Family Practice Grand Rounds

A Case of Insulinoma

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DR. CHARLES W. SMITH (*Chief Resident, Department of Family Medicine*): Insulinoma is a rare but fascinating disease. The case presentation today allows us to focus on several aspects of this entity which are pertinent to family physicians. The wide spectrum of presenting symptoms of hypoglycemia and the differentiation of functional from fasting hypoglycemia are two common problems faced by the family physician. The discussion will focus on a pragmatic approach to the work-up of hypoglycemia, in addition to some guidelines for referral of patients with fasting hypoglycemia. Finally, hypoglycemia as a cause of acute brain syndrome will be discussed.

M.T. is a 70-year-old black female from Alamance County, North Carolina. She is married, the mother of one, and a part-time babysitter.

History of present illness: Nine months prior to admission, she came to the clinic with intermittent, sharp pain in her left thoracic wall in the mid-axillary line. Examination at that time was unremarkable. She was treated with propoxyphene and acetominophen with improvement. Seven months prior to admission, she returned for follow-up at which time there was a question of left costovertebral angle tenderness. She continued to complain of intermittent thoracic wall pain. A urine culture grew greater than 100,000 Escherichia coli. This was treated with sulfamethoxasole. On numerous follow-up cultures, she continued to grow greater than 100,000 E coli in spite of adequate courses of sulfamethoxasole to which the organism was sensitive. An intravenous pyelogram was negative. A voiding cystourethrogram showed a large cystocele. Cystometric examination and cystoscopy were unrevealing. Because of persistence of urinary tract infection, she was admitted for elective vaginal hysterectomy and anterior repair. She was discharged without complication three days prior to the second admission. On the day of this admission, she was restless and unable to sleep. Shortly afterwards, her husband found her confused and with garbled speech. He brought her to the Emergency Room.

Past medical history: She is 25 years postmenopausal. There are no previous hospitalizations, no serious illnesses, and no allergies.

Family history: Her mother and father both died of unknown cause. Her father was a slave in Alamance County. She thought that he had "dropsy" because of intermittent swelling of his face, hands, and legs. She had four brothers, two of whom died in infancy of unknown cause. The other two lived to "old age" (cause of death un-

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known). She is married to a farmer and has a daughter (age 50) who is a reformed alcoholic and has a mild chronic organic brain syndrome.

Social history: She grew up in Alamance County and was married at age 18. She was never formally employed and had no formal education, but does part-time babysitting and helps her husband with the farming. The family lives in a rural area and is "very close."

Review of systems: Noncontributory.

Physical examination: She was an elderly appearing black female in no acute distress. She was afebrile, the pulse was 76 beats per minute and regular, respirations were 18 per minute and unlabored, and the blood pressure was140/100 mmHg. She had a mild right hemiparesis with a question of minimal right central seventh nerve palsy. Her speech was no longer garbled. The remainder of the physical examination was normal.

Laboratory data: WBC 17,800 cu mm with 82 polymorphonuclear cells, 2 bands, 7 lymphocytes, and 8 monocytes. Hemoglobin level was 10.7 gm/100 ml; hematocrit, was 34 percent. Platelet count was 572,000 cu mm. Westergren sedimentation rate was 86 mm/hr. Prothrombin time was 12.4 seconds with a control of 13 seconds. Partial thromboplastin time was 53.4 seconds with a control of 54 seconds. Arterial blood gas on room air: pH 7.41, pO_2 60Hg, and pCO_2 32 mmHg. Urinalysis, chest x-ray, and electrocardiogram were unremarkable. Blood glucose was 55 mg/100 ml, blood-urea nitrogen 15 mg/100 ml, creatinine 2.6 mg/100 ml, calcium 9.0 mg/100 ml. Total protein 7.1 gm/100 ml, sodium was 138 mEq/liter, potassium was 4.1 mEq/liter, chloride was 101 mEq/liter, carbon dioxide content was 26 mEq/liter, albumin was 3.5 gm/100 ml. SGOT 67 IU, SGPT 40 IU, and alkaline phosphatase was 4.5 Bodansky units.

Hospital course: Two hours after admission, she developed a dense right hemiparesis. An emergency computed tomography scan was negative. By the end of the procedure, her neurological deficits had cleared. At this time, the working diagnosis was a transient ischemic attack. A left carotid angiogram showed minimal atherosclerosis. The next day, she had an episode of slurred speech and inappropriate laughter. She was given 50 cc of 50 percent glucose and responded dramatically. An electroencephalogram and a lumbar puncture were both negative. During this episode blood studies were drawn for glucose and insulin levels. The blood glucose was 33 mg/100 ml and the insulin was 34 μU/ml. With the finding of low glucose in the face of elevated insulin level, a celiac arteriogram was performed which showed a 1 cm "tumor blush" between the body and tail of the pancreas. At surgery, an insulinoma was found and a distal pancreatectomy performed.

DR. DENNIS MORGAN(*Third year pathology resident*): Thanks to the astute diagnosis of the clinicians, the pathology department had an opportunity to see this interesting tumor. Among the pathologic features of insulinomas are that they are benign in 90 percent of cases and nearly always (95 percent) solitary. Although tumors up to 8 cm have been reported, most (70 percent) are less than 1.5 cm in diameter. They are evenly distributed along the pancreas, with 60 percent being located in the surgically accessible body and tail.

This patient's tumor was 0.5 cm and localized by arteriography, presenting as a characteristic vascular blush in the body of the pancreas.

Morphologically, the insulinoma is characterized by a well-demarcated area with architectural disarray of islet cells which appear normal. The distinctive feature, however, is the arrangement of these cells in an irregular pattern either of cords or ribbons of tumor. Associated reactive changes sometimes include fibrous trabeculae, calcification, bone formation, and even amyloid.

The criteria for malignancy must be quite stringent because nuclear aberrations and mitotic figures are commonly seen in endocrine tumors that are biologically benign. True malignancy is indicated by stromal invasion or tumor thrombi in walls of veins. Malignant features were not present in this case.

The origin of insulinomas has been a subject of much investigation. In this regard, Creutzfeldt has made some pertinent observations.[1] He feels that insulinomas originate not from mature islet cells, but rather from a primitive precursor cell. Supporting evidence includes the fact that nearly all insulinomas display areas of ductular proliferation such as is seen in the embryologically immature pancreas. Further supporting this concept is the occurrence of relatively undifferentiated function and form in these tumors. Multiple hormone secretion occurs in some cases and presumably represents acquisition of functions which are repressed

in the normal differentiated islet cell. Morphologically, there is variation in the nature of secretory granules seen in a given tumor and even within cells of the same tumor. Some insulinomas have typical beta cell granules (ie, they have crystalline inclusions), others have only atypical secretory granules, alone or in combination with typical ones, and still others have no identifiable granules. This patient's tumor contained cells with exclusively atypical secretory granules.

Regardless of granule morphology, Creutzfeldt feels that the functional defect is the inability to retain and store insulin. Such a cell continues to elaborate insulin despite the presence of hypoglycemia—a stimulus which, in the normal cell, effectively inhibits insulin release. Fasting hypoglycemia and hyperinsulinemia are the well-known clinical manifestations.

Insulinomas, then, are felt to be tumors of relatively undifferentiated percursors of islet cells. Clinical symptoms result from ineffective retention of insulin.

DR. DAVID ONTJES (*Associate Professor, Department of Internal Medicine*): I wonder if I could ask Dr. Smith how long the patient was on the sulfonamide? Had this drug been started during the first hospital admission when the cystocele was repaired?

DR. SMITH: No. Actually, she had been treated intermittently, with several courses, over a three or four-month period.

DR. ONTJES: She had had no unusual neurologic symptoms prior to this episode?

DR. SMITH: No, never.

DR. ONTJES: I would like to talk about the problem of hypoglycemia and to raise two or three points. First, I would like to consider the question of when one should suspect hypoglycemia. I think that this case represents an accidental discovery and it is fortunate that the disease was discovered as soon as it was. Secondly, I would like to talk about the differential diagnosis of hypoglycemia and the measures one would take in working up this problem.

To review, I have divided some of the symptoms of hypoglycemia into two categories. One is related to the activity of the sympathetic nervous system and the other is due to central nervous system effects of hypoglycemia. Most people would define hypoglycemia in biochemical terms as a blood glucose of 50 mg/100 ml or less. Some normal women have fasting levels as low as 40 mg/100 ml. When the blood glucose drops, there are several mechanisms which come into play to cause symptoms. The mechanism which involves a discharge of sympathetic nervous system activity seems to be related to the rate of fall of the blood glucose as much as it does to the absolute level. The kinds of symptoms in this category include increased heart rate, tremor, irritability, pallor, and a feeling of being hungry. All of them are rather nonspecific and do not really point to hypoglycemia per se. If these symptoms are relieved by ingestion of food (particularly by glucose), this suggests more strongly that hypoglycemia is the cause. A second class of symptoms is related to central nervous system dysfunction. This category seems to depend not on the rate at which glucose has fallen but on the absolute level of blood glucose. Below a blood glucose level of 45 to 50 mg/100 ml, the brain may not be able to extract enough glucose to work properly. The nerve cells depend on a minimal concentration of glucose in the blood in order to get enough glucose for their own metabolism. Remember that the brain is one of the few tissues in the body that has an absolute dependence on glucose. Many of the other tissues, such as muscle, adipose tissue, or liver can burn other kinds of fuel such as fatty acids or ketones. But the brain has to have glucose, and this is why symptoms of hypoglycemia are largely related to the nervous system.

The symptoms of neuroglycopenia in the brain are many. They include headache, difficulty in concentrating, and memory failure. There may also be hypothalamic symptoms. The temperature regulating center can be compromised so that hyperthermia is sometimes seen. The physician should take note of the rectal temperature at the time the patient is having symptoms. Patients with hypoglycemia may have somatic complaints such as paresthesias, or, in the case of this patient, even lateralizing signs such as hemiparesis. Usually, hypoglycemia does not cause lateralizing signs, but, in elderly patients who have some cerebrovascular disease, the areas of the brain that are less well supplied with blood are the first areas to feel the effects of the reduced blood glucose. So in elderly patients the physician can see syndromes that mimic vascular accidents due to hypoglycemia. This is one of the reasons that any time a patient comes in with a neurologic complaint,

whether it is lateralizing or not, hypoglycemia should be considered.

I think that if the physicians who were taking care of this patient had relied only on that first blood glucose of 55 mg/100 ml, they would have probably concluded, "Here is an unfortunate woman who has had a stroke." However, a second glucose was drawn during a recurrence of some of her symptoms, and this turned out to be definitively low. This was fortunate. I think many physicians probably would not have drawn that second blood glucose and would have persisted in the idea that this was a cerebrovascular accident.

It is important to emphasize that the central nervous system symptoms are not always accompanied by adrenergic symptoms. If the blood glucose drops gradually enough, it often will not trigger symptoms of sweating or tremor. The neurologic deficit may progress on to unconsciousness, seizures, and irreversible central nervous system damage as the end result.

Now, what are the factors that can cause the glucose to drop to abnormally low levels? I think that it is useful to try to categorize them as occurring during either the fasting state or in the postprandial period (one to five hours after a meal). In the latter case we refer to reactive hypoglycemia. In general, the causes of reactive hypoglycemia are less serious than those which cause hypoglycemia in the fasting period. In taking a history and beginning to evaluate a case of hypoglycemia, it is helpful at the outset to determine whether one is dealing with the fasting or reactive type. The physician can do this by making appropriate blood glucose measurements at different times.

Besides insulinoma, there are several other causes of fasting hypoglycemia. Other tumors have been associated with hypoglycemia. These are usually large and they are most commonly fibrosarcomas, but large adrenal tumors and even lymphomas can be associated with protracted hypoglycemia. The mechanism by which these tumors cause hypoglycemia is unclear. They do not really make insulin, but some feel that they may make an insulin-like substance that can lower the blood glucose. Several kinds of liver disorders can be associated with fasting hypoglycemia. Extensive hepatic destruction can do this since the liver is essential to the maintenance of one's fasting blood glucose. The liver breaks down glycogen and converts amino acids into glucose, which is then released for the rest of the body during normal fasting. Damage to the liver, if it is severe enough, can interfere with these functions. There are some specific enzyme defects which cause fasting hypoglycemia. Several of the enzymes in the pathway that are necessary for gluconeogenesis may be missing and one should think of these. The various glycogen storage diseases, as well as galactosemia, are examples of this. A fairly common cause of hypoglycemia in some populations is alcohol. Alcohol will turn off gluconeogenesis because of an effect on some of the necessary enzymes. Ethanol ingested during fasting, particularly in an individual who has poor nutrition will frequently cause hypoglycemia. It is therefore important to assess a history of ethanol intake in the work-up of this problem. Various endocrine disorders are associated with hypoglycemia, and in most of these there is a deficiency of one or more of the hormones that are anti-insulin-like in their action. These hormones also are necessary to maintain blood glucose in the fasting state. Growth hormone and ACTH deficiency will cause fasting hypoglycemia in hypopituitary subjects. Patients who have primary adrenal failure lack cortisol which is essential for normal gluconeogenesis. Hypothyroid patients are subject to fasting hypoglycemia if severely affected. Also, glucagon deficiency can cause hypoglycemia. A few patients have been reported in whom this seems to be the mechanism.

In the reactive category, several different mechanisms can also operate. One is in early diabetes, where the blood glucose level goes higher than normal after a meal but insulin secretion is delayed. After a time, insulin levels do become high while the blood glucose is falling and absorption from the gastrointestinal tract has ceased. During this period there is an imbalance with an excess of insulin. In this case hypoglycemia usually occurs three to four hours after a meal containing carbohydrate. Patients who have rapid gastric emptying for any cause may also have reactive hypoglycemia. This can occur most often in patients who have had gastrectomies. Thus, hypoglycemia may be one of the components of the dumping syndrome.

Next, I would like to talk about what normally happens to insulin levels during a meal and during the fasting period. When the meal is eaten, blood

glucose typically rises from about 80 to 120 mg/100 ml. The insulin immediately rises from about 10 μU/ml to 100 μU/ml within the first half hour and then comes back down. The abnormal patterns which occur after meals would be characteristic of reactive hypoglycemia. The pattern of rapid gastric emptying mentioned earlier shows that a large load of glucose is dumped into the small intestine and is absorbed more rapidly. Consequently, the blood glucose level rises very rapidly up to 200 or 300 mg/ml in the first 15 to 30 minutes. This provides an intense stimulus for insulin secretion, so the insulin levels rise to 200 or 300 μU/100 ml rather than the usual 100. This creates a high glucose level and a high insulin level, and, because the absorption is completed very quickly, the blood glucose drops very rapidly to low levels within an hour or two. Insulin temporarily remains elevated and that accounts for the hypoglycemia that is seen. Most patients who have the dumping syndrome have glucose tolerance results of this type.

The second pattern that I mentioned was the diabetic, in whom one sees a relative delay in the secretion of insulin while glucose levels go higher than normal. Eventually, the insulin gets up to a high level. This results in temporary imbalance. The hypoglycemia occurs later than it does in the alimentary type (at about three or four hours, rather than at one to two hours).

And finally, there is the category of functional hypoglycemia. This is an entity that is very poorly understood and very widely diagnosed (perhaps overdiagnosed). It is often difficult to document that these patients even have hypoglycemia. In fact, it is hard to distinguish them from healthy patients. There is really no clear-cut abnormality in glucose tolerance except that patients will, at three to five hours after a glucose tolerance test, have a blood glucose level of 50 mg/100 ml or below. In normal people without any complaints, 20 to 30 percent will drop down to the same level with no symptoms. Thus, patients with functional hypoglycemia have mild postprandial hypoglycemia with complaints that are compatible with hypoglycemia. But, they also seem to have psychosomatic problems. It is unclear, at least in my mind, whether this is a disease of psychosomatic origin or whether it is an abnormality in insulin secretion. This remains to be defined.

I will now discuss the causes of fasting hypoglycemia in more detail. The normal blood glucose pattern during fasting starts out at 80 to 90 mg/100 ml and after several days of fasting in normal people, it will only drop to around 70 mg/100 ml. Insulin starts out at around 10 to 15 μU and falls down to less than 5 μU during a three-day fast. In a patient with an insulinoma who is subjected to a three-day fast, the blood glucose may start out at a normal level, but in most cases it will drift down to clearly abnormal levels within 48 to 72 hours. The important thing about the low glucose is that it is accompanied by an inappropriately high insulin level. In today's case, the insulin levels started out at 20 μU/ml which would probably be border line elevated for fasting (usually 15 μU/ml is considered to be an upper level for normal), but they became clearly abnormal when the blood glucose dropped to the 20 to 30 mg/100 ml range and insulin remained in the 20 to 30 μU range. What one must demonstrate in making the diagnosis of an insulinoma is an inappropriately high insulin level in the fasting state when the blood glucose is abnormally low. If this can be shown, then no other tests are needed to make the diagnosis. It can be concluded that the problem is in the secretion of insulin during fasting and that the patient has an insulin secreting tumor!

The primary care physician should be able to distinguish among several diagnostic possibilities and have a good idea of what is going on in a patient who has hypoglycemia. The first task is to distinguish whether this is the reactive or the fasting type. In suspected reactive hypoglycemia, one would usually get a fasting glucose and perform an oral glucose tolerance test to define whether the hypoglycemia really did occur after the oral glucose load. If one thought the patient had gastrointestinal problems, one might do a further GI work-up. If there were a history of gastric surgery, one might consider the possibility of the dumping syndrome. Usually, this work-up does not have to go much further than that. If the patient has early diabetes, then one would recognize that fact, too. In fasting hypoglycemia, once the physician has demonstrated that the fasting glucose is low, and that the insulin is inappropriately high, then any further work-up would probably be done in a referral center.

DR. RICHARD BAKER (*Associate Professor, Department of Family Medicine*): I want to make two points regarding the "somatopsychic" as-

pects of the case before the discussion. First, acute organic brain syndrome (AOBS, which used to be called delirium) is extremely common. About half of unselected inpatients can be determined to have abnormalities of recent memory or other cognitive functions that are significant. It is hard to know what the significance of AOBS is because it is such an ubiquitous manifestation of many stresses, including hypoglycemia.

Two things can happen to brain cells. One is that they can die, and that is irreversible. This usually happens slowly and is responsible for the classic manifestations of *chronic* brain syndrome (or dementia). I am not going to talk about that except to say that most commonly it is associated with cerebral arteriosclerosis. The other response of neurons is injury. This process is reversible. It may be due to direct drug toxicity or withdrawal syndromes (eg, delirium tremens). Other drugs which cause withdrawal syndromes are narcotics and barbiturates. Decreased oxygen levels, chronic obstructive pulmonary disease—or anything that diminishes the pO_2 can cause AOBS. In addition, metabolic and nutritional causes need to be considered, including hypoglycemia. Dr. Ontjes has explained the dependency of central nervous system tissue on glucose levels. Hyponatremia can also cause an acute brain syndrome. There are a variety of endocrine causes such as hyperthyroidism and hypoparathyroidism. Fever may or may not be able to cause brain syndrome by itself, but usually it is referred to as a component of the "infective state."

It can be seen why half of the general medical patients might well prove to have acute brain syndrome if it is looked for carefully. Whether the brain cells are injured, or whether they die, the mental status examination has some similar abnormalities because the final common pathway is a decrease in reality testing. That is just a way of saying that the ability to deal with stimuli that are coming in from the outside is lost. This causes a great deal of anxiety in anyone who is having trouble coping with environmental stimuli.

The hallmark of acute brain syndrome on mental status testing is the state of consciousness. This is *fluctuating* by definition. As with this patient, it varies from lucid status (perfectly normal mental status as far as you can tell) to comatose, including everything in between. Minute-to-minute, you will see this change. There is also disorientation and decreased ability to concentrate. That is measured best by serial 7s (asking the patient to start from 100 and subtract 7s). This may be a manifestation of a recent memory loss, but patients are unable to concentrate on that sort of task for very long. Hallucinations and delusions (especially frightening ones) are characteristic of acute brain syndrome.

The other area that Dr. Ontjes raised, functional hypoglycemia, raises many complex and emotionally laden issues. People who are dealing with stress may get decreased glucose as a physiologic manifestation of psychoendocrinologic changes. It probably does not represent a simple relationship but is a very complex, multifactorial effect. It may depend on many factors, such as genetic, operant conditioning (ie, how you tend to respond to certain situations), nutrition, drugs, and support systems.

We took a group of people who were going through the same stressful procedure (a cardiac catheterization) and measured several endocrine functions. The endocrine response to stress really depends on the way the stress is dealt with. If the anxious person stays engaged with the environment (eg, by talking to the nurses and physicians and their family about how nervous they are about this procedure), he/she will tend to have a moderate elevation of epinephrine. But growth hormone, cortisol, and norepinephrine will stay down. On the other hand, if a person is anxious and *not* talking about it, then he has a different set of responses. There are different endocrinologic profiles depending on how one deals with the situation.[2] So one expects that given certain stresses, there are going to be stimuli to such things as growth hormone which does affect glucose metabolism (and probably has direct effects on insulin secretion).

DR. SMITH: It is interesting that we started out with an esoteric entity and ended up with the ubiquitous phenomenon of stress. Perhaps one of the things we can get out of this is "when you hear hoofbeats, think of zebras as well as horses." The fact that such an unusual diagnosis can be made following such a widespread phenomenon as acute brain syndrome is interesting. In one study, 38 percent of the patients had neurological or psychological symptoms for three years or more prior to diagnosis. Eleven of these patients had permanent brain damage at the time of diagnosis.[3] I know that I seldom think of insulinoma as an etiology of

acute organic brain syndrome.

DR. BAKER: I heard Dr. Ontjes say what an adequate screening work-up would be. It would consist of insulin and glucose levels in the fasting state. But when would the physician do that? Exactly what would be an indication for instituting a look for insulinoma?

DR. ONTJES: The physician would look for it seriously if he found hypoglycemia in the fasting state. He would have the patient come to the hospital or his office fasting and obtain the blood sugars. If he checks the fasting blood glucose several times and it is always 70 mg/100 ml or higher, he can almost rule out the diagnosis of an insulinoma.

DR. BAKER: Would you recommend screening patients over a certain age with a fasting blood glucose?

DR. ONTJES: If they have any symptoms that I thought might be caused by hypoglycemia, I would screen all those patients with a fasting blood glucose. Also, if their history suggested a reactive pattern with the occurrence of symptoms, rather than a fasting blood glucose, I would also order a glucose tolerance test. The best time to draw the blood glucose is whenever the patient is having symptoms.

DR. BAKER: What if it were just anxiety all by itself without any of the other things you described?

DR. ONTJES: I think it would be helpful to have the blood glucose level during the period of the characteristic anxiety, or whenever the patient is describing the anxiety, to determine whether it is normal or not. If it is normal, the physician needs to look for other causes for the symptoms. It is very difficult to document hypoglycemia. There are many patients who complain of symptoms that might be secondary to hypoglycemia.

DR. BAKER: They usually present as obese. This seems a little paradoxical to me. What is your opinion, Dr. Ontjes?

DR. ONTJES: These patients may attempt to compensate by eating more and more. Their caloric intake goes up and they often will gain weight.

DR. SMITH: It seems that the most important thing in making a diagnosis is to document the hypoglycemia, which is one of the most difficult things to do. For how long is it safe to fast a patient with potential insulinoma? 24 hours? 48 hours? 72 hours?

DR. ONTJES: First, the physician should try to document it simply by putting the patient on an overnight fast. If he can get two or three blood glucose levels after an overnight fast, he will usually be able to document it adequately. If he cannot and he still has strong suspicions that the patient is having fasting hypoglycemia, then he would need to bring the patient into the hospital, and under fairly close observation, have him fast for 48 or 72 hours, usually measuring the blood glucose every four to six hours during that fasting period.

DR. BAKER: Do you advise people that have so-called functional hypoglycemia to go on a high protein, low carbohydrate diet?

DR. ONTJES: Diet seems to help in a fair number of cases. If the patient takes in too many carbohydrates, this stimulates too much insulin and interrupts the balance. If they get the proper nutrition, it helps to keep the blood glucose at the proper level. We usually tell such patients to take six feedings a day and avoid sugar. This helps a fair number of patients, but still other patients have symptoms. In these patients, I am often not convinced that they have symptoms due to hypoglycemia.

DR. SMITH: So, in summary, this patient presented with an unusual manifestation of hypoglycemia and a diagnosis of insulinoma was made.

The differentiation of fasting from reactive hypoglycemia is important and can be made by the family physician. Fasting hypoglycemia sometimes causes gradually worsening neurological or psychological symptoms. These are frequently present years before the diagnosis is made. Thus, insulinoma (and other causes of fasting hypoglycemia) should be excluded when evaluating chronic neurologic and psychologic problems.

References

1. Creutzfeldt W: Pancreatic endocrine tumors. Israel J Med Sci 2:762, 1975

2. Greene WA, Conron G, Schlach DS, et al: Psychological correlates of growth hormone and adrenal secretory responses of patients undergoing cardiac catheterization. Psychosom Med 32:599, 1970

3. Gilles P, DeWard OF, Priestly JP, et al: Hyperinsulinism. Arch Surg 96:763, 1968