rated shot and its parent flowmeter. It is likely that the cement originally holding this shot within the bobbin failed, allowing it to be propelled by a high gas flow out of the bobbin and flowmeter tube into the metal tubing system of the machine. The shot was recemented into the bobbin, the flowmeter reassembled, and the calibration verified. Flowmeter behavior has been normal since.

An attempt to contact the Chicago Anesthesia Equipment Company to notify them of this incident was unsuccessful. However, several other sources contacted stated that this firm went out of business approximately seven years ago and has no representative at present.

The purpose of this report is to draw attention to this potential defect in other anesthesia machines still in use made by this manufacturer. Erratic behavior of any of the flowmeters on these machines should be cause to investigate the possibility of bobbin failure as described here.

Prolonged Intraoperative Bleeding Caused by Propylthiouracil-induced Hypoprothrombinemia

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Although hypoprothrombinemia as a result of propylthiouracil therapy was first reported more than 20 years ago, the syndrome is rare, and its existence not generally recognized. In all cases reported previously the initial manifestation was a bleeding tendency, generally associated with metrorrhagia, hematuria, epistaxis, or or pharyngeal bleeding. We present a case of prolonged and troublesome intraoperative bleeding due to hypoprothrombinemia secondary to propylthiouracil therapy, and not recognized prior to operation.

REPORT OF A CASE

A 52-year-old woman was admitted to St. Mary's Hospital with recurrent hyperthyroidism. Three years previously she had developed tremor, palpitations, sweating, and weight loss, for which she underwent subtotal thyroidectomy. The symptoms recurred and, ten months later, the operation was repeated. Despite therapy with methimazole, the symptoms recurred and the patient was clinically hyperthyroid. There was no history of heavy alcohol intake, hepatic disease, or bleeding tendency. On physical examination at the time of admission the pulse rate was 80/min, blood pressure 120/70 mm Hg, and oral temperature 98.6°F. Examination disclosed no abnormalities except an enlarged right lobe of the thyroid. Chest x-ray demonstrated mild cardiomegaly, and the electrocardiogram evidenced left ventricular hypertrophy. Serum electrolytes were normal, as were transaminase and lactic dehydrogenase levels. The hemoglobin was 14.0 g/100 ml and the hematocrit 43 per cent. The leukocyte count was 1,900, with a normal differential and platelets described as adequate. Radioactive iodine uptake was 43.5 per cent, and scan demonstrated that most of the activity was concentrated in the right lobe of the thyroid. Methimazole was discontinued 13 days before operation and replaced by propylthiouracil, 200 mg orally every six hours, and reserpine, 0.1 mg orally daily. Reserpine was discontinued after three days (ten days preoperatively), and propylthiouracil was stopped five days before operation. Lugol's solution, 10 drops three times per day, was started on the seventh preoperative day and continued until the day before operation. The patient was anesthetized with thiopental, nitrous oxide, oxygen, and halothane for right thyroid lobectomy on the thirteenth day after admission. The anesthetic course was uneventful. However, profuse bleeding occurred at the operative site, was controlled only with difficulty, and continued as a troublesome ooze into the postoperative period.

The patient received no blood transfusion during operation. In the Recovery Room prothrombin time was determined to be more than 200 seconds, with a control of 12 seconds. Partial thrombo-
plasmin time was also more than 200 seconds, with a control of 31 seconds. Fibrinogen was 100 mg/100 ml (normal 200–400 mg/100 ml). The patient received 25 mg vitamin K$_1$ intramuscularly and two units of fresh frozen plasma. On the first postoperative day the prothrombin time was 15 seconds, with a control of 11.8 seconds, and the partial thromboplastin time was 38 seconds, with a control of 31 seconds. Several times hematomas developed at the wound site and were aspirated without difficulty. On the first postoperative day the hemoglobin was 11.7 g/100 ml and the hematocrit 38 per cent. The patient is now euthyroid and receiving no medication. She has no signs of increased bleeding tendency.

**DISCUSSION**

Propylthiouracil can depress bone marrow function and cause aplastic anemia, which may manifest as hemorrhage. While aplastic anemia is not uncommon with use of the drug, a more unusual syndrome, i.e., depression of prothrombin activity, with prolonged prothrombin time and bleeding tendency, has been described in patients having in common only that they were hyperthyroid women receiving propylthiouracil. No other common denominator is known, and the patients have ranged in age from 13 to 85 years. The times to onset of recognizable increased bleeding have ranged from 2 weeks to 13 months after the start of propylthiouracil. In one patient four days of therapy with the drug induced the hypocoagulable state. Even after vitamin K$_1$ therapy and discontinuation of propylthiouracil, prothrombin levels have remained depressed for as long as two months. In other cases, there was no discernible cause for depression of prothrombin activity in our patient, other than propylthiouracil. There was no history of exposure to liver toxins, liver function was normal, there was no family history of bleeding diseases, no evidence of malabsorption syndrome, and no history of prolonged or poorly controlled bleeding prior to propylthiouracil therapy.

The mechanism by which prothrombin activity is depressed by propylthiouracil has not yet been elucidated. It has been postulated that the activities of several clotting factors are depressed—e.g., stable factor, Stuart factor, prothrombin, plasma thromboplastin component, and proconvertin, an effect closely resembling that of bis-hydroxycoumarin. In fact, vitamin K$_1$ is usually, although not invariably, effective in restoring normal clotting. In those cases in which vitamin K$_1$ has not proven successful, transfusions of whole blood have been effective. Although the syndrome is rare, its potential danger is great. It is suggested that a prothrombin time determination whenever propylthiouracil is given be routine.

**SUMMARY**

By a mechanism that is not completely understood propylthiouracil exerts a bis-hydroxycoumarin-like effect and causes a hypocoagulable state, usually clinically manifested by hemorrhagic diathesis. A case wherein the condition was not recognized preoperatively is presented. The syndrome is usually responsive to vitamin K therapy. It is suggested that all patients receiving propylthiouracil have their prothrombin times evaluated.

**REFERENCES**