ANAESTHESIA IN GENERAL PRACTICE

This is one of a series of articles, contributed by invitation

NOTES ON THE PHYSIOLOGY AND PHARMACOLOGY OF ANAESTHESIA

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General surgical anaesthesia may be defined as the state of profound insensibility produced by the action of certain drugs on nerve cells of the brain without harming the essential processes of respiration and circulation, and sufficiently profound to allow a surgical operation to be performed. Local anaesthesia comprises loss of sensation over an area caused by a drug acting directly on nervous tissue to which it has been applied. It is the purpose of this article to discuss from a practical point of view the various routes by which these drugs enter the body, the effects they produce, and their ultimate fate.

General anaesthetics are administered in the gaseous or in the liquid state. Solid drugs are given in solution.

Volatile Anaesthetics

Gaseous anaesthetics which enter the body through the lungs are called inhalational anaesthetics. This group includes nitrous oxide, ethylene, acetylene, and cyclopropane, and the vapours of di-ethyl ether, divinyl ether, chloroform, and ethyl chloride. Since an inhalational anaesthetic is speedily absorbed and excreted by the blood through the alveolar epithelium the drug may be given with safety in full pharmacological dose to the point of deep surgical anaesthesia, and provided respiration and circulation are maintained reduction in dosage can be effected readily. On the other hand the dose of non-volatile anaesthetics cannot be reduced rapidly, and therefore deep anaesthesia is not compatible with safety. If a volatile anaesthetic such as ether is administered in solution either intravenously or by the rectum the drug will be excreted by the lungs.

In the upper air passages certain direct effects may be produced: irritation of the mucous membrane accompanied by vasodilatation, secretion of mucus, muscular spasm; after some minutes these signs of irritation may be followed by local anaesthesia of the walls of the air passages and by muscular relaxation. Ether (in the absence of atropine) is especially prone to cause these events, but chloroform and ethyl chloride are less irritating and nitrous oxide and ethylene are non-irritating.

ABSORPTION AND ELIMINATION

The direction of the diffusion of the vapour through the alveolar epithelium depends upon the partial pressure in the alveoli and the tension in the blood. So long as the partial pressure of the vapour in the air cells is higher than its tension in the blood the drug is absorbed by the blood. Although the alveolar epithelium does not appear to suffer damage during anaesthesia of normal duration, high concentrations of ether or of chloroform acting over a long period may cause more or less permanent injury to these cells. Deep inspiration draws a larger volume of gas into the lungs, and at the same time the increased power of the thoracic "pump" promotes a more rapid flow of blood through the heart and lungs. Therefore by full respiratory movements absorption of

anaesthetic gases is increased; or after the administration has ceased excretion of the drug is encouraged.

In the blood the drug is carried partly in solution in the plasma and partly in the red corpuscles, either in a loose chemical combination or by adsorption. After passing through the left heart the anaesthetic-laden blood is propelled to the brain and to the tissues of the body. It is common experience that for a particular anaesthetic the longer the duration of administration the more the delay in recovering consciousness. Brief administration produces a certain tension of the gas in the blood, but the lymph and the body tissues generally do not have sufficient time to store up the drug. On the other hand prolonged anaesthesia causes the anaesthetic to accumulate in all the tissues, although it is necessary to prolong administration for several hours before the concentration in the arterial blood, the venous blood, and the tissues is in equilibrium.

McKesson introduced the method of administering nitrous oxide and oxygen, which he termed "secondary saturation." One hundred per cent. of nitrous oxide is inhaled until the patient is grey, and therefore the blood contains a maximum tension of nitrous oxide, which ensures that the tissues in general and the nerve cells in particular rapidly obtain a maximum concentration of the drug. Oxygen is then driven into the lungs (and into the blood), and thereafter a mixture of nitrous oxide and oxygen in the usual proportions is administered. The period of greyness and anoxaemia which accompanies the saturation with nitrous oxide is considered by many anaesthetists to endanger the safety of the heart muscle.

When the administration is stopped elimination proceeds rapidly at first, particularly if the circulatory and respiratory functions are vigorous, and then more gradually. The last traces of the less volatile drugs may be retained for several days. The bulk of an inhalational anaesthetic drug is excreted through the lungs, a detectable amount through the skin, and possibly traces of ether and chloroform are oxidized by the liver and the products excreted by the kidneys.

EFFECT ON THE BLOOD AND THE NERVOUS SYSTEM

All types of general and local anaesthesia produce a leucocytosis, and among other changes in the blood which have been recorded the following may be mentioned: reduction in the amount of haemoglobin, anaemia, haemolysis, prolongation of the coagulation time, increase in the blood cholesterol, reduction of the oxygen content, and an increased percentage of carbon dioxide. These effects are rare with nitrous-oxide-oxygen anaesthesia, but they have been noted with ether and with chloroform. The alkali reserve of the blood is reduced and some degree of ketosis occurs. The glycogen of the liver is mobilized and the blood sugar rises. Undoubtedly these effects are increased by cyanosis, by prolonged anaesthesia, and particularly by chloroform. The administration, before and after operations, of sodium bicarbonate and of glucose (together with insulin, especially in diabetics) is of much service, good oxygenation is essential, and nitrous oxide and oxygen is the least disturbing (but the weakest) anaesthetic agent.

Anaesthetic drugs are not only readily taken up by the blood but nerve cells have a special affinity for them.

The cells in the higher centres of the cerebral hemispheres are affected first, and the centres for the sensory cranial nerves subsequently—smell, then vision, then hearing. Probably oxidation of the nerve cells, upon which the function of the cells depends, is affected by the drug by interference with the selective permeability of the surface membrane of the cells. If the higher centres are very active at the time of induction a higher concentration may be required to inhibit function. This is the rationale of careful pre-operative sedation, either by natural means or by drugs. An individual in a state of mental excitement may require such a large concentration to control the nerve cells of the higher centres that the function of the lower centres may be affected as well. Anaesthetic agents do not affect the various portions of the cerebrum in quite the same order. Thus chloroform and nitrous oxide usually produce analgesia before confusion of the mind and amnesia set in, but ether confuses the mind at the same time as it abolishes pain.

The concentration of a drug in the blood which is necessary to inhibit the activity of a particular group of nerve cells varies with different drugs. At normal atmospheric pressure the greatest partial pressure of nitrous oxide which permits adequate oxygenation will not produce muscular relaxation. In a pressure chamber, working at a pressure of one and a half atmospheres, nitrous oxide becomes more potent. But ethylene is rather more powerful than nitrous oxide, while ether or chloroform will cause muscular relaxation with adequate oxygenation and unimpaired respiratory and circulatory functions.

TOXIC EFFECTS

In the presence of an adequate oxygen supply nitrous oxide, ethylene, and cyclopropane do not impair liver function; but liver function may be diminished by ether for some hours and by chloroform for days. Permanent degeneration, sometimes fatal, occurs in the condition known as delayed chloroform poisoning. The late Dr. Fairlie of Glasgow, with his great experience of chloroform, considered that minor degrees of damage to the liver were not uncommon. Pre-operative loading of the liver with glycogen is a safeguard, and for this purpose glucose or sodium lactate (the liver converts lactic acid into glycogen) may be given for several days before operation.

Anaesthetics affect the heart by poisoning the neuromuscular mechanism and by causing vagal inhibition. In the early stages of chloroform anaesthesia ventricular fibrillation may follow excitement or the injection of adrenaline. Anoxaemia may lead to failure of the heart muscle itself, and this danger may be caused either by complete displacement of the oxygen (for example, by giving 100 per cent. nitrous oxygen in "dental gas" anaesthesia) or by obstruction to the air intake. Inefficient heart action delays induction and recovery. This is clearly demonstrated when giving gas and oxygen to patients with morbus cordis.

Vasomotor control is usually disturbed by the direct action of the anaesthetic upon the vasomotor centre in the medulla. Thus if the head and shoulders are raised compensatory vasoconstriction of the lower parts of the body will not occur and cerebral anaemia may follow. But lowering of the head, as in the Trendelenburg position, is safe and salutary. Nitrous oxide produces slight vasodilatation, and the blood-pressure readings in the absence of shock in ether and in chloroform anaesthesia are instructive. With ether an initial rise in the systolic pressure is followed by a gradual fall, while the diastolic pressure falls steeply at first and remains low until the

anaesthetic is stopped, when it usually rises rapidly. Thus the pulse pressure under ether is large, the heart has less work against a lowered peripheral resistance, but cut surfaces tend to bleed more freely. Chloroform anaesthesia is accompanied by a slow fall in the systolic pressure and a rise in the diastolic reading. Therefore the pulse pressure diminishes, the heart works against an increased peripheral resistance, but there is a tendency for the bleeding of cut surfaces to be lessened. It is said that etherized patients bleed at the time of operation, but those who have had chloroform bleed after the operation!

The heat centre is also depressed, and as the metabolism of the body is reduced during anaesthesia the lowering of the body heat may be considerable. Adequate covering of the body, the avoidance of draughts, and a well-warmed theatre are called for.

The function of the kidneys is not demonstrably affected by nitrous oxide and oxygen anaesthesia, but ether and particularly chloroform tend to produce oliguria and anuria. Albumin may be detected in the urine after ether and sometimes after chloroform. Acetonuria was present in 67 per cent. of a series of patients upon whom any one of the various forms of general anaesthesia had been used, and "in no less than 85 per cent. under local analgesia" (Schulze, quoted by Hewer). The blood urea shows a slight rise after ether anaesthesia.

Bourne and Burn have demonstrated that the contractile power of the uterus in labour is inhibited by ether and by chloroform. Nitrous oxide and air or nitrous oxide and oxygen permit uterine activity to continue with normal rhythm and contractile power. Spinal analgesia appears to promote tonic contraction of the circular muscle, but the longitudinal fibres do not function effectively.

Non-volatile Anaesthetics

Among those in common use may be mentioned avertin (tribromomethylalcohol) and the rapidly acting barbiturates such as evipan sodium, pentothal sodium (which contains sulphur), pernocton (which contains bromine), sodium amytal, and nembutal. These preparations are all soluble in water, and they are administered by the mouth, by the rectum, by intramuscular injection, or by injection into a vein; but all are not suitable for administration by all routes. Avertin is always administered rectally; evipan sodium and pentothal sodium if injected into the tissues cause severe local reaction, and they are *par excellence* intravenous anaesthetics. If nembutal, the soluble sodium salt of an insoluble barbiturate, is swallowed by a nervous patient the drug may be retained for some time in the stomach by functional pyloric spasm, with the result that the gastric hydrochloric acid may cause precipitation of the insoluble compound and the absorption of the drug may be delayed. Nevertheless nembutal is a useful oral basal anaesthetic.

Each of these substances is detoxicated by the liver, and the oxidized products, together with salts derived from the bromine or sulphur components, are excreted by the kidneys.

The barbiturates not only vary in the particular nerve cells for which they have affinity (luminal has a markedly sedative action in conditions of motor hyperexcitability, such as chorea), but they vary in the rate of detoxication and elimination, sodium amytal being slowly detoxicated, while evipan sodium and pentothal sodium are eliminated with great rapidity. If the property of speedy detoxication is accompanied by a wide margin of safety—that is, if the minimal lethal dose is three or four times the narcotic dose—then the drug may be given into a vein

in sufficient quantity to produce complete narcosis and muscular relaxation. The guide to the dose is the reaction of the patient. Slow administration by other routes—oral, rectal, or intramuscular—is employed for the slowly detoxicated barbiturates and for avertin. The dose is calculated according to the weight of the patient, and unconsciousness only is aimed at, the further depth of anaesthesia being attained by administering a relatively low concentration of an inhalational anaesthetic.

Respiration and the General Circulation

After an operation of average length under either general or spinal anaesthesia there may be marked pallor of the face and body. The prolonged immobility of the body, together with complete muscular relaxation, has reduced the circulation considerably. Deficiency of carbon dioxide (Yandell Henderson) and the reduced metabolism have also tended to produce this appearance.

The administration of carbon dioxide stimulates the respiratory centre and the movements of respiration are increased both in rate and in amplitude. Not only does this improve the colour of the patient by increased ventilation but the return of blood to the heart is also accelerated. On the other hand excess of carbon dioxide may depress the heart muscle. The accumulation of carbon dioxide and other waste products in the muscles tends to cause muscular rigidity.

The administration of oxygen improves the heart's action and helps the functions of other important organs; furthermore, it relieves congestion in the blood vessels of the air passages. Cyanosis after nitrous oxide may lead to vomiting and malaise, but a few breaths of oxygen speedily restore the sensation of well-being. It should be remembered, however, that the pink colour associated with breathing a mixture rich in oxygen may mask defective exhalation of carbon dioxide should the upper air passages or the return flow from an intratracheal catheter be partly obstructed. It is as important to free the body of the waste product carbon dioxide as it is to provide an adequate supply of oxygen. Therefore under general anaesthesia a proper airway is at all times essential.

Local Anaesthetics

These drugs paralyse nerves and nerve endings in concentrations at which they do not injure surrounding tissues and without preliminary excitation. The duration of action is temporary, but more than half an hour (quinine-urea lasts longer and tends to leave permanent effects). They are soluble in water but not destroyed by boiling; they may be combined with adrenaline, and they do not exert a markedly toxic central action. They may be applied by painting on to surfaces; by percutaneous electrolysis; by injection, either hypodermically to paralyse nerve endings or subdurally to paralyse the spinal cord and the spinal nerve roots. These drugs vary in their toxic power upon the brain and other organs, cocaine being potent and novocain relatively innocuous. Adrenaline is injected along with the drug in order that local vasoconstriction and local concentration of the drug may be secured. A large bulk of highly dilute solution increases the tension in the tissues, and thereby pressure paralysis of the nerve fibres is caused.

Patients may suffer discomfort following local anaesthesia. The adrenaline may cause palpitation, pallor, and even alarming derangement of the heart's action. There may be marked idiosyncrasy to the local anaesthetic, and often this effect is not shown immediately but

during the few hours subsequent to the injection when, the local vasoconstriction having relaxed, the drug is being dispersed into the circulation. Novocain is rapidly detoxicated by the liver and the products are excreted by the kidneys, but cocaine is detoxicated slowly and excreted slowly.

Spinal Analgesia

By the direct application to the spinal cord of local anaesthetic drugs (tropacocaine, stovaine, novocain, per-caine, etc.) the passage of both afferent and efferent impulses along the spinal roots may be blocked, the sensory roots being affected more easily. A solution may tend to diffuse up or down the intrathecal space, and dorsally or ventrally as it is heavier, lighter, or of the same specific gravity as cerebro-spinal fluid—that is, hyperbaric, hypobaric, or isobaric—and as the body is prone, supine, upright, or inverted head downwards. The duration of the analgesia is usually from one to two and a half hours, and the drug is ultimately excreted by the same route as other local anaesthetics.

Not only are the motor and sensory actions of the affected nerve trunks and tracts abolished, but should the thoracic region of the spinal cord be affected extensive vasomotor paralysis ensues. The fall in blood pressure may be considerable. It has been suggested that this fall is due to relaxation of the trunk and lower limb muscles, accompanied by stagnation of blood in the capillaries and veins and increased exudation of lymph. In this way the paralysed region of the body becomes a lake of lymph, while the bulk of blood available for return to the heart is greatly reduced. Should the head be raised and the legs lowered cerebral anaemia may produce syncope. In elderly persons the arterial peripheral resistance may be relatively high. According to the formula $S = 2D - 20$ (systolic should be equal to twice the diastolic pressure minus 20 mm. Hg) a diastolic pressure of 120 mm. Hg requires a systolic pressure of 220 mm., but if a pre-operative diastolic reading of 120 mm. were accompanied by a systolic pressure of only 180 mm. a spinal anaesthetic might cause such lowering of the systolic pressure that serious cerebral anaemia might result.

Headache after spinal analgesia may be severe. It may start a few hours after the administration or the headache may not occur for a week. Usually occipital or sub-occipital, it may be exaggerated by raising the head. The intrathecal pressure is raised and the headache is always relieved, temporarily at least, by lumbar puncture. The headache may follow simple diagnostic lumbar puncture, and although injection of air bubbles, intrathecal bleeding, direct effects of the drug, and other possible causes have been deemed responsible, it is probable that the condition is due to the sudden disturbance of the intrathecal pressure associated with lumbar puncture, with or without the injection of a drug. The application of heat to the feet with ice to the head, accompanied by a saline aperient and a mild analgesic, usually relieves the condition.

When spinal anaesthetics are combined with powerful basal anaesthetics whose elimination depends upon detoxication by the liver undesirable effects may result. The drop in blood pressure is more marked than usual, the respiration often is slowed and reduced in depth. The depression of circulation retards detoxication, and until the effect of the spinal anaesthetic has worn off basal anaesthesia will persist. Stimulation of the respiration and of the circulation by means of inhalations of carbon dioxide and oxygen hastens detoxication and helps to break the vicious circle.