ANAESTHESIA FOR PERFUSION WITH CYTOTOXIC DRUGS IN CANCER OF THE HEAD AND NECK

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SUMMARY

Tumours of the head and neck have been treated by a cytotoxic drug given via the arterial supply. A simple anaesthetic technique is described. Related problems are considered, such as difficulty in intubation, difficulty in assessing skin colour following the injection of dye, and acute respiratory obstruction after operation from reactionary oedema in the tumour. Indications for tracheostomy and the value of spontaneous respiration during intubation are mentioned.

The treatment of malignant disease by cytotoxic drugs is now a well-established practice. The dosage of such drugs, however, is limited to an amount which will not produce an accompanying depression of bone marrow. If the drug is given into the artery supplying the tumour, then the dosage can be appreciably increased, without necessarily increasing systemic toxicity. Neoplasms of the head and neck are particularly suitable for perfusion with cytotoxic drugs because the arteries are relatively accessible and the response to therapy can be easily observed.

A series of thirty-five arterial perfusions have been performed, and in this paper the associated anaesthetic problems are discussed. All the patients were suffering from recurrent malignant disease of the head or neck and all had previously undergone conventional surgery, radiotherapy, or both.

The cytotoxic drug used was Epodyl (ICI) which chemically is triethyleneglycol diglycidyl ether, with the formula

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\begin{align*}
\text{O} & \quad \text{O} \\
\text{CH}_2 \text{CH} & \quad \text{CH}_2 \text{O} \text{CH}_2 \text{CH}_2 \text{O} \text{CH}_2 \text{CH}_2 \text{CH}_2 \\
\end{align*}
\]

This is an alkylating agent which is taken up from the blood by actively dividing cells, as for example in tumour, hair and bone marrow. It produces immediate oedema of the tumour area, followed by tissue destruction which in some cases amounts to massive necrosis. In the conscious subject, injection of the drug produces dizziness and pallor.

The surgical procedure involves exposure, on the affected side, of the common carotid artery, the bifurcation and the branches of the external carotid artery. Disulphine Blue is injected into the vessel selected for the perfusion. The area supplied is immediately stained greenish-blue, thus confirming that the correct artery is being used. The Epodyl is then given slowly through the same needle. Subsequently, the patient has a prolonged course of therapy with cyclophosphamide.

The anaesthetic principles are simple, namely to produce and maintain a light plane of anaesthesia, to perform endotracheal intubation, to maintain good oxygenation and to ensure a rapid return of reflexes. Premedication consists of atropine 0.6 mg with pethidine 25 mg and induction of anaesthesia is achieved by intravenous injection of thiopentone (maximum dose 200 mg). This is followed by suxamethonium 40 mg. After ventilation of the lungs with oxygen and intubation, anaesthesia is maintained with nitrous oxide, oxygen and halothane, the patient being given a head-up tilt to reduce venous oozing. Pethidine and suxamethonium are omitted in patients with laryngeal obstruction. Here, it is essential to retain spontaneous respiration in case intubation, which is attempted under nitrous oxide, oxygen and halothane, proves difficult or impossible.

The following are some of the difficulties which have been encountered.
Inability to use a facepiece.

Facial oedema, an underlying large tumour of the maxilla and the bulk of dressings after excision of the cheek and maxilla have all prevented satisfactory application of a facepiece and ventilation with oxygen (figs. 1 and 2).

Difficulty in intubation.

Direct laryngoscopy has been impossible, despite the use of suxamethonium, on three occasions, although the airway has been quite adequate, as shown by the response to manual ventilation. Fibrosis, oedema and extension of the tumour (for example, from the vallecula) may produce a fixed induration of the tissues of the neck which cannot be adequately lifted by the beak of the laryngoscope. In this situation, blind nasal intubation during spontaneous respiration should be attempted.

It may prove possible to expose the region of the larynx readily by laryngoscopy but the final view of the cords and passage of the tube are made difficult by distortion due to large fungating tumours. Spontaneous ventilation is essential in these cases. A wide assortment of endotracheal tubes including gum-elastic catheters, should be available.

On two occasions, both laryngoscopy and blind intubation proved unsuccessful and these patients required immediate tracheostomy.

Determination of the patient's true colour.

After the injection of the Disulphine Blue, the dye is rapidly distributed throughout the body, excretion taking 48 hours. The patient, therefore, is coloured greenish-blue for the latter part of the operation and for the first few postoperative days. Particularly careful observation is required throughout this period in case cyanosis develops.

The development of hypotension.

Immediately after the Epodyl enters the artery, a fall in blood pressure has been noted, which has

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![Fig. 1](image1.png)  
**Fig. 1**  
Woman aged 33  
Both patients were suffering from carcinoma of the antrum and the difficulty of obtaining satisfactory application of a facepiece is apparent.

![Fig. 2](image2.png)  
**Fig. 2**  
Woman aged 60
responded to vasopressor drugs and posture. In some cases this fall appears to be due to a direct effect on the carotid sinus reflex. There is also a central action since a fall has been noted after intravenous injection of cytotoxic drugs.

**Acute respiratory obstruction.**

An intense oedema of the tumour area can be expected as a response to the Epodyl and this swelling may be sufficient to produce acute respiratory obstruction. For this reason, urgent tracheostomy has been twice needed in the immediate postoperative period for neoplasms of the tongue and pharynx. As a result of these experiences prophylactic tracheostomy is now performed prior to perfusion if the larynx, pharynx or tongue is involved.

In addition to these tracheostomies, other procedures which have been combined with the perfusion include lateral rhinotomy and three excisions of orbit and maxilla to reduce the bulk of tumour on which the Epodyl was required to act.

A full account of this work has been given by Harrison (1963). In view of the advanced nature of the disease being treated, it can be said that the results are very encouraging. Neoplasms of the head or neck rarely give rise to metastases, unlike those of the major body cavities. These patients may linger for a considerable time before dying from local extension into a major vessel or from bronchopneumonia. Such patients are often in a poor physical state and present a considerable operative risk. Nevertheless, the anaesthetic hazard must be accepted in order that treatment can be undertaken.

Other reports also illustrate the role of anaesthesia in the use of cytotoxic drugs. Duff and his colleagues (1961) obtain full abdominal relaxation with relaxant drugs during general anaesthesia. Aortic occlusion is then produced by tightly binding sandbags to the abdomen. In this way, the bone marrow is protected whilst the cytotoxic drug is in the circulation.

Stolar and Wynands (1963) base their procedure on the direct relationship between temperature and uptake of certain cytotoxic drugs. Under light halothane anaesthesia and continuous epidural analgesia, hypothermia to 30°C is produced by surface cooling. This protects normal tissue from the cytotoxic perfusion fluid which is administered at 40°C.

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**References**

