

general condition gradually deteriorated and the stools became still looser and more frequent. As B.C.N. was found to be present in them, aureomycin was given. During the first four days there was still some loss of weight, but thereafter rapid improvement ensued with a satisfactory daily gain in weight.

Case 4.—This patient, a twin sister of Case 3, was also admitted for debility. Her development was at first normal, but after two weeks there was a sudden acute onset of gastroenteritis with frequent watery motions, vomiting, and a loss of weight. B.C.N. was isolated on culture and aureomycin therapy was started on the second day. After 24 hours the stools were of half-firm consistency and the loss of weight ceased. From the fourth day of treatment there was a satisfactory daily gain in weight and the stools were firm in consistency.

Case 5.—An 18-day-old baby girl had suffered from vomiting and frequent mucous or watery motions for a week before admission to hospital. At the onset of the illness she was in a home for post-natal care. B.C.N. was found in the faeces on the day of admission. At first streptomycin and penicillin were given as well as fluids by the intravenous route. There was an initial improvement for a few days, but thereafter a marked exacerbation with vomiting and increasingly abnormal motions. Aureomycin therapy was started, and as soon as 48 hours later the stools were half-firm and a satisfactory gain in weight was noted. Improvement continued and the faeces rapidly became normal.

Case 6.—A 2-day-old boy was admitted to hospital for dyspepsia and mucous defaecations. Examination revealed delayed emptying of the stomach, but repeated cultures failed to demonstrate the presence of B.C.N. in the faeces. Penicillin was administered as well as fluids subcutaneously. There was gradual improvement, but after 14 days an acute exacerbation occurred with vomiting and loose stools. Culture then revealed B.C.N. in the faeces, and aureomycin therapy was therefore started. The stools rapidly became normal, but frequent vomiting still occurred and the loss of weight continued. Only after persistent plentiful administration of fluids intravenously did the general condition improve and an increase in weight take place. The protracted course of the illness is presumably to be ascribed to the basic disorder.

Case 7.—A 22-day-old boy had suffered from vomiting and mucous defaecations for one week before admission with an appreciable loss of weight from 3,430 g. to 2,790 g. During the first week of life he was at another hospital for children. On admission he was pale and dehydrated, and there was slight peripheral cyanosis. Oidium was present in the oral cavity. The abdomen was distended and blood oozed from the umbilicus. There was violent watery diarrhoea and vomiting. Fluids were administered intravenously, but he got worse and the loss of weight continued. The presence of B.C.N. was demonstrated already on the day of admission, but aureomycin was not given until the seventh day of illness. After 48 hours the stools became normal and the increase in weight satisfactory. Improvement continued.

Case 8.—A 1-day-old boy was admitted because of prematurity. Apart from the difficulty of keeping his temperature up, there was nothing of note the first week. On the eighth day he became acutely ill with vomiting and watery diarrhoea. The abdomen was distended and his colour was ashen-grey. B.C.N. was present in the stools and aureomycin therapy was started next day. After 24 hours a definite improvement could be noted, and after three days' treatment the stools were normal and the gain in weight satisfactory.

Summary

An investigation at the Sachs Hospital for Children in Stockholm revealed the presence of a special strain of *Bact. coli*—that is, *Bact. coli neapolitanum* (B.C.N.)—in the stools and at times in the respiratory tract of babies suffering from infantile diarrhoea and vomiting. This agrees with the findings of other authors. Eight of the patients were treated with aureomycin. Its effect was marked. Even after a few doses the B.C.N.

present in the stools before the inception of treatment could no longer be found. Only in a few cases did it persist somewhat longer in the respiratory tract. Parallel with this bacteriological effect there was an improvement in the clinical condition.

REFERENCES

- Bray, J. (1945). *J. Path. Bact.*, **57**, 239.
 — and Beavan, T. E. D. (1948). *Ibid.*, **60**, 395.
 Giles, C., and Sangster, G. (1948). *J. Hyg., Camb.*, **46**, 1.
 — and Smith, J. (1949). *Arch. Dis. Childh.*, **24**, 45.
 Holzel, A., Martyn, G., and Apter, L. (1949). *British Medical Journal*, **2**, 454.
 Laurell, G. (1950). In press.
 Rogers, K. B., Koegler, S. J., and Gerrard, J. (1949). *British Medical Journal*, **2**, 1501.
 Taylor, J., Powell, B. W., and Wright, J. (1949). *Ibid.*, **2**, 117.

NITROUS OXIDE ANAESTHESIA WITHOUT HYPOXIA

BY

WILLIAM NEFF, M.D., D.A.
EDWARD C. MAYER, M.D.

AND

RICHARD THOMPSON, M.D.

(From the Department of Surgery (Anaesthesiology), Stanford University School of Medicine, San Francisco, California)

Nitrous oxide possesses many qualities which meet both the clinical and the physical demands for a safe anaesthetic. The ever-present explosion hazard with the inflammable anaesthetics has been increased by the surgical trend towards greater use of the high-frequency electro-surgical unit and has challenged the anaesthesiologist to provide general anaesthesia with non-inflammable and non-explosive agents of low toxicity.

Neff, Mayer, and Perales (1947), in a preliminary report, outlined a method of potentiating the anaesthetic action of nitrous oxide by the intravenous administration of "demerol" (pethidine hydrochloride). Thompson (1950), in an experimental and clinical investigation of two new analgesics closely related to pethidine, during nitrous oxide anaesthesia compared the effects of these drugs with morphine and pethidine. Neff and Thompson (1948) later concluded that these new analgesics were less satisfactory than pethidine for fortifying the anaesthetic action of nitrous oxide. Mushin and Rendell-Baker (1949) confirmed the efficacy of pethidine for the supplementation of nitrous oxide anaesthesia, and Brotman and Cullen (1949) emphasized its usefulness in geriatric anaesthesia.

An extensive study of the problems incident to the use of nitrous oxide and pethidine anaesthesia has been in progress for the past five years. During this period nitrous oxide anaesthesia has been employed for all kinds of intra-abdominal, intrathoracic, and other extensive operations. Experience gained through the administration of nitrous oxide on several thousand occasions since the preliminary report has provided the stimulus to attempt to review and re-evaluate the present status of this gas.

Nitrous Oxide Anaesthesia without Oxygen Restriction

Modern anaesthesia with gases or volatile liquids presupposes a combination of these agents with oxygen. One uses the terms ether anaesthesia, cyclopropane anaesthesia, and chloroform anaesthesia, but in the case of nitrous oxide the more cumbersome and very often less descriptive

expression nitrous oxide and oxygen is more common. Preference is here given to the designation nitrous oxide anaesthesia.

One of the masters, Dr. Wesley Bourne, was so convinced of the value of nitrous oxide without oxygen restriction that he actually induced anaesthesia for dental operations with a mixture containing higher than atmospheric proportions of oxygen. Clinical and laboratory evidence was offered (Raginsky and Bourne, 1934) to support his contention that nitrous oxide with 20% oxygen could produce anaesthesia for operations not requiring great muscular relaxation. The induction of anaesthesia using nitrous oxide with a high complement of oxygen has in recent years received little attention.

Paul Bert (1878) reported on the harmlessness of nitrous oxide for prolonged administration to animals when a mixture of five parts of nitrous oxide to one part of oxygen was given under one and one-fifth atmospheres of pressure. Referring to the degree of anaesthesia obtained, he stated: "In this condition the animal after a couple of minutes of agitation is completely anaesthetized. The corneal reflex disappears; you can pinch a sensitive nerve and do an amputation without any movement of the animal; the muscular relaxation seems extraordinary, and if the regular respiratory movements were not present you could think him dead. It can last one-half hour to one hour without any change. The blood is of normal red colour, rich in oxygen, the heart strong, and the pulsations normal. At the same time excitation of any centripetal nerve will give the same results as on a normal animal. When you take off the bag with the gas after three or four inspirations of the free air the animal gets back the sensitivity, intelligence, independence, and tries to bite rather often. As soon as the ties are off it runs away and seems gay and vivacious."

Henderson, Brown, and Lucas (1927) were unable to duplicate Paul Bert's results with nitrous oxide and oxygen under pressure, and concluded that oxygen lack was a necessary accompaniment of anaesthesia with this gas. Most pharmacologists and many anaesthetists accepted their results as conclusive evidence that, although nitrous oxide did possess some analgesic properties, it was not an anaesthetic unless its administration was accompanied by periods of oxygen restriction.

Faulconer, Pender, and Bickford (1949) demonstrated rather conclusively in man that the depth of anaesthesia produced by nitrous oxide in the presence of excess oxygen is directly proportional to the partial pressure of the anaesthetic gas. They were able to demonstrate the soundness of Paul Bert's reasoning when he projected the results of his animal experiments into clinical application as follows: "The fact that anaesthesia could be obtained only by the inhalation of pure nitrous oxide means that for a sufficient saturation of the organism it should be in a tension equal to one atmosphere. Under normal pressure it means a proportion of the gas of 100%. If we could place the patient in an apparatus where the pressure would be two atmospheres we could obtain the necessary pressure of the gas by using a mixture of 50% nitrous oxide and 50% air; in this way it will be possible to attain sufficient anaesthesia with a normal amount of oxygen in the blood and a normal respiration."

Object of Oxygen Restriction during Nitrous Oxide Anaesthesia

Oxygen restriction during nitrous oxide anaesthesia was directed mainly towards the attainment of relaxation of the skeletal musculature. Nitrous oxide combined with oxygen in atmospheric proportions will usually result in only a

very moderate degree of muscular relaxation in the adequately premedicated patient. Superimposing oxygen lack will result in additional relaxation. Severe hypoxia will cause the muscles to become rigid.

Oxygen lack is often considered to be the only important factor in the response of the patient to nitrous oxide when the oxygen concentration falls below atmospheric proportions. The fact that the replacement of oxygen with nitrous oxide produces slightly more profound anaesthesia is often overlooked. The response of the patient must be attributed to a combination of drug action plus oxygen lack. The reduction of the oxygen concentration by 1 or 2% will not adversely affect the average patient, and yet it might afford the additional depth needed to avoid the administration of other less readily eliminated drugs. In practice it appears best arbitrarily to limit this reduction in oxygen concentration to 2% below its concentration in the atmosphere. The muscles may become somewhat relaxed but never flaccid as a result of so moderate a reduction in oxygen tension. Flaccidity can be accomplished only by expanding the lungs with oxygen immediately after a period of severe hypoxia.

The introduction of curare into anaesthesiology has provided the anaesthetist with an agent by means of which muscular relaxation may be provided during light surgical anaesthesia.

Use of Oxygen in Higher than Atmospheric Proportions

There is no good reason to believe that because 20% oxygen is good for the body economy 30, 40, or 50% is better, unless there is evidence of pre-existing hypoxia. An excess of oxygen will not ensure good ventilation in the patient who is suffering from depressed respiration and a consequent accumulation of carbon dioxide. The higher the oxygen concentration the lower the nitrous oxide and the weaker the anaesthetic, and the greater will be the demand for supplementation with other agents. Oxyhaemographic studies support the clinical observation that it is more rational to increase the proportion of nitrous oxide than arbitrarily to maintain oxygen in excess and therefore be obliged to administer larger doses of hypnotics, narcotics, or muscular relaxants than would otherwise be required for light anaesthesia.

Analgesic Properties of Nitrous Oxide

The subjective nature of analgesia makes its evaluation rather difficult, and yet it is of fundamental importance in the study of an anaesthetic of relatively low potency such as nitrous oxide.

SeEVERS, BENNETT, POHLE, and REINARDY (1937) studied the action of sub-anaesthetic concentrations of nitrous oxide in man. They found the optimum concentration of nitrous oxide for continuous inhalation which would produce a maximum degree of analgesia and yet retain the co-operation of the subject to range between 35 and 40%. BENNETT and SEEVERS (1937) found that there was little difference in the analgesic action of nitrous oxide whether diluted with oxygen or with air. Their results indicated that if there is any difference better analgesia is obtained when oxygen is the diluent. They also showed that the greatest reduction in pain sensitivity occurs within the first five minutes, with the greatest elevation of the threshold in ten minutes.

The demonstrated analgesic property of nitrous oxide offers further proof that oxygen lack does not account for the pain-relieving qualities of the gas, and may even interfere with the production of anaesthesia.

Rapid Induction of Anaesthesia

The rapid induction of anaesthesia with nitrous oxide required oxygen exclusion for its success. This requirement was readily admitted by McKesson, a leading exponent of the method, who did not believe that short periods of even complete oxygen lack were necessarily harmful. When nitrous oxide is administered without oxygen the induction may be smooth, but with the addition of oxygen in atmospheric proportions anaesthesia lightens and the more vigorous patients will enter the stage of delirium. It would appear that oxygen lack so limits the time available that adequate tissue saturation of nitrous oxide is not accomplished by this method despite the higher partial pressure.

Compromise Induction of Anaesthesia

Some anaesthetists, not having sufficient confidence in their ability to induce anaesthesia without oxygen restriction and at the same time being fearful of the rapid induction with pure nitrous oxide, try to effect a compromise. The usual procedure is to administer first a combination of nitrous oxide with 6 or 8% oxygen. One has only to compare the loss of consciousness incident to the inhalation of 100% nitrous oxide with the unpleasant subjective sensations associated with the slow development of oxygen lack to realize why this manner of induction is usually very unsatisfactory. Sensations of shortness of breath, suffocation, or choking are not entirely compatible with mental tranquillity.

The patient struggles, whereupon the oxygen consumption of the body increases fourfold to eightfold. The anaesthetist responds to the struggling of the patient by further reducing the oxygen in the anaesthetic mixture in order to "get him deeper"; the demand for additional oxygen is met by restriction. Finally, the patient loses consciousness, but slight muscular twitchings may be observed around the face, while the larger skeletal muscles begin to stiffen. The addition of oxygen at this point renders the patient less rigid at once, although not well relaxed.

Slow Induction of Anaesthesia

The slow induction of nitrous oxide anaesthesia was advocated by Guedel in 1922. At that time he stated: "Rapid induction of nitrous oxide is a heritage of the past. Anaesthesia as a rule is smoother as induction is slower." Later in the same article, referring to difficulties encountered in the "so-called stimulated types," he went on to say: "Time and oxygen should be the rule for these cases. The time necessary in some extreme cases to consummate a nice induction may be ten or fifteen minutes. If fifteen minutes is not enough time take more. Maintain ample tissue oxygenation while allowing time for the nerve-cell absorption of the nitrous oxide, and it is probable that any patient will be quietly anaesthetized and will like the sensation."

In the presence of adequate oxygen the time of induction is not limited, and despite the lower partial pressure the maximum tissue concentration compatible with safety is ultimately achieved.

Breathing nitrous oxide with a high complement of oxygen promotes a receptive attitude on the part of the patient to the anaesthetist's reassuring remarks. It is rather difficult for the anaesthetist to gain the patient's confidence while forcing him to breath a choking gaseous mixture. The faith which the patient has in the anaesthetist as a result of the pre-anaesthetic visit may be destroyed in a few suffocating moments.

Pre-oxygenation

Pre-oxygenation with 100% oxygen for five or ten minutes before the addition of nitrous oxide facilitates the induction of anaesthesia. The optimum action of nitrous oxide seems to be more quickly effected if the patient is first permitted to breath pure oxygen. It is possible that this may be explained on the basis of an initial elimination of some of the body nitrogen, reducing the tension of this gas in the alveoli and allowing a corresponding increase in space for nitrous oxide. The concentration of nitrous oxide may be rapidly or slowly increased, and as long as the percentage of oxygen is held near atmospheric the patient will not experience the unpleasant sensations associated with hypoxia. Many patients show an initial rise in blood pressure of approximately 10 mm. of mercury as the face mask is applied, although 100% oxygen is being delivered at a brisk flow rate. The blood pressure rapidly assumes its pre-existing level as the patient becomes accustomed to the face mask. Usually no further increase occurs as nitrous oxide is introduced. It is worthy of note that when nitrous oxide is slowly added first-plane anaesthesia usually occurs within ten minutes and while the oxygen concentration is still 40 or 50%.

Elimination of carbon dioxide will prevent the occurrence of subjective disturbances incident to its accumulation in the respired atmosphere. Rebreathing without carbon dioxide elimination may cause the patient to be conscious of a feeling of impending suffocation, even though the oxygen concentration of the inspired mixture is abnormally high.

Supplementation of Anaesthesia

In view of the foregoing evidence, which strongly suggests that the depth of nitrous oxide anaesthesia is limited entirely by the oxygen requirements of the body, it is reasonable for the anaesthetist to try to gain the full benefit of the action of nitrous oxide independent of oxygen lack before considering its supplementation with drugs whose action is less readily reversed. At the present time we are not in a position to take clinical advantage of the increased depth of anaesthesia produced by administering nitrous oxide under a significant positive pressure, but we can realize the benefits of slow induction and pre-oxygenation. Supplementation will usually be required to provide adequate reflex obtundation with an 80/20% mixture of nitrous oxide and oxygen.

Since the preliminary report (Neff, Mayer, and Perales, 1947) in which pethidine ("demerol"; ethyl-1-methyl-4-phenylpiperidine-4-carboxylate) was recommended for the supplementation of nitrous oxide anaesthesia, we have experimented with and, later, clinically employed two of its analogues for this purpose. These drugs—namely, "bemidone" (ethyl-1-methyl-4 (3-hydroxyphenyl) piperidine-4-carboxylate hydrochloride) and "ketobemidone" (ethyl-1-methyl-4 (3 hydroxyphenyl) piperidine-4-ketone hydrochloride)—proved to be considerably more powerful as analgesics than pethidine. Bemidone proved to possess twice the analgesic activity, milligram for milligram, of pethidine, while ketobemidone was approximately 15 or 20 times more powerful. The respiratory depression resulting from comparable analgesic doses indicated that they possessed no significant advantages over pethidine. Dolophine was tried as a supplement to nitrous oxide anaesthesia in dogs, and the respiratory depression associated with its intravenous administration was so great that it was considered to be unworthy of clinical trial.

In reviewing the records of the supplemented nitrous oxide anaesthetics administered during the past eight

months some outstanding developments were observed. First, the dose of pethidine was approximately one-half the amount used five years ago. Secondly, in operations lasting over three hours 50% or more of the total dose of pethidine was given during the first hour. One of the reasons for the reduction in the amount of pethidine used was the substitution of ether supplementation for pethidine and curare for endotracheal intubation in extensive surgical operations. In those cases not requiring endotracheal intubation the practice of first obtaining the full effect of nitrous oxide before pethidine supplementation has been a factor in the successful employment of smaller doses of this drug. In all cases it was found that the average dose level for any particular type of operation, such as cholecystectomy, pneumonectomy, or fenestration, could be reduced by closer attention to the response of individual patients to small amounts of pethidine. In many instances where we formerly gave an initial dose of 50 mg. of pethidine we subsequently found that 20 or 30 mg. was often satisfactory. In other cases additional amounts of 10 mg. were needed to obtain the desired effect.

Maintenance of Anaesthesia

Nitrous oxide supplemented with pethidine, plus curare in cases requiring muscular relaxation, will provide satisfactory anaesthesia for most surgical operations. Where ether was used to facilitate endotracheal intubation the anaesthetic mixture was found to be sufficiently free of ether to be non-explosive within ten minutes of its discontinuance, provided the period of its administration did not exceed eight minutes. Tests for explosibility were made with the Mine Safety Appliance Company's explosimeter.

Anaesthesia was maintained with a continuous flow of an 80/20% mixture of nitrous oxide and oxygen. Carbon dioxide was eliminated with soda-lime by the to-and-fro method. The oxygen concentration was checked at frequent intervals by the Beckman gas analyser. The usual flow rates of the gases were 4 litres per minute for nitrous oxide and 1 litre per minute for oxygen. These flow rates were, as a rule, doubled before, during, and for a short time after any interruption in the anaesthesia for the insertion of an airway or the changing of a canister. It is advisable to limit so far as possible the number of interruptions in the anaesthesia during the maintenance period. A pharyngeal airway should be inserted early in all cases, whether the patient appears to require one or not. In operations such as lobectomy for bronchiectasis, where frequent interruptions in the anaesthesia are necessary for the recovery of secretions, nitrous oxide anaesthesia is probably contraindicated.

Intra-abdominal Operations

Extensive intra-abdominal operations performed under nitrous oxide anaesthesia require less pethidine supplementation for the control of traction reflexes when the patients are given the benefit of a splanchnic block with 60 ml. of 1% procaine with adrenaline in 1 in 200,000 concentration. For example, the average gastric resection lasted four hours in nine cases chosen at random. The average dose of pethidine per case was 131 mg. In one case lasting three hours in a patient who was given a splanchnic block the total dose of pethidine was 50 mg. The average dose of curare administered to these patients was 140 units or 21 mg. of *d*-tubocurarine, and the patient who received the splanchnic block required 120 units or 18 mg. of *d*-tubocurarine. As might be expected, when curare is administered only for the purpose of obtaining muscular relaxation, the required dose will vary very little in those

patients who have received and those who have not received a splanchnic block. The dose of pethidine, on the other hand, is appreciably reduced by the block.

Intrathoracic Operations

Nitrous oxide was used for all kinds of intrathoracic operations, with several notable exceptions. Ether anaesthesia with the highest possible percentage of oxygen was considered more suitable for the Blalock operation for pulmonary stenosis, where a patient already suffering from oxygen lack must be subjected to additional hypoxia during the operation. Supplementation of nitrous oxide anaesthesia with non-volatile drugs in order to permit an extremely high concentration of oxygen must be of such magnitude as to render the nitrous oxide almost impotent.

The unsuitability of nitrous oxide for patients undergoing lobectomy for bronchiectasis has already been mentioned, and the advantages of the slower emergence from ether anaesthesia should be emphasized.

In 24 consecutive operations, including 5 patent ductus operations, 10 transthoracic oesophageal and gastric resections, 2 diaphragmatic herniorrhaphies, 3 pneumonectomies, 3 exploratory thoracotomies, and 1 resection of a mediastinal tumour, only 12 received any curare. The average duration of these operations was 2.7 hours and the average dose of pethidine was 79 mg., or 28 mg. an hour. In the 12 cases in which curare was administered the average dose was 100 units or 15 mg. of *d*-tubocurarine, or 5.25 mg. an hour.

Recently it has been found that nerve block of the sympathetic chain, the phrenic, and the vagus under direct vision will provide better operating conditions and ensure greater freedom from traction reflexes than can be obtained directly from profound anaesthesia or indirectly by the use of curare.

Other Operations

Of 100 consecutive extra-abdominal and extrathoracic operations 25 required more than three hours of anaesthesia. The procedures included radical mastectomies, laminectomies, radical neck dissections, and extensive orthopaedic procedures.

Nine of the 25 patients were given a thiopentone induction, while the remainder were not. It is interesting to note that, while the average dose of pethidine for all cases was 30 mg. an hour, 37 mg. an hour was the average dose for the patients who received a thiopentone induction. This might reasonably be explained on the basis of slower saturation of nitrous oxide incident to the respiratory depression of thiopentone.

Premedication.—Adult patients rarely received doses of morphine exceeding $\frac{1}{4}$ gr. (11 mg.) combined with 1/150 gr. (0.43 mg.) of scopolamine one and a half hours pre-operatively. A short-acting barbiturate was administered the night before operation.

Recovery from Anaesthesia

Recovery from nitrous oxide anaesthesia is almost immediate when it has not been complicated with hypoxia. Patients who have received pethidine supplementation during nitrous oxide anaesthesia regain their mental faculties before perceiving pain. In those cases in which pethidine has not been given, post-anaesthetic analgesia is rarely a feature of nitrous oxide anaesthesia. Emergence delirium, a rather common complication of thiopentone hypnosis, cyclopropane anaesthesia, and nitrous oxide complicated with hypoxia, has not been noted in any case.

The cough reflex returns quickly after the termination of the anaesthesia. The early return of this reflex is in agreement with the general observation that pethidine is rather ineffective in causing its abolishment. Control of cough with pethidine during nitrous oxide anaesthesia is probably due to the slightly greater depth of anaesthesia which it provides, and when the nitrous oxide is discontinued pethidine itself will not inhibit the cough reflex.

The pharyngeal reflex usually becomes active only after consciousness has returned. Many patients do not object to the presence of a pharyngeal airway even after they awaken. On request they will open their mouth to facilitate its removal.

Summary

A further report on nitrous oxide independent of oxygen restriction has been presented.

The factors which we consider important, based on our experience in over 2,000 administrations for all kinds of operations, including intra-abdominal and intrathoracic procedures, have been emphasized.

Pethidine and curare continue to be the preferred drugs for enhancing respectively the reflex obtunding and relaxing qualities of nitrous oxide.

REFERENCES

- Bennett, J. H., and SeEVERS, M. H. (1937). *J. Pharmacol.*, **61**, 459.
 Bert, Paul (1878). *C. R. Acad. Sci., Paris*, **87**, 728.
 Brotman, M., and Cullen, S. C. (1949). *Anesthesiology*, **10**, 696.
 Faulconer, A., Pender, J. W., and Bickford, R. G. (1949). *Ibid.*, **10**, 601.
 Guedel, A. (1922). *Curr. Res. Anesth.*, **1**, 59.
 Henderson, V. E., Brown, W. E., and Lucas, G. H. W. (1927). *Ibid.*, **6**, 21.
 Mushin, William W., and Rendell-Baker, L. (1949). *British Medical Journal*, **2**, 472.
 Neff, W., Mayer, E. C., and Perales, M. (1947). *Calif. Med.*, **66**, 67.
 — and Thompson, R. (1948). Analgesics During Nitrous Oxide Anaesthesia, Scientific Exhibit, American Medical Association Convention, 1948.
 Raginsky, B. B., and Bourne, W. (1934). *Anesth. Analg.*, **13**, 152.
 SeEVERS, M. H., Bennett, J. H., Pohle, H. W., and Reinardy, E. W. (1937). *J. Pharmacol.*, **59**, 291.
 Thompson, R., and Neff, W. (1950). *Anesth. Anal.*, **29**, 75.

PROLONGATION OF THE INITIAL STARVATION PERIOD IN PREMATURE INFANTS

BY

WILFRID GAISFORD, M.D., F.R.C.P.

Professor of Paediatrics, University of Manchester; Honorary Paediatrician, St. Mary's Hospital, Manchester

AND

SHEILA SCHOFIELD, M.B., D.C.H.

Paediatric Registrar, Neonatal Department, St. Mary's Hospital, Manchester

Prematurity still ranks high among the causes of neonatal death. Its prevention is a matter of obstetric concern. The successful rearing of a premature infant is one of the paediatrician's major tasks, and any method of removing one of the hazards associated with prematurity is worthy of consideration. The special hazards operate particularly in the first three days of life, during which period about 75% of the fatalities occur. Intracranial trauma, congenital malformations, and atelectasis may be beyond therapeutic care, but asphyxia following inhalation of fluid—which is a common cause of death—can be avoided if no fluid be given during these first few days.

It is the purpose of this paper to describe the rationale and the routine followed in the care of a group of premature infants weighing between 2 and 5 lb. (0.9 and 2.3 kg.) at birth.

Premature infants may suffer considerable shock at birth and their immature respiratory centres be further adversely affected by anaesthetics or analgesics administered to the mother as well as by cerebral oedema or actual intracranial haemorrhage. The sucking reflex may be absent and the swallowing and coughing reflexes inadequate. As a result a spill-over of ingested fluid from the oesophagus into the trachea may easily occur and lead to asphyxia. Death due to this cause in premature infants often occurs following an attack of cyanosis during or immediately after a feed.

The lungs are deficient in elastic tissue and are slow to expand, so that pulmonary collapse occurs easily. The ingestion of fluid may lead to abdominal distension, and this results in an elevation of the diaphragm and a further tendency to pulmonary collapse.

Time of First Feeding

For these reasons delaying the initial feeding from the customary 24 hours after birth to 70 hours or more would seem a logical procedure if it did no harm to the infant.

During the past two and a half years this principle has been applied to 231 premature infants. The time of initial feeding has been in every case determined by the infant himself or herself. The routine is to place the infant in a cot immediately after his airway has been cleared, maintain an equable temperature (varying from 75 to 85° F. (23.9 to 29.4° C.) according to weight) and an adequate humidity (65%), and administer oxygen as necessary. The infant is kept as quiet as possible and away from bright light. The position in the cot is changed three-hourly and a fresh napkin applied when the previous one is soiled or wet. Recently some of these infants have been nursed naked and they have proved more active, so that routine three-hourly position-changing becomes less important.

After a variable number of hours the infant begins to cry—feebly at first and readily ceasing when his position is changed—but gradually the cry increases in strength and persistence and sucking movements of the lips are evident. When this occurs the first feeding is given. Table I

TABLE I.—Hour at Which First Feed was Given in 231 Cases

Weight in lb. and oz.	No.	Hour of First Feeding		
		Max.	Min.	Average
2-2.7 (0.9-1.1 kg.)	9	96	26	60
2.8-2.15 (1.13-1.33 kg.)	23	102	31	73
3-3.7 (1.36-1.56 kg.)	35	105	15	61
3.8-3.15 (1.58-1.78 kg.)	58	111	28	61
4-4.7 (1.8-2 kg.)	67	106	19	53
4.8-4.15 (2.04-2.24 kg.)	39	105	20	48

shows the hour at which this happened. By this time the shock of birth and the effects of any maternal anaesthetic have passed and the increasing crying has led to some further expansion of the lungs.

Effects of the Starvation Period

What have been the effects of this period of starvation? First, the weight loss, as might be expected, has been greater than in infants fed earlier. Table II shows the weight loss in the various groups. The interesting features are that the average loss is similar, irrespective of the birth weight. But when this loss is recorded as a percentage of the birth