American Association for Clinical Chemistry Chicago

Amino Acid Alterations in Head Injury

The brain accounts for approximately 2% of an adult's body weight, but consumes 20% of all oxygen and glucose. Studies on normal volunteer subjects, say Jerry C. Goodman and his associates at the Pathology Department of Baylor University in Houston, have shown that the brain is in a continuously positive amino-acid balance. They have discovered that after a head injury, alterations occur in the amino-acid balance of the brain which are similar to those occurring in sepsis, burns, multiple organ injury or failure, and hepatic encephalopathy. There is an increase in the plasma aromatic acid and sulfur-containing amino acids, and a decrease in the branched-chain amino acids. These changes could result in an alteration of the cerebral amino-acid metabolism.

Goodman's group studied twelve patients with head injuries. The patients were between 15 and 45 years old; there were nine males and three females. The injuries included an eipidural hematoma in one patient, a penetrating gunshot wound in another, subdural hematoma in four patients, intracerebral hematoma in three patients, and diffuse brain injury in three patients.

In each patient the researchers daily measured the arterial whole-blood amino acids, internal-jugular-bulb-venous whole-blood amino acids, and cerebral blood flow by the Kety-Schmidt method, using nitrous oxide as a diffusible indicator. Leucine, isoleucine, valine, serine, arginine, and threonine were decreased, while methionine, tyrosine, phenyalanine, taurine, and glutamate were increased. All of the patients were in negative cerebral amino-acid balance at some point. The changes may reflect a disruption in the blood-brain barrier and amino acid leakage from the injured tissue, says Goodman, or the changes in cerebral amino-acid metabolism may parallel decreases in brain oxidative metabolism following an injury.

Goodman believes that neurologists and others treating head-injured patiens should follow the treatment methods used for patients with sepsis, burns, and other injuries to help the brain maintain a more normal balance. These measures include feeding the patient earlier—by parenteral means if necessary—to help restore the brain's normal, negative amino acid balance. Also, the diet should be high in the branched-chain amino acids.

The drugs the patients got, including corticosteroids, appeared to make no difference in their condition, according to Goodman. Three patients had a good outcome, one had a moderate disability, one a vegetative disability, and two died.

Lipid Metabolism Studies

A major concern in preventing coronary heart disease (CHD) is the level of its probability. Will a particular risk factor improve or reduce the risk of heart disease, and will the intervention be worse than the disease? There have been many studies of hyperlipidemia and risk factors for CHD, but the risk factors are present by the time the disease is diagnosed. Prospective studies are needed to show that certain risk factors will lead to disease, says Evan A. Stein of the University of Cincinnati Medical Center, or that the prevention of various factors will reduce coronary disease.

In lipid metabolism, Stein continues, lipids must be transported through the bloodstream without causing damage to the arterial wall. The different lipid fractions are delivered to various cells, predominately in the liver, and then taken up in the body's adipose tissues.

The first lipoprotein synthesized is the large, lipid-rich, very-low-density (VLDL) particle. The VLDL is broken down and its triglyceride is stored in adipose tissue. High-density lipoprotein (HDL) helps break down VLDL so it becomes a less lipid rich particle—an intermedidiate density lipoprotein (IDL)—in which the cholesterol and triglyceride have almost the same concentration. IDL is a short-lived lipoprotein and is rapidly metabolized to low-density lipoprotein (LDL).

There is some evidence, says Stein, that not all IDL or VLDL goes to LDL, but is instead removed from the circulation between IDL and LDL. Basically, though, LDL is the catabolic product of VLDL. LDL is taken up by specific receptor sites, the tightly controlled number of which depends to some extent on

how much cholesterol is present.

The receptors play an important role in removing lipoproteins and preventing atherosclerosis. But a number of receptor abnormalities may occur and affect this process. HDL is thought to be able to remove cholesterol from the cell surface and transport it back to the liver, where it can be eliminated or recycled between VLDL and LDL.

This entire process relates to atherosclerosis. According to Stein, the more HDL present, the more cholesterol will be removed from the peripheral circulation. HDL can thus be considered good cholesterol and LDL bad cholesterol.

The tests that give fairly good risk data for hyperlipidemia or coronary artery disease are cholesterol and triglyceride, observes Stein. These are also relatively easy to measure in the laboratory. Electrophoresis is useful for measuring them only in exceptional circumstances and in research.

Some clinicians, says Stein, like to discuss risks in terms of ratios of HDL to LDL. He believes this comparison may be useful in some circumstances, but can also be misleading. Two men with the same total cholesterol and HDL or HDL- to -LDL cholesterol ratios may nevertheless have an entirely different risk of developing CHD because of other factors. Each lipoprotein should be looked at individually, Stein warns, and interpretations should be made according to what is known about the physiology of lipids.

It is also important to have accurate reference ranges, says Stein; data from the Lipid Research Clinics study provide an acceptable standard, but also have some drawbacks as applied to many individual persons. They are usually given by age and sex, and go from pediatric to older ages; LDL slowly increases as age increases. HDL would be expected to increase in older individuals, but does not. However, many people still survive into their 80's and 90's. The most protective factor, says Stein, is a low LDL, as exists in most animal species except man. Therefore, he adds, probably the biggest problem facing laboratories today is standardizing and interpreting their overall lipoprotein data.

Stein believes that the growing area of apolipoprotein technology will take years before it provides clinically useful measurements of the apolipoproteins. At present, he explains, there is no consistent methodology and no decent data base for using apolipoproteins—which are potentially and pathophysiologically better indicators and the latter cannot be developed without the former.

Neonatal Drug Withdrawal Screening

Infants born to mothers who are drug abusers may become addicted to the drugs *in utero* and experience withdrawal symptoms like those of any addict. The blood or urine of women suspected of or known to be drug abusers, and their infants—especially for infants showing signs suggesting drug withdrawal—should be screened to support the diagnosis, say Dr. Anne C. Halstead and her associates at the Children's Hospital in Vancouver, British Columbia, following an investigation of 57 mother-infant pairs. Also, they add, if results are positive for a drug, specific therapy can be given to the infant to help ease withdrawal symptoms.

Urine from pregnant or peripartum women and their infants had been analyzed by thin-layer chromatography, with confirmation by a variety of methods. Clinical data on both the mothers and infants was obtained by chart reviews. The drug screens were ordered by either the obstetrician or pediatrician because of a history of drug use in the mother or withdrawal symptoms in the infant. By history, the drugs used were ethanol, pentazocine, methylphenidate, benzodiazepines, heroin, marijuana, methadone, amphetamines, cocaine, barbiturates, inhalants, hallucinogens, analgesics, and others. All of the mothers were long-time drug users, one had been taking an opiate for migraine headaches.

Unsuspected drugs were found in 2 of the 6 mothers who had negative drug histories, and in 8 of 22 who had a positive drug history. The drugs found in 8 of these mothers could have contributed to their infants' withdrawal symptoms. Unsuspected drugs were also found in 2 of the 17 infants whose mothers had a negative drug history, and in 6 of the 35 whose mothers had a positive drug history.

False-negative results in the mothers were caused by late urine collection, infrequent use of drugs, or use of a drug not detected by the screen. The urine of some mothers showed drugs given in the hospital. The false-negative results in infants mainly occurred because the urine was collected late. Discrepancies between the results in the mothers and those of their infants were believed to result from late collections from the infants and from drugs given the mother in the hospital.

Halstead says the study showed that urine drug screens on mothers and infants can provide useful information in some instances, but that some precautions must be kept in mind. False-positive and -negative results were common, especially when enough attention was not paid to the time the sample was collected; 50% of the study was affected. The mother's urine should be collected as close to admission as possible, says Halstead, and before any drugs are given in the hospital. The infant's urine should be collected during the first 24 hours of life; later specimens will not provide as accurate a picture of the drugs in the infants's system.

Halstead explains that the collection bags used on the infants frequently came off, or the infant's skin