

## THE ANESTHETIC MANAGEMENT OF HYPOPHYSECTOMIZED PATIENTS

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TOTAL hypophysectomy for pituitary tumor, advanced carcinoma of the breast, fulminant juvenile diabetes, and other conditions is now being performed with increasing frequency (1, 2). Recent advances in endocrine replacement therapy have reduced the postoperative mortality. The hypophysectomized patient, with this increased longevity, may develop conditions which might require further operative procedures. Since these patients have a delicate hormonal balance it is important for the anesthesiologist and the surgeon to become familiar with the possible abnormal physiologic responses of these patients and their proper management. In the past few years, we have administered general anesthesia to 4 hypophysectomized patients at 6 operations performed at the Memorial Center for Cancer and Allied Diseases. This report reviews briefly some of the important physiologic factors in hypophysectomized patients and presents our experience in the management of patients during these operations.

### PHYSIOLOGIC ASPECT OF HYPOPHYSECTOMY

The hypophysis has many known functions, and some not yet recognized. The complete operative removal of the pituitary gland is not usually fatal in itself, although the physiologic derangements which it engenders result in shortening of the life span. By proper treatment and management, these derangements can be effectively combated. They can be outlined as follows:

*Sensitivity to Stress.*—Hypophysectomized animals are extremely sensitive to stress, especially an acute one (3, 4). Selye and Heuser (5) believe that adrenal response during the alarm reaction is prevented. Experimentally, in hypophysectomized rats, epinephrine or stimuli which provoke the release of epinephrine do not bring about any fall in the circulating eosinophils or adrenal ascorbic acid content, which are generally recognized as responses to an increased blood level of adrenal cortical hormones. This is, however, not the sole explanation for sensitivity to stress. Possibly there are other factors involved which are not yet understood (3, 4, 5).

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*Altered Metabolism.*—Hypophysectomy alters the metabolism of carbohydrate, fat, and protein. This includes a hypersensitivity to insulin, a tendency toward hypoglycemia, a slower rate of absorption of carbohydrates and storage of glycogen in tissue, a diminished fat catabolism, an alteration of nitrogen balance and retention of nitrogen, and a reduction in glyconeogenetic activity. Starvation results in a rapid and severe hypoglycemia in the hypophysectomized animal, followed by death (6, 7).

*Anemia.*—An anemia develops in the hypophysectomized animal which can be effectively treated by pituitary extract or combination of various endocrine preparations. This anemia has been duplicated in rats by a combined removal of the thyroid and adrenal glands and can be prevented by daily subcutaneous injection of thyroxine and cortisone (8). Others have suggested that the anterior pituitary contains a specific erythropoietic hormone acting on the bone marrow (9, 10).

*Diabetes Insipidus.*—According to Pearson and others (2) most patients develop polyuria, two to twenty-four hours after hypophysectomy, which can usually be controlled by parenteral pitressin. Pitressin tannate, 2 to 5 units, intramuscularly, has been recommended if the urinary output exceeds 150 cc. per hour. One injection is effective for one to three days or longer (2, 11).

*Adrenal Insufficiency.*—The completely hypophysectomized patient develops adrenal insufficiency or crisis within two to seven days when cortisone or ACTH replacement therapy is withdrawn (2). There is atrophy of the adrenal cortex with subsequent metabolic derangements; therefore, cortisone or ACTH is essential in such patients.

*Thyroid Insufficiency.*—Hypophysectomy results in atrophy of the thyroid and a deficiency in thyroid hormone. Myxedema usually appears within one to two months after a complete hypophysectomy. The PBI and  $I^{131}$  uptake are both lowered (12). Furthermore, the lack of thyroid hormone may lessen the effect of adrenal cortical hormone on the body tissues. On the other hand, adrenocortical hormones have been shown to be antagonistic to the thyroid metabolic effect in man (13, 14). Thus, thyroid replacement therapy is essential after hypophysectomy. Thyroid extract, thyroxine, or triiodothyronine can be used in such cases. Since triiodothyronine has a metabolic activity 4 to 10 times that of an equimolecular quantity of thyroxine and also acts 4 to 10 times faster than thyroxine, triiodothyronine is preferred for emergency use (15).

*Growth and Gonadal Change.*—It is well known that hypopituitarism results in dwarfism and infantilism before puberty. Testicular atrophy becomes apparent a few weeks after hypophysectomy in the human male. In the female, menses cease and the vaginal mucosa and endometrium undergo atrophy (2). Urinary gonadotrophin excretion is reduced to an immeasurable level.

*Electrolytic Imbalance.*—Owing to the effect of pituitary and

adrenal insufficiency, the hypophysectomized patient is apt to have water imbalance and an abnormal electrolyte pattern. The daily fluid intake and urinary output should be recorded accurately. Normal saline in conjunction with desoxycorticosterone is sometimes necessary (11, 16). However, Hollander and others (17) reported that in adrenal insufficiency, electrolyte balance can be maintained by cortisone alone in addition to the normal salt intake.

#### CASE REPORTS

During the past two years, 6 anesthetics have been administered to 4 hypophysectomized patients. General anesthesia was used in all 6 operations. In 4 operations, cyclopropane was used; in 2, ether was the main agent. Premedication was Demerol® (25-75 mg.) and scopolamine (0.3-0.4 mg.) atropine (0.3-0.4 mg), or atropine (0.3-0.4 mg.) alone, depending upon the daily requirement of sedatives or analgesics by the patient and his general condition. For induction, 100 to 200 mg. of thiopental sodium were given to all but one patient, who received only cyclopropane and oxygen. The operations in this series consisted of bilateral adrenalectomy, bilateral oöphorectomy, repair of perforation of the bowel (2), and hip nailing for pathological fracture (2). The anesthesia time varied from one hour and fifteen minutes to two hours and twenty minutes. The maintenance of anesthesia in all 6 operations was uneventful with no marked deviations in blood pressure or pulse. Because of the adequate preparation no additional hydrocortisone was required in 3 of the operations, and in the remaining 3 hydrocortisone (100 to 200 mg.) was given during the procedure. The awakening time after 4 of the operations was on arrival in the recovery room in 3 cases and thirty minutes in one case. The 2 anesthetics with an awakening time of two hours were in the patients with obvious liver metastasis at the time of the operations. The use of thiobarbiturate in these patients is open to question.

*Case Report 1 (F. H.)*—A 51-year-old white female had an hypophysectomy for metastatic carcinoma of the breast in September, 1954. Postoperatively she developed immediate and permanent diabetes insipidus, which required periodic injections of pitressin. She also required daily doses of cortisone and thyroid extract. Nine months later, because of progression of her disease and an increase in pain, she was admitted for bilateral adrenalectomy and oöphorectomy. At this time the patient was obese with questionable myxedema and had obvious liver metastasis. The blood volume was normal, the bromsulfalein test showed 40 per cent retention, and the basal metabolic rate was minus 30 per cent. Preoperatively she was given cortisone, 100 mg., once daily and triiodothyronine, 25  $\gamma$ , three times daily. On June 20, 1955, a bilateral adrenalectomy was performed with ether analgesia. The operative course was uneventful except for a preoperative hypotension that was believed to be due to the premedication (Demerol, 75 mg., and atropine sulfate, 0.4 mg.). The patient was awake on return to the recovery room and maintained a satisfactory blood pressure for

the next twenty-four hours. In the postoperative period she received cortisone, 50 mg., every four hours which gradually was changed to cortisone, 50 mg., once daily. She also received triiodothyronine, 25  $\gamma$ , three times daily for several days. Her convalescence was uneventful. On June 21 blood chemistry determinations showed: calcium, 10.8 mg. per cent; chloride, 102 mEq./l.; carbon dioxide content, 27 mEq./l.; sodium, 138 mEq./l.; and potassium, 3.57 mEq./l. On June 29 a bilateral oöphorectomy was performed with cyclopropane anesthesia. Premedication consisted of 50 mg. of Demerol and 0.4 mg. of atropine sulfate. The operative course was uneventful, and the patient returned to the recovery room awake. The patient received cortisone, 50 mg., every four hours on June 29 and was reduced to 50 mg. every four hours on June 30 and to 50 mg. three times daily on July 7. The patient's convalescence was slow and marked by lethargy and unexplained abdominal pain. Because of fluid imbalance on July 10 pitressin tannate in oil was given. By July 13 the patient had developed an anemia (hemoglobin, 9.3 Gr. per cent) for which she received 500 cc. of whole blood.

*Case Report 2 (M. H.)*—A 72-year-old white female had an hypophysectomy for advanced carcinoma of the left breast with extension to her right breast and left lower neck on September 13, 1954. Postoperatively she was treated with cortisone, pitressin, electrolytes, and fluid. Her immediate recovery was uneventful. On October 1, 1954, because of sudden onset of abdominal pain, tenderness and rigidity, and roentgenographic evidence of free air under the diaphragm, she was scheduled for exploratory laparotomy. Her physical status was fair except for questionable fluid and electrolyte imbalance. Preoperatively she was given triiodothyronine, 100  $\gamma$ , and hydrocortisone, 200 mg., in 5 per cent dextrose in water by intravenous drip. Premedication consisted of atropine sulfate, 0.4 mg., intramuscularly, forty minutes prior to the time of starting anesthesia. Anesthesia was induced with 0.1 Gr. of thiopental sodium and maintained with cyclopropane by endotracheal inhalation. Succinylcholine, 0.1 per cent solution, by intravenous drip was used as a relaxant. There was a relatively slight hypotension immediately after starting anesthesia, restored to normal tension by 2 units (approximately 500 cc.) of plasma and 500 cc. of whole blood. During the one and half hour of the operative procedure, evidence of peritonitis and retention of fluid in the bowel was found, but no definite underlying cause was demonstrated. Postoperatively her blood volume was estimated as normal for her status. She received cortisone, 50 mg., every four hours, then gradually reduced to 50 mg. each day; triiodothyronine, 25  $\gamma$ , three times daily; intermittent doses of pitressin in oil; electrolytes and fluid as indicated from blood chemistry determinations. Her recovery was uneventful. On October 12, 1954, she suddenly developed a similar attack of abdominal pain, which was suspected to be due to perforated bowel. She received whole blood, 500 cc.; plasma, 300 cc.; hydrocortisone, 200 mg., and triiodothyronine, 35  $\gamma$  in 5 per cent dextrose in water, intravenously, before the scheduled operation. Premedication consisted of atropine sulphate, 0.4 mg., one hour before operation. Repair of a perforated sigmoid colon and a transverse colostomy were done under light cyclopropane endotracheal anesthesia with succinylcholine by intravenous drip for relaxation. During the two hour and twenty minute-operative procedure there were slight fluctuations of blood pressure and pulse rate, which was treated by 500 cc. of blood. Postoperatively she received hydrocortisone, 150 mg., intravenously, followed by 50 mg. every four hours, triiodothyronine,

50  $\gamma$ , intravenously, followed by 25  $\gamma$  three times daily, antibiotics, electrolytes, fluid, and intermittent doses of pitressin in oil, whenever indicated by the fluid intake and urinary output. Her convalescence was gradual but uneventful.

#### DISCUSSION

Operations for the hormonal control of cancer have been done for years, including bilateral orchiectomy, bilateral oöphorectomy, bilateral adrenalectomy, and total hypophysectomy. Hypophysectomy has been well tolerated by most patients. Operations in hypophysectomized patients can now be performed if particular care is given to hormone replacement.

Although the problem would seem more complex, hypophysectomized patients require only adrenal and thyroid replacement therapy, and careful observation of the fluid and electrolyte requirements, and adequate blood volume to withstand anesthesia and surgery. In the preoperative period the dosage of cortisone and thyroid extract, or triiodothyronine, should be increased above the maintenance requirements. All patients in this series also needed an increased dosage for several days postoperatively. Careful fluid intake and urinary output records will detect the increase in severity of the diabetes insipidus which may result in dehydration. In these cases pitressin tannate should be given until the fluid balance is under control. In the 4 operations in which there were no bowel lesions the electrolyte pattern and acid-base balance were not disturbed.

#### SUMMARY

The physiologic aspect of hypophysectomy has been reviewed. Complete operative removal of the pituitary gland is not usually fatal in itself, but the resulting physiologic derangements must be adjusted in order to keep the patient alive. This regimen includes adrenocortical and thyroid replacement, attention to nutrition, and a carefully controlled water balance.

Six general anesthetics in 4 hypophysectomized patients are reported, and 2 case reports are presented. With proper treatment and management, all of these patients recovered uneventfully. Adrenal cortical and thyroid hormone replacement was given in increased doses before and after anesthesia and operation. Adequate blood volume and electrolyte and water balance were maintained.

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