to be greatly increased in depth, and therefore a further three-minute period of hyperventilation through the canister was undertaken. At the end of this the child's respiration was noted to be normal in depth and character. The endotracheal tube was therefore removed, and an airway was substituted. No further oxygen administration was required.

COMMENT

The remarkable features of this case appear to be: (1) Persistent respiratory paralysis, apparently due to the residual effect of a relaxant, seems to have been caused by carbon dioxide retention. Possibly an increased carbon dioxide tension is capable of producing myoneural block. (2) The child did not recover consciousness for some four hours, although recovery would normally have been anticipated within one hour after operation; it therefore seems likely that the degree of carbon dioxide retention was sufficient to produce narcosis.

It is unfortunate that carbon dioxide estimations were not possible in this case. The difficulty of the treatment of prolonged respiratory depression is illustrated. Such depression has been attributed to hyperventilation: it now appears that underventilation also may perpetuate respiratory depression. It is possible that an electronic apparatus may in future be devised which, by means of an electrode inserted into the tissues, may give continuous measurement either of pH or of carbon dioxide concentration. Such an instrument would obviously be of the greatest value in cases requiring controlled ventilation.

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A Possible Method of Pre-operative Anticipation of Thrombo-Embolic Episodes

In recent years major advances have been made in the preparation of patients for the stress and eventualities of surgical procedures, and many previously fatal secondary factors can now be evaluated and corrected pre-operatively to prevent a fatal outcome. Not so post-operative thrombo-embolic episodes: the majority still occur apparently unexpectedly and in spite of increasing awareness of the condition and diligent attempts to anticipate its occurrence.

Ochsner has shown that approximately 50% of pulmonary emboli occur in patients without recognizable preceding peripheral stigmata. Sulamaa and Pentti (1949) reported 170 cases of thrombo-embolic disease, 20 being fatal pulmonary emboli: of the latter, 14 were not diagnosed or were not suspected before their occurrence. Felder (1949) reported 27 cases of pulmonary emboli; in 10 the chest and peripheral signs occurred simultaneously and in 11 cases the chest signs were the first indication. In 78% of his cases treatment began after the chest signs were manifest.

Active prophylactic therapy, excluding routine use of anticoagulants, has not lowered the incidence; 0.57% of patients are liable to pulmonary infarction and 0.22% to fatal pulmonary emboli. A perusal of gastrectomy fatalities shows that about 20% are due to pulmonary emboli.

It is thus the more apparent that pre-operative diagnosis of the thrombophilic type of patient would present a major advance in the selection of those patients who require post-operative anticoagulant therapy. At present it would be unwise to adopt routine anticoagulant treatment owing to its cost, its sequelae, and the labour involved.

It seems reasonable to postulate that clotting *per se* is a normal physiological accompaniment to wound-healing, and that in association with any trauma, definitive or accidental, there is a general and a local mechanism which ensures clotting at the breaches in vascular continuity; likewise, this process is graded in degree to meet the local requirement, and its duration should be proportional to the initial lesion. This effector mechanism has already been discussed in detail by many authors, and no useful purpose will be served by repeating their observations.

Previous attempts have been made to prevent patients from developing thrombo-embolic episodes—the construction of a coagulation graph post-operatively and detection of fibrinogen B in the plasma (Cummine and Lyons, 1948). Ochsner also propounded the theory of a lowered anti-thrombin titre, and advocated the use of alpha-tocopherol and intravenous injections of calcium to raise a lowered titre. No case selection was made, and such a method, even if it proved to be effective, would be costly and, like coagulation-graph charting, could be conducted only in well-staffed institutions. If it could be foreseen which patients were liable to thrombo-embolic phenomena, active measures could be taken with this smaller group.

It is possible that an increased post-operative clotting tendency is a function of the general response of the body to the strain applied to it by a surgical operation and that the degree of clotting is an indication of adrenal cortical function. During recent years there have been increasing records of spontaneous thromboses and embolic phenomena occurring during cortisone therapy. Cosgriff (1951) recorded the increased coagulability of the blood during treatment and an unexpectedly high incidence of thrombo-embolic complications. The patient liable to post-operative thrombotic episodes may thus respond abnormally to stress or prolongation of the post-operative state.

Godlowski (1951) demonstrated that changes in the eosinophil count could be modified by the administration of heparin, and this suggested that such changes may bear some relation to blood coagulability. Post-operative eosinophil counts were charted on several cases, but the results were not uniform.

An effective reproduction of stress to the body can be secured by the adrenaline test, as used extensively in America to ascertain the resistance to stress of a patient about to undergo a given major operation.

Adrenaline hydrochloride, 0.3 mg., was given to pre-operative patients, and their clotting-times and eosinophil counts were recorded half-hourly during the next four hours. It was found that varying results were obtained. These same patients had coagulation graphs taken post-operatively and were examined clinically for thrombotic stigmata. In all, about 50 patients have been examined and a certain pattern is developing.

The majority of those patients examined showed a rapid shortening of their coagulation time during the first hour and then a fairly quick return to normal time inside the four-hour period of examination. Six of them showed a shortened coagulation time, but it persisted at a low level and was still present after six hours. They also were followed up post-operatively, and all six developed thrombotic episodes, two of a major nature and one fatal. The other patients demonstrated shortening of their coagulation time for four days and then elongation to normal.

All patients were treated identically: pre-operative and post-operative physiotherapy, early rising, and routine examination for tender calf muscles and calf-muscle spasms. The duration of stay on the operating table was almost identical, and the operative procedures were of a similar magnitude and location.

Application.—Given forewarning of subjects who are likely to develop post-operative thrombotic episodes, it is possible to provide selective treatment with anticoagulants 24–48 hours after operation; and, in the event of the discovery of a more innocuous replacement therapy on the lines of the antithrombin hypothesis, treatment could be given post-operatively to those subjects showing a suggestive adrenaline response and liable to undergo major surgery.

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