaks causing mediastinitis, empyema, or peritonitis according to the site of the anastomosis. This big number reflects on the poor healing quality of the premature infant's tissues especially in the presence of infection. Five further deaths were due to septicaemia, two were secondary to sepsis at the site of intravenous transfusion, one almost certainly secondary to umbilical sepsis, and in the remaining two the cause of the septicaemia was undetermined. Nine children died from haemorrhage, usually widespread. Bleeding into the lungs, retroperitoneal tissues, peritoneum, intracranial cavity, etc., was common, and any combination of bleeding sites was seen. The cause of this bleeding tendency was somewhat obscure. All our infants receive vitamin K pre-operatively; the bleeding and clotting times in all infants were normal. In some there was an absence of platelets; in some no chemical or microscopical abnormality of the blood could be discovered and an immaturity of the capillaries was postulated. Two infants had another intravascular complication, massive venous thrombosis. In one the whole of the inferior vena cava and portal vein thrombosed post-operatively, in the other there was bilateral thrombosis of the renal veins. In seven children death was associated with severe congenital malformations of the heart.

One very premature infant operated for malrotation of the midgut and volvulus died of kernikterus. Kernikterus of prematurity develops when the serum bilirubin level rises above 18 mg. (Meyer, 1956); the cause is often excessive vitamin K administration. At the time of this death we still used vitamin K in dosages of 10 mg. We have since reduced the dosage to 2.5 mg.

The Management of Premature Infants Requiring Surgery

There are several important aspects in the management of premature infants requiring surgery which have to be discussed in some detail.

Anaesthesia. This is not the place to discuss neonatal anaesthesia in detail, but only to point out the differences between premature infants and full-term infants in their reactions to anaesthesia. The liability of the premature infant to pulmonary complications has already been mentioned. It is partly due to the fact that the premature infant's respiratory system is rudimentary both in the histological development of the lung and its mode of ventilation, partly because the cough reflex in premature infants is either deficient or absent. Aspiration of vomitus or mucus is therefore even more common in premature infants undergoing surgery than in full-term babies. In order to minimize the complications, all infants should be nursed in incubators in an atmosphere of 100% humidity, which in our experience is the most important single factor in preventing pulmonary complications. The constant temperature in such incubators allows these infants to be nursed naked so that no clothing or blankets hinder respiratory movements. For the same reason the only type of dressing which we use is a $\frac{1}{2}$ in. broad plastic strip. The infant should be nursed lying on his side, the head slightly elevated, to allow for the maximum freedom of diaphragmatic movement. The position should be changed from side to side every two hours, in order to reduce the chances of massive pulmonary collapse. In cases operated upon for intestinal obstruction constant gastric suction should be prolonged, until all risk of vomiting due to ileus has disappeared. Even in the uncomplicated cases we rarely discontinue suction earlier than the third post-operative day, and often employ it for considerably longer periods. In premature infants operated upon for oesophageal atresia a gastrostomy is always necessary. No feeds are given via the gastrostomy for at least three days after operation in order to minimize regurgitation from the stomach when feeding is started. Feeds are very slowly dripped into the gastrostomy tube and the level of the reservoir is

FIG. 1.—This emergency trolley is standing in the neonatal ward ready for use in any emergency. On the top shelf are laryngoscope, endotracheal tubes, Ree's modification of the Ayr's T piece and rubber bag, various rubber catheters, syringes and drugs. On the bottom shelf stands a powerful electric sucker.

never raised higher than 10 cm. above the infants' abdomen. The baby is not fed orally until it has been shown by 'lipiodol' swallow that there is no hold-up or stricture at the site of the anastomosis.

In spite of these precautions aspiration of mucus or vomitus is all too common. An emergency trolley with endotracheal tubes, laryngoscopes, a powerful electric sucker and rubber catheters thin enough to pass through the endotracheal tubes must therefore always be at hand (Fig. 1) and an anaesthetist skilled in passing these tubes must be constantly on call.

In infants under $3\frac{1}{2}$ lb. in weight pulmonary collapse is very common, because their swallowing and cough reflexes are very rudimentary. Luckily even massive pulmonary collapse can usually be rapidly cured by positioning. Sucking out of the bronchi through an endotracheal tube is only very occasionally necessary and bronchoscopy is only rarely resorted to. This infant, weighing 3 lb. 6 oz., whose radiographs are shown in Figs. 2 and 3 was successfully operated upon for oesophageal atresia but he invariably collapsed the lung on the side on which he lay. He was then nursed for a few hours on the opposite side, which re-expanded the lung lying uppermost, but then the other lung collapsed. This went on for

nearly three weeks after operation in spite of the fact that he was entirely fed through the gastrostomy.

The passing of an endotracheal tube does not appear to present any difficulties to the skilled paediatric anaesthetist (even the smallest infant will take an 00 endotracheal tube), neither have there been any complications from this procedure despite the numerous statements to the contrary. There is no great difference in the reaction to anaesthesia between the premature and the full-term infant.

Premature infants appear to exhibit the peculiar response of newborn babies to muscle relaxant drugs of the anti-depolarizing type. Frequently they show a myoneural block of the anti-depolarizing type after long administration of drugs of the depolarizing type, such as succinylcholine (Rees and Stead, 1957).

During the first few post-operative days all these premature infants need nursing in an oxygen-enriched atmosphere. Our incubators leak in so many places that the maximum oxygen concentration which is possible is in the neighbourhood of 50%. We have seen no cases of retrolental fibroplasia. This we believe to be due to the fact that it is the concentration of oxygen in the blood that matters. Practically all these premature infants have considerable respiratory difficulties during the post-operative period, and, even in an atmosphere with a high oxygen concentration, oxygenation of blood is imperfect.

Prevention and Treatment of Infections. The most important single factor in the prevention of infection is nursing in a special unit, isolated from all other infants and children. The usual isolation precautions are of course essential. Nursing in incuba-

FIG. 2.—Infant of 3 lb. 6 oz. in weight with oesophageal atresia 12 hours after operation. The whole of the right lung is collapsed.

tors further reduces the chances of airborne infections.

All infants receive penicillin and streptomycin before operation and for five days after operation. Although there might be objections to this on the grounds that it may produce the growth of resistant organisms, in practice this method has proved its value. In infants with infective conditions, the organism is cultured, tested for antibiotic sensitivity, and the appropriate antibiotic is given. In cases with fulminating peritonitis when the organism is unknown intravenous terramycin has occasionally been very useful.

Transport. The transport of the larger premature infants, even over long distances (we receive infants from as far away as 100 miles and more) presents no special difficulties. They should be transported in a carry-cot adequately supplied with blankets and hot

water bottles. The accompanying nurse must be able to suck out the pharynx and clear the air passages at a moment's notice. The infant should be transported lying flat on his side. A vomiting or distended infant must have a rubber catheter passed into the stomach and the nurse must aspirate the stomach at 10-minute intervals.

Infants under 4 lb. in weight are best transported in a portable incubator at a temperature of 85° F., an atmosphere of 100% humidity and an oxygen concentration of 50%. We have a home-made incubator, which we send out when the condition demands it (Fig. 4).

Control of the Body Temperature: Sclerema. It has been known for a long time that because of their relatively large body surface and immature temperature regulating centres premature infants need to be

FIG. 3.—The same infant as in Fig. 2 three hours after the first radiograph was taken. The right lung has re-expanded. There is now collapse of the left lung. In the period intervening between the two radiographs the infant was lying on his left side.

FIG. 4.

FIG. 4.—This portable incubator is heated by a hot water tank beneath the mattress. Infants are transported in a high oxygen concentration and an atmosphere of 100% humidity. There is a large sliding door and an attachment facilitating gastric suction.

FIG. 5.—Premature infant nursed in a surgical incubator. The incubator has a double hinged lid, allowing for the small side doors to be opened without a marked fall in the temperature, humidity and oxygen concentration. Transfusion stands are incorporated in the design. The baby is nursed on a radio-translucent tray. The drawer underneath facilitates the introduction of x-ray plates.

FIG. 5.

kept at a high environmental temperature. Full-term infants can be operated upon without any special protection against heat loss; the body temperature often drops to 90° F. or below without any ill effects. Premature infants, however, stand a fall of body temperature very badly; they should therefore be nursed in incubators at a temperature of 90° to 95° F. The special surgical incubators we use are so designed that the infant can be continuously nursed inside them (Fig. 5). Large side flaps allow handling and feeding of the baby without an appreciable lowering of the temperature. The infant lies on a plastic tray, which can be tilted from the outside and which is radio-translucent, so that radiographs can be taken while the child is in the incubator. The incubator has its own oxygen supply and an attached drip stand, which allows the infant to be transported in the incubator from the ward to the operation table.

At operation these infants are placed on an electric, thermostatically controlled blanket and wrapped as far as possible in gamgee wool. They are returned to the incubator immediately after operation.

There is one post-operative complication, which

we have as yet not discussed, although it causes perhaps more deaths of operated premature infants than all the conditions mentioned above; this is sclerema neonatorum. This condition, which is supposed to be a very rare one, is characterized by a hardening of the subcutaneous fat, due, it is presumed, to solidification. Although sclerema was recognized in the eighteenth century (Usenbenz, 1722; Underwood, 1784) the condition is still very incompletely understood. It occurs in infants who are exposed to cold, but is so rare that even single cases are reported in the literature. We have found that in very ill premature infants who undergo severe operations, especially if operation is coupled with post-operative infection, some degree of sclerema is invariable. If sclerema were due to exposure of the infant to low temperatures, one would suppose that it would be noticed immediately after operation, as this is the only time the infant is outside the incubator. This is not so; the condition usually develops during the second, third, or fourth post-operative day. If severe, the infant will succumb within 24 to 48 hours of pneumonia secondary to respiratory difficulties. Nearly half of our premature infants who died had some degree of sclerema, but this is not recognized at necropsy, because of the stiffness of rigor mortis. Sclerema, therefore, does not figure as a cause of death at necropsy.

We have found that the treatment of sclerema is very difficult. The accepted method of treatment

consists in the administration of cortisone in doses of 10 to 25 mg. t.d.s. (Wickes, 1956). We have used this method for over three years, but we found that in premature infants who have undergone an operation it is most unsatisfactory. In these infants cortisone inhibits healing and

anastomotic leaks readily occur. After laparotomy a ruptured abdomen, which in our experience is the greatest rarity in neonatal surgery, is not at all uncommon (Fig. 6). Because of these unfortunate side-effects, we stopped giving cortisone and have tried giving D.O.C.A. instead on the somewhat hypothetical basis that mineralocorticoids and glucocorticoids might have antagonistic actions on the intercellular ground substance (Foster, 1957). However, although D.O.C.A. does not inhibit healing, it is ineffective in curing or preventing sclerema. We have, therefore, returned to the administration of cortisone in doses of 5 mg. b.d., whenever there is clinical evidence of sclerema. In addition we raise the incubator temperature to between 98 and 100° F. and attempt to administer a maximum of glucose either orally or intravenously. The cortisone is immediately discontinued when the sclerema begins to subside. This treatment has on the whole been quite successful and gross sclerema has only rarely developed since this regime has been employed.

Fluid and Electrolyte, Plasma, and Blood Therapy. This is not the place to go into detailed consideration of fluid and electrolyte therapy (Rickham, 1957). Kidney function in premature infants is poor. If there is no gross dehydration and no post-operative fluid loss, as for instance, in oesophageal atresia, the premature infant does not usually require any fluids for two to three days after operation. After abdominal operations necessitating continuous post-operative gastric suction, 5 ml. of fluid per hour is the maximum intravenous requirement. In order to administer accurately such small quantities, it is important to incorporate a burette measuring up to 1 ml. in the intravenous set (Fig. 7).

It is extremely easy to over-infuse a premature

FIG. 6.—Infant weighing 3 lb. 8 oz. at birth who was operated on for intestinal atresia. Post-operatively she was put on cortisone and the abdomen ruptured and was resutured. At 7 months of age she has a large incisional hernia.

FIG. 7.—Measuring burette holding 30 ml. and graduated in millilitres incorporated into an intravenous giving set.

infant and so to produce fatal pulmonary complications.

The sodium and chloride requirements of the premature infant are also small. If there has not been any vomiting nothing but 5% glucose water should be infused for dehydration. With continuous gastric suction N/5 normal saline and 5% glucose is the infusion of choice.

Premature infants need hardly any potassium replacement as there is no post-operative potassium shift. When continuous suction is employed for more than three days, some potassium should be replaced. This is conveniently done by giving small (30 to 40 ml.) daily infusions of Darrow's solution.

The serum protein level of premature infants is always low and falls rapidly during starvation. While the infant is on intravenous therapy it is best to replace proteins by infusing small daily amounts of half-strength plasma. This is important, as a low plasma protein concentration may easily produce generalized oedema, or aggravate the oedema often present in newborn premature infants.

The haemoglobin concentration of premature infants at birth is usually very high. Nevertheless any blood loss at operation should be meticulously replaced and even slight over-transfusion at operation does not do any harm. During the first few weeks of life the haemoglobin level drops sharply and anaemia is common (Arthurton, O'Brien and Mann, 1954). Iron preparations must be administered and occasional small blood transfusions are very valuable.

The sooner the infant can come off intravenous therapy and alimentary fluids can be taken the better. Starting with 1 dram of glucose water, given

every two hours, the amount is gradually increased. When the amount has reached 4 drams two hourly, half strength breast milk should be given. When the feed reaches 6 drams two hourly, full-strength breast milk is substituted. The bigger infants take feeds readily from a pipette, the smaller may occasionally need feeding by gavage. In cases operated upon for intestinal obstruction a tube should be passed into the stomach before each feed and the stomach aspirated for the first 48 hours after feeding has started. If more than 10 ml. are aspirated the oral feeds must be decreased or stopped. After 48 hours the tube needs only to be passed four hourly, after 72 hours, six hourly, and suction can usually be discontinued after the fourth day. This method might seem unduly elaborate, but it ensures that there is little chance of vomiting and obviates the danger of aspiration. In general we do not start feeding by bottle before the child weighs 4½ lb. and bottle feeding is then only gradually introduced.

Once the infant is on full feeds it must be remembered that the premature infant needs 3 oz. of milk per pound of body weight, and that the infant who has undergone a severe operation and subsequent weight loss may need even more. We have occasionally given 3½ or 4 oz. of milk per pound of body weight before the child started to gain weight.

Surgical Technique. This does not differ in any respect from that employed in operating upon full-term infants. It goes without saying that without a really good operating light, small instruments and the finest needles and sutures it is futile to attempt operations. In very small infants anastomosis may be a strain on the eyes and there may be a place for

FIG. 8.—The smallest infant to survive operation, a premature infant weighing 2 lb. 8 oz. operated upon for pyloric stenosis.

FIG. 9.—Same infant as in Fig. 8 when 13 months old.

FIG. 10.—Smallest infant with oesophageal atresia to survive (birth weight 2 lb. 15 oz.).

FIG. 11.—Same child as in Fig. 10 when 20 months old.

FIG. 12.—The smallest child with intestinal atresia to survive operation (birth weight 3 lb. 4 oz.).

FIG. 13.—Same child as in Fig. 12 when 9 months old.

operating magnifying spectacles such as are used by many American paediatric surgeons.

Discharge and Follow-up. The infants are discharged when their condition is satisfactory and when they weigh at least 5 lb. It is advisable to admit the mother two or three days before the infant's discharge in order to accustom her to looking after the baby. The infant should be established on one of the dried milk preparations before discharge. After discharge the supervision of these infants has been made much easier by making use of the premature infant district nursing service which has been established in Liverpool. The infants are followed up in the Out-patient Department. On the whole their subsequent progress has been most satisfactory (Figs. 8, 9, 10, 11, 12, 13).

It is perhaps one of the most gratifying experiences in surgical practice to watch such a premature infant developing through the months and years. Most of them do very well indeed. The surgery of premature infants is full of disappointments and an inordinate amount of labour has to be expended in order to achieve occasional successes but the few successes make it all very much worth while.

This paper is based on the work of a large team. Space does not allow me to mention all those who have

helped. About half the cases included in this paper were operated upon by Miss Isabella Forshall. I wish to thank her for her help and advice and for assistance in the preparation of this paper. Dr. G. J. Rees and Dr. A. Stead, consultant paediatric anaesthetists to the Unit, have given invaluable assistance, not only by their skill in the administration of the anaesthetics, but also by their help in pre- and post-operative supervision. Dr. E. G. Hall and Dr. C. Jones, pathologists to Alder Hey Children's Hospital, have supplied much of the information upon which this paper is based. Mr. J. T. Ireland has been responsible for the biochemical data for control of treatment.

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