COMMENTS

Approximately 100 patients per month have been admitted to our 16-bed intensive care unit. About half of them have received prolonged artificial ventilation via endotracheal or tracheostomy tubes. There were approximately five life-threatening accidental airway disconnections per month until October 31, 1970. These occurred in spite of the routine practice of taping all connectors. The newly-designed adaptors have been used since November 1, 1970, for all ICU patients needing artificial ventilation. There has been no accidental disconnection during the two months these adaptors have been in use.

Almost as many life-threatening disconnections occur at other sites in the air-train path of the ventilator-to-patient assembly as occur in the endotracheal airway, including separations of ventilator tubings from nebulizers, valves, or ventilators; leaking nebulizers; and electric wall-plug slippage.

Manufacturers should be encouraged to design and produce dual-swivel adaptors which incorporate the nonslipping characteristics shown here and, in addition, are small, short (not protruding more than necessary beyond the end of the tube), lightweight, without leaks, and have a 15-mm female patient end, a 15-mm male ventilator end, a lumen equal to or larger than that of the tracheal tube, and a slip-proof suction port which can be opened and closed quickly.

Dr. Peter Safar and Dr. Ake Grenvik made valuable suggestions.

REFERENCE


Clinical Implications of the Effect of Halothane on Depressed Rat Bone Marrow

DAVID L. BRUCE, M.D.,* AND JOHN A. KOEPKE, M.D.†

We have reported that halothane interferes with granulopoiesis in rats1 and have investigated the kinetics of DNA synthesis in myeloid cells of these animals.2 In the latter study, the rats received 0.55 per cent halothane for four hours, beginning concurrently with injection of tritiated thymidine (3HT). We learned that rat bone marrow takes two hours to equilibrate with inspired halothane, so only a portion of the four-hour exposure really tested the effect of halothane on the kinetics of myeloid precursor flow. The current study was undertaken to correct this flaw in experimental design, and the results of this and the previous...
experiment are compared and assessment of the possible clinical implications is made.

**Materials and Methods**

Male Sprague-Dawley rats weighing between 180 and 200 g were used. They were given cyclophosphamide, 30 mg intraperitoneally, then allowed to eat and drink normally for the remainder of the day. The following morning, 22 hours after the drug had been injected, ten rats were put into a chamber and exposed to 10 l/min of air, and ten others were exposed to 0.35 per cent halothane and air. Neither group was given food or water. Two hours later, each animal was given $^3$HHTip in a dose of 250 microcuries (specific activity 5.0 c/mMl). Four hours following this injection, all rats were killed by cervical dislocation and their femurs prepared for radioautography, as described previously. Results were analyzed statistically by chi-square tests.

**Results**

The rats receiving halothane all retained at least a sluggish righting reflex. As in previous studies, we divided the myeloid marrow cells into two compartments: cells which divide (myeloblasts, promyelocytes and myelocytes) and those which do not divide but continue to mature (metamyelocytes, stab neutrophils). The proportions of total marrow cells in these two categories were the same for air- and halothane.

**Fig. 1.** Schematic representation of sizes of granulocyte compartments and fluxes of cells under normal conditions, with inflammation, and with inflammation in the presence of halothane.

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**Table 1. Percentages of Rat Bone Marrow Granulopoietic Cells Having Labelled Nuclei Four Hours after Administration of 250 μc $^3$H**

<table>
<thead>
<tr>
<th></th>
<th>Dividing Cells*</th>
<th></th>
<th>Maturing Cells†</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Air</td>
<td>Halothane</td>
<td>$P$</td>
<td>Air</td>
</tr>
<tr>
<td>Present study</td>
<td>66</td>
<td>51</td>
<td>&lt; 0.001</td>
<td>13</td>
</tr>
<tr>
<td>Previous study</td>
<td>55</td>
<td>55</td>
<td>N.S.</td>
<td>11</td>
</tr>
</tbody>
</table>

* Myeloblasts, promyelocytes and myelocytes.
† Metamyelocytes and stab neutrophils.
thane-treated rats. The numbers of these cells carrying a radioactive nuclear label did differ (table 1). For comparison, data from our earlier study are included.

**DISCUSSION**

We believe that we have defined the degree of interference by halothane with granulopoiesis in these experiments more clearly than in the previous report. Halothane not only led to greater depression of labelling in the maturing cell compartment but also caused a diminution of dividing cell labelling not seen previously. Cyclophosphamide was given the day before this study to stress the granulopoietic system. It has been shown in the mouse and rat that a single dose of this drug will profoundly depress the number of nucleated cells in the bone marrow, reaching a low point 48 hours after injection, followed by rapid recovery. We chose to do our experiments during this period of depression in order to mimic the clinical situation in which the marrow is depressed from intrinsic disease, immunosuppressive drugs, or cancer chemotherapy. It has become increasingly common to anesthetize patients during these conditions; if anesthesia contributes to a worsening of leukopenia in such circumstances, we should be forewarned and attempt to minimize total anesthesia time.

During six hours of very light halothane anesthesia, only a fourth as many cells made the myelocyte–metamyelocyte transition as in the control animals. The significance of this derives from the knowledge of granulopoietic kinetics in man, a review of this comprising the source for the following information. The total blood granulocyte pool in man is about 44 per cent circulating cells and 56 per cent marginal cells; these two compartments being in equilibrium. It takes 11.4 days for a myelocyte to divide, mature, and appear in the blood. The total pool turns over 2.3 times a day, and once a cell disappears from the blood it does not return. A granulocyte stays in the circulation only seven hours.

From these data we can see how important it is to keep the flow of neutrophil precursors moving. There is a high rate of loss of circulating neutrophils which must be balanced by a continuing input from the maturing compartment marrow cells. Interference with the production of these precursors may result in a deficiency of neutrophils several days later. It is at this time that problems such as wound infection, pneumonia, atelectasis and the like are apt to occur.

Figure 1 depicts these concepts schematically and suggests two possible sites of action by halothane. The first is interference with the flow of bone marrow cells from dividing to maturing compartments, to which reference has been made. A second possibility is an inhibition of egress of marginal peripheral leucocytes into tissues. There is evidence that halothane inhibits mouse peritoneal neutrophil mobilization in response to intraperitoneal injection of endotoxin or live Salmonella. Anesthesia apparently interferes with the immune response. This, plus interference with the capacity of neutrophils for phagocytosis of bacteria, might make the anesthetist and prolonged operative procedures unwitting contributors to postoperative morbidity.

**SUMMARY**

Halothane (0.35 per cent) for six hours in rats previously given cyclophosphamide caused marked depression in labelling of maturing granulocytic marrow cells and moderate inhibition of labelling by dividing cells. This interference with the flow of neutrophil precursors might be reflected in a relative neutropenia several days postoperatively, and would be of clinical importance, particularly in patients with pre-existing bone marrow depression.

The authors thank Harold Traurig, Ph.D., for preparation of the radioautographs.

**REFERENCES**


A Variable-deadspace Device for Use with the Engström Respirator

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During long periods of artificial ventilation it is important to keep PaCO₂ constant, slightly below the normal range. In practice, this can be difficult. Studies of patients requiring long-term ventilation have shown that large tidal volumes at slow frequencies are necessary to expand the lung and prevent atelectasis. Further, this ventilatory pattern minimizes excessive shunting and compensates for the increased physiologic deadspace. An undesired sequel of this process has been a very low PaCO₂. Three methods are available to maintain a near-normal PaCO₂: 1) decrease respiratory rate; 2) increase inspired CO₂; 3) add mechanical deadspace. Since it is not always possible to decrease the respiratory rate sufficiently, and the addition of CO₂ to the inspired gas mixture necessitates additional flow-meters, tanks, and computation, the only practical method is the use of additional mechanical deadspace.4 4

This report describes a mechanical variable-deadspace device for use with the Engström Respirator. The device, which replaces the Y piece of the respirator, is made from a Foregger to-and-fro canister. Two sizes are used, the smaller with a volume of 315 ml, the larger with a volume of 510 ml (fig. 1). The canister is connected to the patient’s tracheostomy or endotracheal tube via a Foregger right-angle adaptor. The wire mesh at the patient end is fastened and left in place. At the other end, a 20 mm hole is drilled into the cylindrical body of the canister and a short metal pipe of the same diameter is soldered to it at a right angle to its central axis. A 17.5-cm-long metal pipe 20 mm in diameter is now pushed through the opening at the distal end of the canister, after removal of the wire mesh normally closing this side of the canister. This 20-mm pipe is supported by a rubber ring, which also seals the canister. The function of the device is that of a Y piece. The central long pipe is connected to the inspiratory tubing from the ventilator; the expiratory tubing is connected to the short pipe soldered to the canister.

Since the centrally located metal pipe is movable, it can be pushed in until its tip...