A REPORT OF SEVEN ADMINISTRATIONS OF CHLOROFORM FOR OPEN THORACIC OPERATIONS

KARL L. SIEBECKER, M.D., AND O. SIDNEY ORTH, M.D.

There has been controversy over the use of chloroform since 1847 when Sir James Y. Simpson successfully used it as an anesthetic agent for major operations and in midwifery. Ralph M. Waters (1) in 1951 edited a monograph (from the Department of Anesthesiology of the University of Wisconsin Medical School) in which there was reported the study of chloroform by modern methods as would be done with a new agent. It was found to be a potent anesthetic agent, safe to use in trained persons’ hands, provided certain specific precautions were observed. These are, primarily, assurance of adequate oxygenation of the patient at all times, and prevention of hypercarbia. In the Wisconsin series of 1,111 administrations there were only 2 intrathoracic cases done in which chloroform was the primary anesthetic agent. No untoward results were noted in these 2 patients, or in 3 other patients who underwent open thoracic procedures where other anesthetic agents were used. It was noted in dogs that hepatic damage was quite likely if hypoxia or hypercarbia or both were allowed to occur during the administration of chloroform.

Clinically it is difficult to judge “low-grade” chronic hypoxia. Conrowe and Botelho (2) showed that blood oxygen saturation may drop to 70 per cent or below before it is recognized by supposedly competent observers. Many writers have noted the presence of acidosis during open thoracic procedures (3–8), and have attributed the acidosis to various causes. It is somewhat commonly agreed, however, that it does occur and unusual caution as to adequate assistance of respiration is necessary throughout all phases of the anesthetic administration. It has been noted that changes in acid-base balance can occur quite rapidly (9). Also, elevations in carbon dioxide levels are easily attained in patients without the knowledge of the anesthesiologist when he is depending only on ordinary clinical signs (10). The existence of the above evidence in the literature would make it appear that the administration of chloroform for open thoracic procedures would be a precarious undertaking. As further evidence in support of this view the following 7 cases are reported.

Case No. 1.—A 28-year-old male patient was admitted to the hospital in March, 1952. He had had tuberculosis with intermittent hospitalization and occasional varied treatment since 1948. He was treated medically with strep-

Accepted for publication July 9, 1956. Dr. Siebecker is Assistant Professor, and Dr. Orth is Professor and Chairman, Department of Anesthesiology, Medical School, University of Wisconsin, Madison, Wisconsin.

792
tomycin, sodium para-aminosalicylate and isonicotinic acid hydrazide. His sputum had been found positive for tubercle bacilli on both smear and culture. The disease was bilateral, most marked in the right upper lobe. The disease remained stable through three months of medical treatment, and he was brought to the operating room for segmental resection of the right upper lobe in June, 1952. He was anesthetized with sodium thiopental and ether for a three hour procedure, consisting of segmental resection of the upper lobe of the right lung. Chloroform was added to the anesthetic mixture for the last few minutes, during closure of the wound. The course of anesthesia was uneventful and there were no postoperative complications.

In August, 1952 (two months later) he was anesthetized with sodium thiopental and cyclopropane for a segmental resection of the upper lobe of the left lung. The procedure lasted two hours. The course of the anesthetic was uneventful, and the postoperative course was uncomplicated.

Case No. 2.—A 30-year-old male patient was admitted to the hospital in August, 1952. He had been known to have tuberculosis since 1949, and had been treated in and out of sanatoriums intermittently. On admission, his roentgenogram showed progression of the disease, but sputum and gastric tests were negative for tubercle bacilli. He was treated with streptomycin, sodium para-aminosalicylate and isonicotinic acid hydrazide, with marked regression of the disease. In January, 1953, he was brought to the operating room for segmental resection of the upper and lower lobes of the right lung. He was anesthetized with sodium thiopental, d-tubocurarine, nitrous oxide and chloroform. The operation lasted one and three-quarter hours, and the course of the anesthetic was uneventful. Postoperatively he had marked hemorrhage, which required a thoracotomy for removal of a blood clot and hemostasis 24 hours later. At this time he was anesthetized with nitrous oxide, sodium thiopental and gallamine with no untoward effects. His postoperative course was uneventful.

In March, 1953, a left upper lobectomy was done, at which time he was anesthetized with nitrous oxide, sodium thiopental and gallamine. As before, he bled postoperatively and it was necessary to perform a thoracotomy for hemostasis and clot removal. Nitrous oxide, a barbiturate, and a relaxant were again used with no apparent ill effect.

Case No. 3.—This 50-year-old man developed symptoms of tuberculosis in March, 1952. He was hospitalized at that time, and transferred to this hospital in June, 1952. He responded well to treatment with streptomycin and sodium para-aminosalicylate. In January, 1953, he underwent segmental resection of the upper and lower lobes of the right lung. He was anesthetized with chloroform, nitrous oxide, sodium thiopental and curare without difficulty. There were no postoperative complications.

Case No. 4.—A 57-year-old male patient developed tuberculosis in June, 1952. He received antimicrobial therapy consisting of isonicotinic acid hydrazide beginning in August, 1952. In January, 1953, a right upper lobectomy was done. Anesthesia was induced with sodium thiopental and gallamine. An endotracheal tube was placed and anesthesia for the thoracotomy was maintained for four hours and fifty minutes with nitrous oxide, oxygen and chloroform. Chloroform was used for a period of two hours and forty-five minutes. The first 24 hours postoperatively, the patient’s condition was apparently satisfactory. The evening of the first postoperative day, however, the patient began to have high “spiking” fever, hypotension, and auricular fibrillation. The latter
was controlled by the administration of digitalis. He became comatose and
developed progressive jaundice. He died on the third postoperative day. No
laboratory tests relative to the jaundice were done on this patient.

Post-mortem examination revealed acute central necrosis of the liver. This
was attributed to the chloroform anesthesia with probable inadequate oxygena-
tion for a prolonged period.

Case No. 5.—A 48-year-old male patient developed tuberculosis in December
of 1950. He entered this hospital in August, 1952, and was treated with strep-
tomycin and isonicotinic acid hydrazide. There was a history of chronic
alcoholism and early Laennec’s cirrhosis. In January, 1953, a segmental resec-
tion of the upper lobe of the right lung was done. Anesthesia was begun with
sodium thiopental and d-tubocurarine for intubation. Anesthesia was main-
tained with nitrous oxide and oxygen for two hours and fifteen minutes. Chloro-
form was added for a period of almost two hours.

During the first postoperative day a sample of blood, taken for a hematocrit
determination, showed an icteric tint of the plasma. On the second postopera-
tive day the patient developed vomiting, hypotension and “mental cloudiness.”
The sclerae became icteric and the blood icterus index rose to 120. The cephalin
cholesterol flocculation test was four plus. The patient failed to respond to
supportive therapy and died on the fourth postoperative day. Post mortem
examination revealed extensive, severe centrlobar necrosis of the liver. Renal
tubular degeneration was present and considered to be secondary to the hepatic
necrosis. This liver damage was considered to be due to chloroform poisoning
in the presence of probable chronic hypoxia during the course of the anesthetic.

Case No. 6.—A 30-year-old male patient first developed tuberculosis in
1946. He was treated by bed rest for a short time, and received checkups at
six month intervals. The disease became active again in 1952, and the patient
was admitted to the hospital in September. He was treated with streptomycin
and isonicotinic acid hydrazide. In January, 1953, an apical posterior seg-
mental resection of the upper lobe of the left lung was done. Anesthesia was
begun with sodium thiopental and d-tubocurarine for intubation and then main-
tained with nitrous oxide and oxygen for two hours and ten minutes. Chloro-
form was added for a period of one and one-half hours. The course of the
anesthetic period was apparently uneventful.

This patient developed symptoms of toxic hepatitis manifested by anorexia
and nausea on the second postoperative day. His icteric index was 80 units on
the third postoperative day, declining to nine units on the twenty-third day.
The cephalin cholesterol flocculation test ranged from three plus to zero.

He recovered clinically with no apparent permanent damage. This episode
was also attributed to chloroform intoxication in the presence of mild to moderate
hypoxia and hypercapnia.

Case No. 7.—A 29-year-old male patient who developed symptoms of tuber-
culos is in 1948. He received various forms of therapy for four years, including
pneumoperitoneum, pneumothorax, pneumonolysis and antimicrobial therapy.
He received courses of streptomycin, sodium para-aminosalicylate, and isoni-
oc tinic acid hydrazide. He entered this hospital in July, 1952, and was brought
to the operating room for a segmental resection of the upper and lower lobes
of the right lung in January, 1953. He was anesthetized with sodium thiopental
and gallamine for endotracheal intubation and anesthesia was maintained for
three hours and forty-five minutes with nitrous oxide and oxygen. Barbiturate
and curare were added as deemed necessary, and chloroform was added "in minimal amounts" intermittently during the course of the operation. On the second postoperative day a blood sample was drawn for hematocrit determination and the plasma was noted to be icteric. An icterus index done this day showed 40 units. The cephalin cholesterol flocculation test was two plus. The only clinical symptom of hepatitis was an icterus of the sclerae. On the fourth postoperative day the icterus index had risen to 80 units. All laboratory and clinical evidence of hepatitis had disappeared by the eighteenth postoperative day.

In March, 1952, the patient was again anesthetized for a segmental resection of the upper lobe of the left lung, and decortication of the lingula and lower lobe of the left lung. At this time anesthesia was induced with thiopental sodium and succinylcholine for intubation. Anesthesia was maintained with ether and cyclopropane for a period of three hours. It was noted by the anesthesiologist that it was difficult to keep the patient adequately oxygenated and normocapnic whenever the lung had to be compressed by the surgeons for any length of time. The postoperative course was completely uneventful for this operation, and all liver function tests were normal.

**Discussion**

Examination of the anesthesia records of both patients who received severe enough hepatic damage to cause death reveals that there were periods of hypotension and bradycardia during the administration of chloroform. These are danger signals during the administration of this agent and should be considered indicative of overdose.

The salient facts from the 7 patients who had open thoracic operations are summarized in table 1. There is indicated the surgical procedures performed, the length of the anesthetic period, the duration of chloroform administration and a detailed report of the postoperative course, including laboratory and pathological studies. It is evident that in 4 of the 7 patients severe hepatic damage developed which was sufficient to cause death in 2 of the patients. It is fair to assume that the administration of chloroform in the presence of possible hypoxia or hypercarbia or both was the cause of the hepatic damage.

It is believed that the results from these 7 cases should be recorded in the literature, again to emphasize the fact that adequate assurance of oxygenation and ventilation, in order to remove carbon dioxide, are primary requisites in the safe use of chloroform. The monograph (1) reporting the evaluation of this agent by modern methods on its centenary emphasized these facts very explicitly. They should be kept in mind constantly if chloroform is employed for anesthetizations.

**Summary**

Seven instances of chloroform administration during open thoracic procedures are presented. The case reports are summarized in tabular form as to the postoperative course, laboratory findings and the patho-
<table>
<thead>
<tr>
<th>Case Number</th>
<th>Operation</th>
<th>Postoperative Complications</th>
<th>Laboratory Results</th>
<th>Pathological Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Segmental resection R. upper lobe*</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>Segmental resection L. upper lobe*</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>3</td>
<td>Segmental resection R. upper lobe*</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>4</td>
<td>Segmental resection L. upper lobe*</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>5</td>
<td>Chronic alveolar pneumonia, L. upper lobe*</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>6</td>
<td>Segmental resection R. upper lobe*</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>7</td>
<td>Segmental resection L. upper lobe*</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

*Premedication 0.3 mg. atropine.  
1 Premedication 0.3 mg. atropine.  
2 Premedication 0.3 mg. atropine.
logical reports. Two of the 7 patients died due to acute centrilobar necrosis of the liver, and 2 more presented clinical and laboratory evidence of toxic hepatitis.

The dangers of chloroform administration under other than optimal conditions are emphasized. Possible contraindications to the use of chloroform during anesthesia for open thoracic procedures are noted. It is re-emphasized that the precautionary measures of adequate ventilation to remove carbon dioxide and to provide adequate oxygen for the patient must be maintained continuously during the administration of chloroform.

ACKNOWLEDGMENT

The authors are indebted to the individuals who supplied the reports for this paper and the hospital where the chloroform administrations occurred for permitting publication.

REFERENCES