

# Postoperative Respiratory Effects of Morphine and Halothane Anesthesia:

A Study in Patients Undergoing Cardiac Surgery

Robert F. Bedford, M.D.,\* and Harry Wollman, M.D.†

Lung volumes, deadspace, ventilation, and ventilatory response to  $\text{CO}_2$  challenge were studied on the day before and for the first three days after corrective cardiac surgery. Ten patients underwent coronary artery bypass grafting and ten patients had mitral valve prostheses inserted. Half of the patients in each group received halothane as the major anesthetic, and the other half received morphine sulfate (1–2 mg/kg). Mitral valve-replacement patients anesthetized with morphine showed lower  $\text{CO}_2$  sensitivity on the first postoperative day than those who received halothane. Patients who had coronary artery bypass grafts tended to hyperventilate during the postoperative period, but this did not occur on the first postoperative day in those who received morphine anesthesia.

Respiratory rate was always higher postoperatively, most markedly in patients who received halothane for coronary artery bypass grafts. Vital capacity was diminished by 67 per cent in all groups postoperatively.  $V_D/V_T$  tended to increase during the first and second postoperative days and then decrease toward control values on the third postoperative day in all groups except valve-replacement patients who received morphine. Morphine anesthesia may increase the period of mechanical ventilation necessary after cardiac surgery partly as a result of impaired  $\text{CO}_2$  sensitivity. (Key words: Ventilation, postoperative; Surgery, cardiovascular; Analgesics, narcotic, morphine; Anesthetics, volatile, halothane.)

SPONTANEOUS VENTILATION is occasionally not possible for a number of days following corrective cardiac surgery, and there is evidence that the postoperative period of assisted ventilation may be prolonged by the use of large-dose morphine anesthesia.<sup>1</sup> Because opioids depress the ventilatory response to carbon dioxide, this study was undertaken to compare some of the postoperative respiratory effects of morphine and halothane anesthesia in patients undergoing open-heart surgery. Since it has been observed that patients who have mitral valve replacement tend to require longer periods of assisted ventilation and that those undergoing coronary artery bypass grafts require shorter periods,<sup>1</sup> both types of patients were studied in order to compare their postoperative respiratory performances.

## Methods

Twenty consecutive patients undergoing cardiac surgery (ten coronary artery bypass

1 Lecky J, Ominsky A, Wollman H: Postoperative ventilatory requirement in open heart patients—a prospective randomized study. Abstracts of Scientific Papers, American Society of Anesthesiologists, 1971 Annual Meeting.

\* Research Fellow in Anesthesia. Present address: Department of Anesthesia, Mary Imogene Bassett Hospital, Cooperstown, New York 13326.

† Professor of Anesthesia and Pharmacology.

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Address reprint requests to Dr. Bedford.

## ABBREVIATIONS

FEV<sub>1</sub>/FEV = ratio of forced expiratory volume in 1 second to total forced expiratory volume

$\text{Pa}_{\text{CO}_2}$  = arterial partial pressure of  $\text{CO}_2$  (torr)

$\text{Pa}_{\text{O}_2}$  = arterial partial pressure of  $\text{O}_2$  (torr)

$\text{P}\bar{\text{E}}_{\text{CO}_2}$  = mean expired partial pressure of  $\text{CO}_2$  (torr)

$\text{PET}_{\text{CO}_2}$  = end-tidal partial pressure of  $\text{CO}_2$  (torr)

VC = vital capacity

$V_D/V_T$  = deadspace-to-tidal volume ratio

$V_E$  = minute ventilation

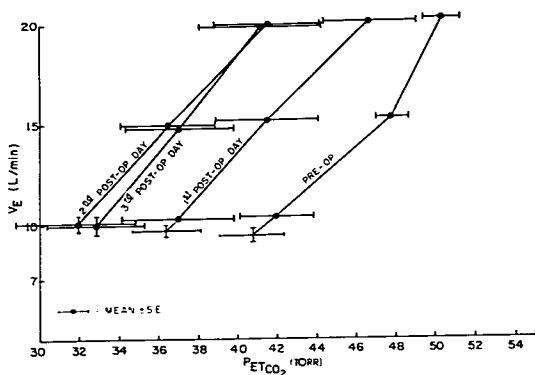


FIG. 1. Ventilatory responses to  $\text{CO}_2$  before and after coronary artery bypass grafts with halothane anesthesia. Moderate hyperventilation was present on the first postoperative day, progressing to marked hyperventilation on the second and third postoperative days.

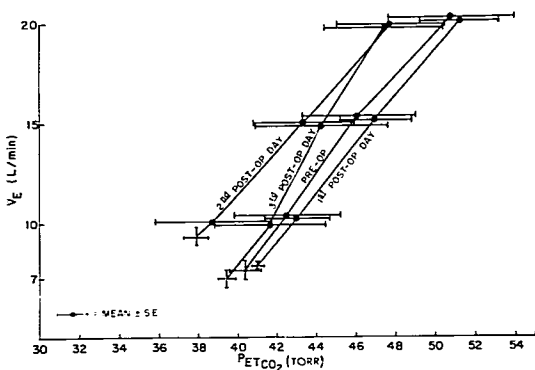


FIG. 2. Ventilatory responses to  $\text{CO}_2$  before and after coronary artery bypass grafts with morphine anesthesia. An insignificant decrease in  $\text{CO}_2$  sensitivity was present on the first postoperative day, followed by moderate hyperventilation on the second and third postoperative days.

grafts and ten mitral valve replacements) were studied after informed consent was obtained. All were New York Heart Association Class III, and none had evidence of pre-existing pulmonary disease. Control measurements were made the day before surgery. Half of the patients in each group received morphine, 1–2 mg/kg, with 50 per cent  $\text{N}_2\text{O}$  as the primary anesthetic, and the other half received halothane (.5 to 1.5 per cent) with 50 per cent  $\text{N}_2\text{O}$ . The anesthetic was chosen by coin toss. Preoperative medication consisted of morphine (0.1 mg/kg) and

scopolamine (0.6 mg), given intramuscularly 1 hour prior to induction of anesthesia. Muscle relaxation was afforded by administering *d*-tubocurarine (.5 mg/kg) at the beginning of operation in all cases. Chlorpromazine (1–2 mg) was given in iv boluses as necessary to control hypertension during morphine anesthesia (mean dosages: 4.2 mg for graft procedures and 2.3 mg for mitral valve operations). After operation, all patients were mechanically ventilated overnight. Morphine (2–4 mg, iv) was given as needed to alleviate discomfort until 2 A.M. of the

FIG. 3. Ventilatory responses to  $\text{CO}_2$  before and after mitral valve replacement with halothane anesthesia. There was a moderate decrease in  $\text{CO}_2$  sensitivity on the first and second postoperative days, followed by a return toward control sensitivity on the third postoperative day.

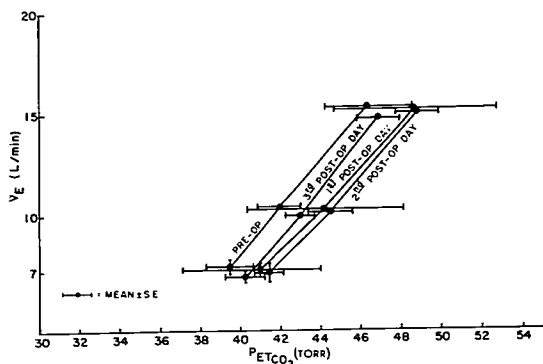
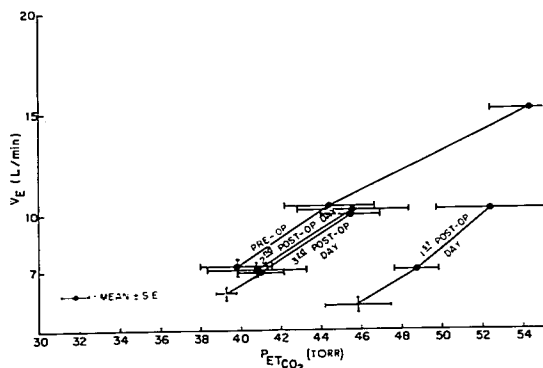


FIG. 4. Ventilatory responses to  $\text{CO}_2$  before and after mitral valve replacement with morphine anesthesia. There was marked depression of  $\text{CO}_2$  sensitivity on the first postoperative day, followed by a return to control  $\text{CO}_2$  sensitivity on the second and third postoperative days. Postoperatively, these patients could not increase minute ventilation to preoperative values.



morning after operation (mean dosages: 12.3 mg for grafts with halothane, 8.2 mg for mitral valve operations with halothane, 6.5 mg for grafts with morphine, 4.8 mg for mitral valve operations with morphine). Beginning at 8 A.M., all patients were allowed to breathe humidified 60 per cent  $\text{O}_2$  spontaneously via a T-piece and endotracheal tube for one hour. All studies on the first postoperative day were performed with the endotracheal tubes in place, since we could not be certain of the safety of extubating the trachea until respiratory studies were completed. None of

the patients showed signs of respiratory failure. The tracheas of all patients were then extubated and repeat studies on the second and third days were performed via a mouthpiece.

Patients rebreathed into a Collins 13.5-liter spirometer adapted for simultaneous determination of end-tidal  $\text{CO}_2$  concentration and minute ventilation as previously described.<sup>1</sup> When steady-state  $\dot{V}_E$  and  $\text{PETCO}_2$  had been achieved, baseline respiratory rate,  $\dot{V}_E/\dot{V}_T$ , and vital capacity were determined. Simultaneously, arterial blood was withdrawn via

an indwelling cannula for determination of  $P_{aO_2}$ ,  $P_{aCO_2}$ , pH, and base excess. The  $CO_2$  absorber was then bypassed and the ventilatory response to  $CO_2$  observed. End-tidal  $CO_2$  concentration increased at approximately 1 torr/min during rebreathing. Minute ventilation and end-tidal  $CO_2$  were plotted simultaneously on a dual-channel recorder (Texas Instruments), and recorded at 20-second intervals during  $CO_2$  response.  $CO_2$  challenge was terminated when patients complained of dyspnea or tightness in the chest, or when end-tidal  $P_{CO_2}$  exceeded 55 torr. Circuit resistance to breathing was 0.2 cm  $H_2O/l$  per minute. All postoperative studies were performed with continuous monitoring of arterial and central venous pressures and the EKG. None had to be terminated due to deterioration in vital signs.

$CO_2$  concentration was measured with a Godart infrared  $CO_2$  analyzer calibrated with gases of known concentration.  $PET_{CO_2}$  was determined by continuous sampling from the spirometer mouthpiece.  $P\bar{E}_{CO_2}$  was sampled

from a 2-liter baffled mixing chamber on the expiratory limb of the spirometer.

$V_D/V_T$  was determined by the formula:

$$\frac{PET_{CO_2} - P\bar{E}_{CO_2}}{PET_{CO_2}}$$

$V_E$  and VC were determined from the spirometer tracing and corrected to BTPS.  $CO_2$  sensitivity curves were compared statistically at a minute ventilation of 10 liters, BTPS, because many patients could not achieve higher values in the postoperative period.

Since there were several experimental groups, statistical comparisons were made by analysis of variance and critical difference testing.<sup>2</sup>

## Results

Figures 1-4 summarize the results of the  $CO_2$  response studies. Coronary artery bypass graft patients anesthetized with halothane (fig. 1) tended to hyperventilate on the first

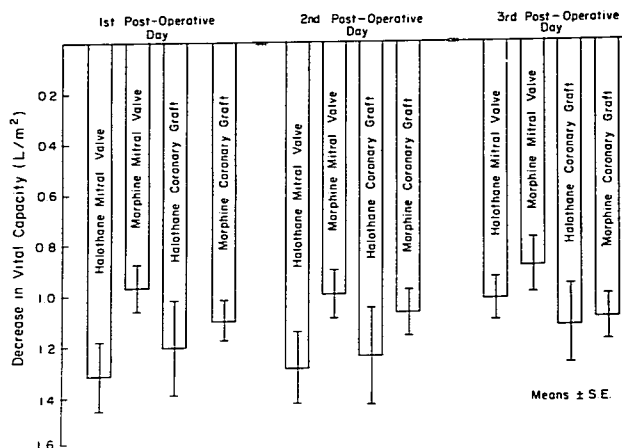


FIG. 5. Changes in vital capacity from preoperative values following cardiac surgery. There was a 67 per cent overall reduction in VC postoperatively. Patients anesthetized with morphine tended to have less impairment in VC than those who received halothane, although the difference was not statistically significant.

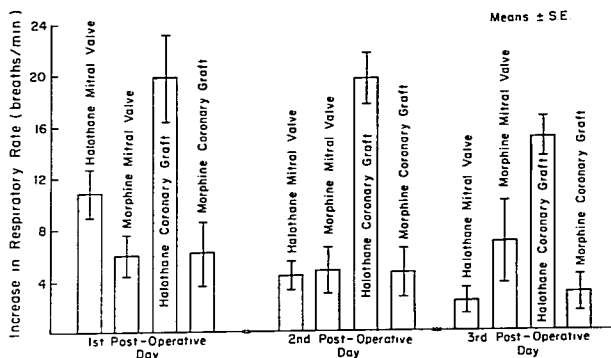


FIG. 6. Changes in respiratory rate from preoperative values. Patients anesthetized with halothane had greater increases in respiratory rate than morphine-anesthetized patients on the first postoperative day. The graft-halothane group hyperventilated throughout the postoperative course.

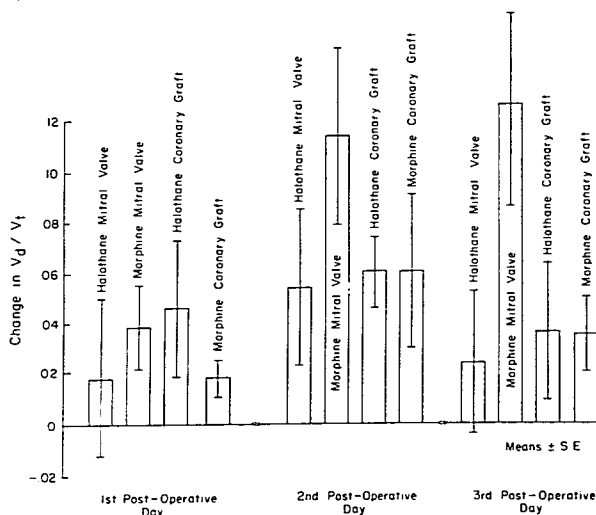


FIG. 7.  $V_D/V_T$  ratios following cardiac surgery.  $V_D/V_T$  rose on the second postoperative day after the endotracheal tube had been removed, and tended to return toward control by the third day, except in the morphine-valve-replacement group.

postoperative day and hyperventilated more markedly ( $P < .05$ ) on the second and third postoperative days. Those graft patients anesthetized with morphine (fig. 2) had  $\text{CO}_2$  response curves unchanged from preoperative values on the first postoperative day, but the curves then tended to shift to the left (hyperventilation) on the second and third postoperative days, although this shift was not significant at the .05 level.

Patients undergoing mitral valve operations responded differently. Those anesthetized with halothane (fig. 3) did not show a significant change from control  $\text{CO}_2$  sensitivity. Valve-replacement patients who received morphine (fig. 4) showed marked impairment of ventilatory response to  $\text{CO}_2$  on the first postoperative day, with a significant ( $P < .05$ ) shift of the curve to the right from control measurements. On the second and third days this group returned to preoperative  $\text{CO}_2$  response, although the patients were unable to increase minute ventilation to preoperative values.

Vital capacity was markedly impaired ( $P < .001$ ) in the postoperative period for all patients (fig. 5), resulting in a 67 per cent overall reduction from control values. There was no significant difference among the experimental groups, and there was no significant improvement in vital capacity during the first three postoperative days.

Respiratory rates were always higher after operation than before (fig. 6). Patients who received halothane showed greater increases in respiratory rate on the first postoperative day than did the morphine-anesthetized patients ( $P < .05$ ). The patients in the graft-halothane group continued to hyperventilate significantly throughout the postoperative study period.

The  $\dot{V}_D/\dot{V}_T$  ratio tended to increase over control values following cardiac surgery (fig. 7), although the only significant ( $P < .05$ ) elevation occurred in the valve-replacement-morphine group on the second and third postoperative days after the endotracheal tubes had been removed.

End-tidal  $P_{\text{CO}_2}$  values differed from simultaneous arterial  $P_{\text{CO}_2}$  values by  $\pm 1.68$  torr, with a standard deviation of 1.42 torr. There was no significant difference among the

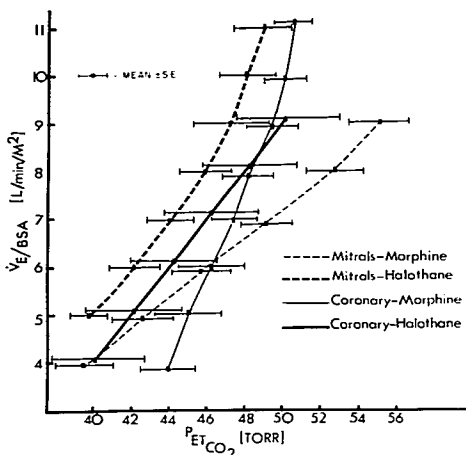
groups studied.  $\text{PaO}_2$  was always more than 100 torr during  $\text{CO}_2$  rebreathing.

## Discussion

Control  $\text{CO}_2$  response curves were similar for all groups of patients except those who were about to undergo mitral valve replacement with morphine anesthesia. The slope of their ventilatory response curve was consistently flatter than those of the other groups. The only explanation for this appears to be the differences in the sizes of the patients. The mean body surface area of the valve-replacement patients was  $1.68 \text{ m}^2$  compared with  $2.1 \text{ m}^2$  for the graft patients. Correcting minute ventilation for the differences in patient size results in more uniform control  $\text{CO}_2$  response curves (fig. 8), and although curve for the valve-replacement-morphine group is still somewhat flattened, it is probably within the range of normal variation. We elected not to present the data corrected for discrepancies in patient size, since the majority of adult  $\text{CO}_2$  response studies have measured minute ventilation alone. However, pulmonary function data for our patients were remarkably similar to data obtained by Weintraub *et al.*<sup>2</sup> in cardiac patients prior to corrective surgery. Preoperative  $\text{PaO}_2$  breathing room air was always higher in graft patients (mean 68 torr) than in valve-replacement patients (mean 59.2 torr).

Mitral valve-replacement patients anesthetized with morphine consistently showed a significant rightward shift of the curve of the ventilatory response to  $\text{CO}_2$  on the first postoperative day. Lecky *et al.*<sup>1</sup> observed that this group of patients required longer periods of postoperative ventilation following heart surgery than did mitral valve-replacement patients who received halothane anesthesia. Using Lecky's criteria for extubation following cardiac surgery, several of our valve-replacement-morphine patients would have been ventilated for another 24 hours before their tracheas were extubated, primarily because of elevated resting  $\text{PaCO}_2$  levels. The tracheas of all our patients were extubated after studies had been completed on the first postoperative day, and patients who had marginal respiratory function received more intensive inhalational and physical

FIG. 8. Ventilatory responses to  $\text{CO}_2$  before cardiac surgery. Control  $\text{CO}_2$  response curves corrected for patients' sizes. While the curve for the valve-replacement-morphine group is slightly flattened compared with the others, this graph shows them to be in fact closer than in figure 4, where patient size was not considered.



therapy thereafter. No attempt was made to reverse residual narcotic effects.

It is possible that intraoperative chlorpromazine and postoperative morphine administration augmented the observed respiratory depression in the valve-replacement-morphine group. However, these patients received considerably less of these drugs than did the graft-morphine group, whose  $\text{CO}_2$  sensitivity was unchanged from control values. Stanley (personal communication) measured morphine in blood and urine after its use for anesthesia in both mitral valve replacement and coronary artery bypass graft operations and observed considerably slower morphine excretion and higher postoperative blood levels in valve-replacement patients. This may explain the prolonged respiratory depression seen in these patients.

By the second and third postoperative days, valve-replacement-morphine patients had  $\text{CO}_2$  sensitivities unchanged from control values, except that they were unable to achieve as great a peak minute ventilation during  $\text{CO}_2$  rebreathing as they had been able to attain prior to operation. The  $\text{V}_E/\text{V}_T$  ratio was also significantly elevated in this group on the second and third postoperative

days, but respiratory rate and vital capacity were not significantly different from those in the other groups.

Mitral valve-replacement patients anesthetized with halothane responded differently. There was no significant change from preoperative  $\text{CO}_2$  sensitivity, and  $\text{V}_E/\text{V}_T$  was not significantly greater than control. Peak minute ventilation during  $\text{CO}_2$  rebreathing was unchanged after operation, although postoperative vital capacity was reduced as much in this group as in the morphine-anesthetized patients. None of these patients would have needed additional mechanical ventilation after the first postoperative day.

Patients who had coronary artery bypass grafts showed increased sensitivity to  $\text{CO}_2$  after operation, with a leftward shift of the  $\text{CO}_2$  response curve that was most pronounced on the second postoperative day. There was no evidence of metabolic or pulmonary factors that could cause this. Rather, the resistance of the spirometer and a slight metabolic alkalosis should have decreased  $\text{CO}_2$  sensitivity. However, the graft patients, as a group, were more alert and active than the valve-replacement patients, and their sternum-splitting incisions were less uncomfortable than the thoracotomy inci-

sions used for mitral valve replacement. Initially, the graft patients responded to spirometry by hyperventilating. This was most apparent in the halothane group on the first postoperative day, despite relatively large postoperative doses of morphine. The morphine-anesthetized patients were more sedated on the first postoperative day, possibly as a result of chlorpromazine given in addition to morphine during operation. They did not respond by hyperventilating until the second and third postoperative days. Concomitant with the leftward shift in the  $\text{CO}_2$  response curve was a significantly increased respiratory rate in the halothane group. We attribute this to psychogenic factors rather than true respiratory stimulation. Comparing morphine and halothane for coronary artery bypass graft procedures, there was no significant postoperative difference in  $\text{V}_\text{E}/\text{V}_\text{T}$  ratio, vital capacity, or peak  $\text{V}_\text{E}$  during  $\text{CO}_2$  rebreathing.

In comparison with the valve-replacement patients, graft patients had superior overall respiratory function. By purely clinical criteria, many of those who received halothane anesthesia could have had their tracheas extubated safely within 4 to 6 hours of operation. They were ventilated overnight only to insure that all experimental groups were treated in a similar fashion.

Many factors affect the ventilatory response to  $\text{CO}_2$ . Narcotics,<sup>1</sup> metabolic alkalosis,<sup>4</sup> increased resistance to breathing,<sup>5</sup> and obstructive airway disease<sup>6</sup> have all been shown to decrease  $\text{CO}_2$  sensitivity. None of our patients had significant obstructive pulmonary disease: preoperative  $\text{FEV}_1/\text{FEV}$  was greater than 75 per cent in all cases. All had similar metabolic alkalosis in the postoperative period (mean base excess = +4.18 mEq/l; SE = 1.6) and all breathed against the same spirometer resistance. We attribute the low-normal control  $\text{CO}_2$  sensitivity slopes to the resistance to breathing within the spirometer system.

Vital capacity was reduced by 67 per cent in the postoperative period, with no significant difference among the four groups of patients. Vital capacity did not improve significantly during the first three postoperative days. Weintraub *et al.*<sup>3</sup> found that vital capac-

ity returned to preoperative values within 50 days following corrective cardiac surgery.

The main problem in studying the ventilatory response to  $\text{CO}_2$  was patient reluctance to continuing  $\text{CO}_2$  rebreathing after an increase of only 5–10 torr  $\text{PET}_{\text{CO}_2}$ . Graft patients frequently developed angina during preoperative studies, and many valve-replacement patients were slightly dyspneic at rest and refused to breathe more than twice their resting minute ventilations. Postoperatively, graft patients were free of angina, but complained of incisional discomfort over the sternum as minute ventilation surpassed 20 liters. Valve-replacement patients had right thoracotomy incisions and seemed to complain of discomfort much earlier during  $\text{CO}_2$  rebreathing. Frequently, they would initially respond with increasing minute ventilation as  $\text{PET}_{\text{CO}_2}$  increased, but would then level off, although  $\text{CO}_2$  continued to accumulate. When requested to breathe harder, they were unable to do so and refused to continue the experiment.

In summary, we found that patients who receive morphine anesthesia for corrective heart surgery have impaired ventilatory responses to  $\text{CO}_2$  in the postoperative period compared with patients who receive halothane as the major anesthetic. Patients who underwent mitral valve replacement were more sensitive to the residual respiratory depression from morphine than were those who underwent coronary artery bypass grafts. Patients who had grafts tended to hyperventilate postoperatively, and this was most marked in those who received halothane. The clinical implication of this study is that the requirement for prolonged mechanical ventilation observed in some patients who receive morphine anesthesia, particularly for mitral valve replacement, may be in part the result of impaired  $\text{CO}_2$  sensitivity.

Many other factors may dictate the need for long periods of postoperative assisted ventilation following corrective cardiac surgery. Heart failure, renal shutdown, CNS dysfunction, pulmonary disease, and sepsis are some of the most common of these complications. However, in the preoperative choice of an anesthetic, the clinical advantages of large-dose morphine administration should be



weighed against the prolonged postoperative respiratory depression that may result.

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### Pulmonary Circulation

#### X-RAYS AND PULMONARY VASCULARITY

The authors present a radiologic technique to evaluate pulmonary vascularity in children suspected to have congenital heart disease. They used the diameter of the right descending pulmonary artery (RDPA) by correlating the diameter of the RDPA with that of the trachea. The growth curves with the RDPA and the tracheal diameters are not strictly parallel, according to the authors, but are quite close. It was found that when a left-to-right shunt existed the RDPA never had a diameter less than that of the trachea. They reviewed 120 chest radiographs of normal children and 102 of children with left-to-right shunts and in so doing substantiated this observation. (Cousement, A. M., and Gooding, C. A.: *Objective Radiographic Assessment of Pulmonary Vascularity in Children. Radiology* 109:649-654, 1973.)

**ABSTRACTER'S COMMENT:** This particular method of determining the state of pulmonary vascularity in children is fraught with danger.

So much depends on the technique and positioning of the child. Surely in children less than 2 years of age one cannot use this method because of the presence of the thymus, making it more difficult to assess both tracheal and RDPA diameters. In addition, the cooperation of the pediatric patient is needed and rarely obtained in an effort to have a proper film obtained, and inflammatory changes in the lungs can make measurements difficult and unreliable. As the authors mention, some children have unusually small or large tracheas, and false-positive or false-negative findings may result. Fortunately, the conclusion of the authors is that assessment of increased pulmonary vascularity should not be based on these measurements alone. This is still for the most part a clinical judgement in assessment of a chest x-ray, though the authors suggest that if the RDPA has a diameter less than that of the trachea a left-to-right shunt is improbable.