Endocrine Responses During Stress

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Although the stress syndrome has many facets, this discussion will be limited to some responses of the endocrine glands during the stress of surgery and anesthesia. The major effects are produced by the pituitary and adrenal glands. We will briefly refer to the chromaffin cells of the gastrointestinal tract. A summary of the normal and desirable effects seems in order and then the abnormal and undesirable responses will be presented.

NORMAL RESPONSES

Insult to the body tissues as infection, trauma (surgical or accidental), burns, or anesthesia alone will set off a chain of events. The body has two methods of transmitting signals of distress which are carried very rapidly via the nervous system and less rapidly by the chemical, or humoral, system by way of the hormones. The word hormone means "to arouse or to activate." Each hormone is secreted by specific gland cells and has its effect on specific body cells only. Chemically, the hormones fall into the following categories: 1. The pituitary hormones which are proteins; 2. The adrenocortical hormones which are steroids, and 3. The adrenomedullary hormones which are catechol amines.¹

The stimuli of stress will probably rouse or force both the nervous and humoral systems into action. First of all, the hypothalamus is probably stimulated, activating the sympathetic nervous system, which stimulates the adrenal medulla to secrete adrenaline and noradrenaline. These in turn cause peripheral vasoconstriction, contraction of the spleen, glucogenolysis, etc. At the same time, the anterior pituitary (adrenohypophysis) secretes more adrenocorticotropic hormone (ACTH) which causes an increase in the production of the adrenocortical steroids. Two of these steroids are of prime importance, i.e., mineralo-corticoids and gluco-corticoids. The former, with aldosterone as its principal hormone, is chiefly concerned with water balance and electrolyte balance. It is greatly responsible for regulating the retention of sodium and elimination of potassium.² This accounts for part of the sodium retention and oliguria during anesthesia. Gluco-corticoids, better known as hydrocortisone and cortisone, have their effect on carbohydrates, fat and protein metabolism, and if the need arises, convert proteins and fats to carbohydrates (gluconeogenesis).³ Such metabolism is vital during stress for additional resistance and energy.

In addition, the posterior pituitary or neurohypophysis will probably also be stimulated by the hypothalamus

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and produce its antidiuretic hormone which will also induce retention of water. If large amounts are produced, vasoconstriction will be increased as well.

Briefly then, the body normally has a tremendous reaction toward insult. The hypothalamus triggers the sympathetic nervous system and posterior pituitary into action. The anterior pituitary secretes ACTH causing production of mineralo-corticoids and gluco-corticoids by the adrenal cortex. These responses are essential to life with or without anesthesia and surgery.

**ABNORMAL RESPONSES**

Adrenal Medulla. Adrenalin and noradrenalin, known as catechol amines, are the hormones to be considered. Recently, I had the privilege of attending a lecture by Dr. J. H. Burns of London. He explained that normally the blood vessel walls and chiefly those of the arterioles, contain little pockets of noradrenalin. During sympathetic stimulation this substance is activated and causes constriction of the vessel wall. We have known for some time that the rauwolfa drugs, i.e., Reserpine and Serpasil, reduce blood pressure in the hypertensive. It is now understood that they deplete the vascular reservoirs of noradrenalin to a greater or lesser degree, depending upon dosage of these drugs.³

If these patients must submit to surgery they may not respond to the stress involved. If possible, the rauwolfia drugs should have been discontinued for two weeks prior to surgery, permitting a buildup of noradrenaline reserve. If emergency surgery is necessary and the patient does not respond to the usual treatment of shock, noradrenaline (Levophed) should be given promptly. Sometimes it may take 5 or 8 hours for a patient to build up his reservoir. If, after that length of time, he is still in need of vasopressors it is well to use other peripheral constrictors such as Vasoxyl.

Pheochromocytoma, a tumor of the adrenal medulla, presents an interesting abnormality. At present there is an over enthusiastic interest in this tumor and it is quite "in vogue" to speak of it. Nevertheless, some 800 people in the United States die yearly of this tumor. Usually it is found in the adrenal medulla, but the secreting cells have been found in the thorax and abdominal cavity. The tumor cells produce an excessive amount of catechol amines at various times and may lie dormant at other times. This causes the diagnosis to be overlooked. If pressure is applied on the tumor it may release such large amounts of the catechol amines as to cause extreme hypertension with instantaneous death due to a cerebral vascular accident or produce extreme pulmonary edema.⁴

If the correct diagnosis is made and the tumor removed the prognosis is usually good for they are seldom malignant. During surgical removal, we as anesthetists are faced with two hazardous situations. First, during surgery and manipulation of the tumor, large amounts of catechol amines will be secreted into the blood stream. The blood pressure must be monitored constantly. As soon as marked hypertension is evident, Regitine should be given until the readings are near normal range. As soon as the tumor and gland have been removed, the body will suddenly be without its accustomed large supply of noradrenalin, and because of the previous activity of the tumorous gland,
the remaining adrenal gland may be somewhat inactive. Acute hypoten-
sion may follow. This again is the
time for Levophed infusion. Other
vasopressors should be available
should the Levophed be ineffective
after a time.4

Adrenal Cortex. In a rather re-
cent survey, Gillies noted that 5.6% of
their surgical patients had received
cortisone therapy prior to surgery.5
Steroid therapy will cause atrophy of
both the adrenal cortex and the cells
in the anterior pituitary gland pro-
ducing ACTH. Schneewind and Cole
state that, "It is probably a safe rule
that any patient who has received
steroid therapy for five days or more
during the year preceding operation
should receive prophylactic treatment
to prevent adrenal cortical insuffi-
ciency during an operative pro-
cedure."6

If these patients are submitted to
the stress of anesthesia and surgery
they may tolerate the procedure with-
owout incident. However, should the
patient show persistent hypotension
even after adequate blood replace-
ment and after ruling out other causes
such as coronary disease, adrenocor-
tical insufficiency must be suspected.
Rapid therapy with intravenous hy-
drocortisone sodium succinate (Solu-
cortef) should be instituted. Cornejo7
has recently written of this treatment
in greater detail.

Hypnotics as well as anesthetic
drugs may produce profound effects
in the patient with adrenocortical insufficiency. Morphine sulfate seems
to be a great offender. It has been
suggested that the opiate dose for
pre-anesthetic medication should be
reduced to about one-half the normal
dose.8

Patients with previous steroid ther-
apy are not the only ones who may
suffer from adrenocortical imbalance.
The extremes of age may not respond
normally. Smith states that the new-
born probably has very little adrenal
function for the first 3 or 4 weeks of
life. 10 The very old, especially those
who have been chronically ill for
some time, may have marked adrenal
insufficiency and if these patients
have persistent hypotension during or
following surgery, steroid therapy
may be a life saving measure. Another
instance is the patient who has had
major surgery and responded well,
but needs to be exposed to a second
anesthetic and operation within a day
or two. The patient may have little
or no response to stress situations and
steroid therapy should be contem-
plated. 2

Still another interesting observa-
tion has been suggested by Hausmann
and Lunt. It is known that during
pregnancy the patient has an increase
in ACTH and gluco-corticoids. The
placenta may be responsible. After
delivery and loss of the placenta, the
patient may not be able to stand
sudden stress such as the aspiration
of gastric contents. I believe this is
worthy of consideration for aspiration
is still one of the major causes of
post-partum deaths and why should
these patients be more susceptible
than general surgical emergencies.2

Posterior Pituitary. Diabetes in-
sipidus is a condition resulting from
tumors or lesions of the posterior
pituitary or hypothalamic region.
There is a lack of antidiuretic hor-
mone and the kidney will be unable
to re-absorb water at the distal tubule.
From 5 to 10 liters of urine may be
excreted daily. Many of the patients
respond well to posterior pituitary
preparations but about 10% do so
very poorly. 1 We do not encounter
these patients very often, but occa-
sionally they must submit to surgery.
Probably our chief concern is their tendency toward dehydration and since patients are deprived of fluids during the pre-anesthetic period the dehydration may be extreme. Water intoxication may occur if the patient responds to posterior pituitary extract and infusion is excessive.

CHROMAFFIN CELLS OF THE GASTROINTESTINAL MUCOSA

The chromaffin cells secrete a substance known as 5 hydroxytryptamine and abbreviated as 5-HT. However, the earlier name "serotonin" is more frequently used. Normally, 5-HT is found in an inactive form and has been found abundantly in the hypothalamus and blood, principally in platelets. When activated it exerts its effect on smooth muscle and nerve tissue. Much of its action is unknown but it seems to cause constriction of peripheral, pulmonary and coronary circulations. This may be followed by bradycardia and hypotension. The smooth muscle of the gastrointestinal tract shows increased peristalsis and excessive amounts may cause nausea, vomiting, abdominal distention and diarrhea. Bronchiolar spasm with resultant wheezing may also present itself. Of interest, although not to anesthesia, wasp venom contains a high concentration of 5-HT.\(^1\)

Although poorly understood, this hormone is necessary for normal physiology. Should chromaffin cells give rise to tumors, excessive amounts may be produced. Such tumors belong to the carcinoid classification. Patients suffering from the tumors show dyspnea, paroxysms of vascular collapse, sweating, flushing or mottling of the skin changing from red to blue and white. In order to demonstrate the complexity of the hormone, Drill says 5-HT can be eliminated from the blood with Reserpine but amphetamine (Benzedrine and Dextedrine) also reduces its concentration. The totally different effects of Reserpine and amphetamine are well known.\(^1\)

Anesthesia and surgery for the patient with a secreting carcinoid tumor may be hazardous or uneventful. Perhaps the most important factor to bear in mind is the avoidance of hypotension. Sudden decrease in systolic blood pressure causes secretion of 5-HT in excessive amounts. Therefore, it is best to avoid spinal anesthesia, drugs such as Fluothane and perhaps pentothal unless very little is used. It is also advisable to avoid any spasmogenic drugs which might initiate bronchiolar constriction for the bronchodilators seem to have had little effect in correcting the constriction.\(^1\)

SUMMARY

Regardless of how minor or major the surgery and how safely the anesthetic is administered, the body is placed into a situation of stress. How the normal endocrine glands respond to maintaining physiology has been briefly stated followed by some of the pitfalls one may encounter during anesthesia when either hyper- or hypofunction of these glands is present. Lastly, the carcinoid tumor is discussed although knowledge of its secreting hormone is limited.

The old adage of "care, prayer and plenty of air" will still apply to the majority of anesthetics we administer. This is because the endocrine and autonomic nervous systems are ever vigilant keepers of body physiology. Interference with either should be contemplated only after judicious

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consideration. In studying the endocrine system we are again reminded that we are indeed "fearfully and wonderfully made." 13

REFERENCES


