Questions and guide to answers

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Q: Discuss important recommendations of the ACCORD study for diabetic patients.

Important recommendations of the ACCORD study for diabetic patients.

Action to Control Cardiovascular Risk in Diabetes (ACCORD) was specifically designed to determine the effects of intensive treatment of blood glucose and of either blood pressure [Action to Control Cardiovascular Risk in Diabetes Blood Pressure (ACCORD BP)] or plasma lipids (ACCORD Lipid) on atherosclerotic cardiovascular disease outcomes in patients with type 2 diabetes who were at high risk for such an outcome. The primary outcome of all three ACCORD trials was the first occurrence of a major cardiovascular event, which was defined as the composite of nonfatal myocardial infarction, nonfatal stroke, or cardiovascular death. Prespecified secondary outcomes included the combination of the primary outcome and revascularization or hospitalization for congestive heart failure (termed the ‘expanded macrovascular outcome’) and the combination of a fatal coronary event, nonfatal myocardial infarction, or unstable angina (termed ‘major coronary disease events’). The ACCORD Lipid trial tested the hypothesis that treatment of type 2 diabetes patients with fenofibrate to increase plasma high-density lipoprotein (HDL) cholesterol levels and reduce plasma triglyceride concentrations, on the background of simvastatin therapy, would result in additional cardiovascular benefit compared with simvastatin therapy alone. There is no evidence from this trial to indicate that fenofibrate should be routinely added to a statin for the treatment of lipids in patients with type 2 diabetes. Indeed, routine addition of fenofibrate might be harmful for women with type 2 diabetes. However, the ACCORD data, together with post-hoc analyses of three other fibrate trials, suggest that, after statin therapy has significantly reduced LDL cholesterol levels and when triglyceride level is greater than 200 mg/dl and HDL level is less than 35 mg/dl, fibrate treatment can be considered, at least in men [1]. The ACCORD BP trial tested the effect of a target systolic blood pressure below 120 mmHg on major cardiovascular events among high-risk persons with type 2 diabetes. Intensive antihypertensive therapy in the ACCORD BP trial did not significantly reduce the primary cardiovascular outcome or the rate of death from any cause, despite the fact that there was a significant and sustained difference between the intensive-therapy group and the standard-therapy group in mean systolic blood pressure. There was also no significant benefit with respect to most of the secondary trial outcomes. At a significance level of less than 0.05, intensive blood-pressure management did reduce the rate of two closely correlated secondary outcomes, fatal stroke and nonfatal stroke [2].

With respect to intensive blood sugar control and cardiovascular events, they randomly assigned participants with type 2 diabetes and cardiovascular disease or additional cardiovascular risk factors to receive intensive therapy (targeting a glycated hemoglobin level<6.0%) or standard therapy (targeting a level of 7–7.9%). After termination of the intensive therapy, because of higher mortality in the intensive-therapy group, the target glycated hemoglobin level was 7–7.9% in all participants, who were followed until the planned end of the trial. Before the intensive therapy was terminated, the intensive-therapy group did not differ significantly from the standard-therapy group in the rate of the primary outcome (a composite of nonfatal myocardial infarction, nonfatal stroke, or death from cardiovascular causes) but had more deaths from any cause, primarily cardiovascular and fewer nonfatal myocardial infarctions. These trends persisted during the entire follow-up period. After the intensive intervention was terminated, the median glycated hemoglobin level in the intensive-therapy group rose from 6.4 to 7.2%, and the use of glucose-lowering medications and the

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rates of severe hypoglycemia and other adverse events were similar in the two groups. Hence, they concluded that, as compared with the standard therapy, the use of intensive therapy for 3.7 years to target a glycated hemoglobin level below 6% reduced 5-year nonfatal myocardial infarctions but increased 5-year mortality. Such a strategy cannot be recommended for high-risk patients with advanced type 2 diabetes [3].

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Discuss the diagnosis and significance of covert hepatic encephalopathy

Diagnosis and significance of covert (minimal) hepatic encephalopathy

Covert hepatic encephalopathy (HE) is defined as abnormal performance on psychometric testing when a standard neurological examination is completely normal [1].
It is present in >50% of patients with cirrhosis.
It has a significant negative impact on the quality of life and is associated with poor driving skills, impaired navigational skills, and increased traffic violations and accidents.
It is shown to increase the risk of progression to overt HE.

The Working Group on Hepatic Encephalopathy divides the diagnosis of HE into three categories: A (acute liver failure), B (portosystemic bypass without liver disease), and C (cirrhosis).

Clinical significance

Minimal hepatic encephalopathy (MHE) reduces patients QOL, increases their incidence of disability, and has a significant impact on their daily activities such as sleep, rest, eating, work, home management, recreation, ambulation, daily care, movement, and emotional behavior. All scales were significantly reduced in patients with MHE compared with individuals without MHE.

Predicting future episodes of hepatic encephalopathy

In a study of 116 patients with cirrhosis, those with MHE had a 3.7-fold increased risk of developing HE compared with patients without MHE. MHE significantly increased mortality in certain studies, and, although its economic burden is not known, it is likely to increase the cost and resource burdens to the healthcare system.

MHE slows psychomotor functions; hence, it is more detrimental to patients with manual labor professions (which involve operation and driving of machinery) than those with desk jobs (which involve verbal and intellectual skills).

Schomerus *et al.* [2] reported that 44–60% of patients with cirrhosis were unfit to drive. Driving competence was scored lower in patients with MHE.

They reported impairments in attention, response inhibition, and visuomotor coordination, as well as in working memory for navigational purposes.

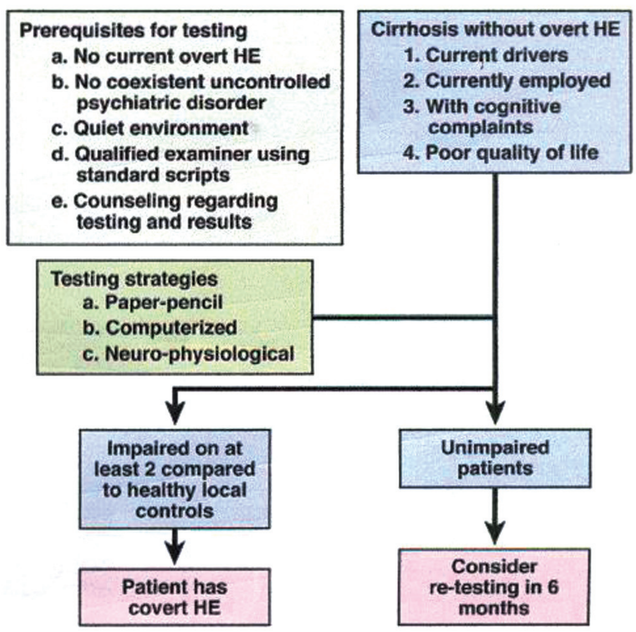
Roman *et al.* [3] reported that patients with cognitive dysfunction, diagnosed by the psychometric hepatic encephalopathy score (PHES), fall more frequently than patients without MHE. The greater number of falls increased the need for primary healthcare services and hospitalization among patients with MHE.

Although MHE is an early stage in the spectrum of cognitive disorders associated with cirrhosis, it was found to increase mortality in selected studies.

Diagnosis

One of the difficulties in recognizing MHE as an entity is the challenge of accurate diagnosis because of the time and psychological expertise required, financial burden, and copyright constraints of the psychometric tests recommended by the Working Group of Hepatic Encephalopathy. A model for conducting an evaluation is presented in Figure 1.

Figure 1



Flowchart for testing patients with MHE.

Once it is confirmed that a patient does not have another cognitive deficit, specific results from psychometric tests can help diagnose MHE. Patients frequently have defects in visuomotor coordination and response inhibition (which are important for operating a motor vehicle). These attention deficits affect a patient's ability to orient and perform executive functions and impair learning and working memory. When data from psychometric or neurophysiological tests are used, traditional paper-and-pencil or computerized tests can be accurately performed.

Grading hepatic encephalopathy

Traditional scores for grading HE identify patients with overt hepatic encephalopathy (OHE) and can be used to exclude MHE. The West Haven criteria were developed in 1977 by Conn *et al.* [4] to grade levels of encephalopathy. These criteria use subjective assessments of behavior, intellectual function, and alterations of consciousness and neuromuscular function. On the basis of several studies, the West Haven criteria are often subjective and prone to poor inter-rater and intrarater reliability, especially in identifying patients with grade I HE.

These scoring systems are most valuable in identifying or excluding OHE. Mini-mental examination status has been used to estimate the severity of cognitive impairment, on the basis of arithmetic, memory, and orientation analyses; a cutoff value of less than 25 has been used to exclude OHE. The Clinical Hepatic Encephalopathy Staging Scale is a simple, nine-question test used to characterize orientation and awareness; it might also be used to exclude OHE. Similarly, the Modified Orientation Log has been used to predict the outcomes of hospitalized patients with HE; it is objective, and scores less than or equal to 23 indicate that a patient is beyond MHE. The HE scoring algorithm combines patients' clinical features with neuropsychological and affective factors to better characterize HE and minimize variations in grading. The HE scoring algorithm performed well in characterizing OHE, but its components, including cognitive portions, are too simple to identify patients with MHE.

Psychometric tests performed with a pencil and paper

Psychometric hepatic encephalopathy score

PHES centers on the detection of deficits in attention and processing speed. Impairments in visuospatial function, attention, response time, and inhibition are specific to MHE in the absence of other neurocognitive disorders. The PHES comprises five different tests: the number connection test-A (NCT-A), the number connection test-B (NCT-B), the digit symbol test (DST), the line-tracing test, and the serial dotting test (SDT). NCT-A and NCT-B evaluate concentration, mental tracking, and visuomotor speed (the NCT-B is more complex). The DST evaluates psychomotor and visuomotor speed, whereas the line-tracing test examines visuomotor and visuospatial skills, with attention on speed and accuracy. The SDT is a test of psychomotor speed. These tests are each scored on a scale of 1–3 on the basis of SDs; scores range from +6 to −18. A value from −4 to −6 indicates MHE, depending on the country.

Computerized psychometric tests

Computerized psychometric tests offer an advantage over the traditional paper-and-pencil tests, which rely on motor function and involve multiple cognitive functions. These tests use reaction time, and patients must only push buttons. We review the available testing modalities.

Choice tests and Sternberg paradigm [5]

It measures mean reaction times and ability to recognize common numbers in pairs of digits displayed on a computer screen.

Inhibitory control test

The Inhibitory Control Test (ICT) is a computerized test of attention and response inhibition.

The ICT not only identifies these errors in patients with MHE, but also quantifies them. The ICT measures target detection rate, and errors in not detecting targets are considered errors of omission. These errors are considered primary errors of attention and are commonly associated with reduced processing speed and impaired visuomotor function.

Central nervous system vital signs

The assessment of Central Nervous System Vital Signs is a multifaceted system that has been validated in patients with other neurological diseases but has only recently been compared with PHES in patients with cirrhosis. Central Nervous System Vital Signs is a computerized battery of tests to evaluate verbal memory, processing speed, executive function, reaction time, cognitive flexibility, and complex attention [6].

Neurophysiological assessments

Electroencephalograms

Patients with HE have a reduced mean dominant frequency, higher π-relative power, and lower B relative power in the parietal regions of the brain compared with controls. As cirrhosis worsens, EEG slowing in the parietal regions worsens [7].

Psychometric batteries have proved to be more sensitive in detecting MHE than the neurophysiology tests.

Identifying a reliable method to diagnose patients with MHE will overcome multiple logistic and cost issues. There is an evidence that the diagnostic accuracy increases with the number of tests performed.

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Discussion of body water in elderly

Decreased body water in elderly

Water is essential for the human body to function. The body cannot store water and must have fresh supplies everyday to perform virtually every metabolic process [1].

The human body can last weeks without food but only days without water. The body is made up of 55–75% water. Water forms the basis of blood, digestive juices, urine, and perspiration and is contained in the lean muscle, fat, and bones. Babies and the elderly are vulnerable to lack of water or dehydration. Not drinking enough water increases the risk for kidney stones and, in women, urinary tract infections [2]. As the body cannot store water, we need fresh supplies everyday to make up for losses from the lungs, skin, urine, and feces. The amount we need depends on our body size, metabolism, the weather, the food we eat, and our activity levels.

Water is needed for most body functions, including the following.

(1) Maintain the health and integrity of every cell in the body.
(2) Keep the bloodstream liquid enough to flow through the blood vessels.
(3) Help eliminate the by-products of the body's metabolism, excess electrolytes (for example, sodium and potassium), and adult serum urea, which is a waste product formed through the processing of dietary protein.
(4) Regulate body temperature through sweating.
(5) Moisten mucous membranes such as those of the lungs and mouth.
(6) Lubricate and cushion joints.
(7) Reduce the risk for cystitis by keeping the bladder clear of bacteria.
(8) Aid digestion and prevent constipation.
(9) Moisturize the skin to maintain its texture and appearance.
(10) Carry nutrients and oxygen to the cells.
(11) Serve as a shock absorber inside the eyes and the spinal cord.

Older people who get enough water tend to suffer less constipation, use less laxatives, have fewer falls, and, in men, it may have a lower risk for bladder cancer. Less constipation may reduce the risk for colorectal cancer. Drinking at least five to eight glasses of water daily reduces the risk for fatal coronary heart disease among older [3].

Approximate adequate daily intake of fluids in liters per day:

Male:	
51–70 years	2.6 l/day (about 10 cups)
>70 years	2.6 l/day (about 10 cups)
Female:	
51–70 years	2.1 l/day (about eight cups)
>70 years	2.1 l/day (about eight cups)

Lack of water in the body leads to decline in renal blood flow and glomerular filtration rate, distal renal tubular diluting capacity, renal concentrating capacity, sodium conservation, and renal response to vasopressin. This decline in kidney function together with hormonal changes and factors, such as decreased thirst perception, medication, cognitive changes, limited mobility, and increased use of diuretics and laxatives, makes older adults a group of particular concern. Numerous studies have shown diminished thirst sensations in the elderly. Despite the fact that these changes may be normal adaptations of the aging process, the outcomes of dehydration in the elderly are serious and range from constipation to cognitive impairment, functional decline, falls, or stroke.

Fluid and sodium balance is impaired in elderly [4]. The ability of the aged kidney to conserve Na^+ in response to Na^+ deprivation is impaired. Plasma renin, aldosterone, and angiotensin II levels decline with the advancing age. Two other factors place the elderly at risk for dehydration: altered thirst sensation and relative renal resistance to vasopressin. Renal diluting and sodium excretion abilities are also impaired.

Table 1 Classification of hepatic encephalopathy for research and clinical use

Clinical features	Clinical definition	Research definition
No specific symptoms and normal specialization testing results	Unimpaired	Unimpaired
No specific symptoms but abnormal specialized testing results	Covert	Minimal
Nonspecific changes without asterixis with abnormal specialized testing results		Grade I
Disorientation, asterixis, change in consciousness through coma. Specialized testing not required for diagnosis	Overt	Grade II
		Grade III
		Grade IV (coma)

Dehydration of as little as 2% loss of body weight results in impaired physiological responses and performance. The reported health effects of chronic mild dehydration and poor fluid intake include increased risk for kidney stones, urinary tract cancers, colon cancer, and mitral valve prolapse as well as diminished physical and mental performance.

Sudden shifts in the body's water balance can frequently result in dehydration, and the physical changes associated with aging expose the elderly, in particular, to the risks for dehydration [5]. The danger is that they may not know about their dehydrated condition, which could lead to more serious consequences.

Dehydration can cause headaches, tiredness, and loss of concentration. It is a problem particularly associated with aging, as older adults are less sensitive to mild dehydration, they drink less, and take longer time to rehydrate.

It is important for caregivers of the elderly to be more aware of the ways to prevent dehydration, recognize its signs, and treat it promptly.

The earliest manifestations are dryness of mouth, dry tongue with thick saliva, inability to urinate or pass only small amounts of urine, dark or deep-yellow urine, cramping in the limbs, headaches, weakness, general feeling of being unwell, and drowsiness or irritability. However, with more serious dehydration, the patient may have low blood pressure, severe cramping and muscle contractions in the limbs, back, and stomach, rapid but weak pulse, dry and sunken eyes with few or no tears, and wrinkled skin. If dehydration is not identified and treated, the consequences to health are significant, including reduced or even loss of consciousness and lowered blood pressure. If rehydration is not started, the situation can become life-threatening.

Everyone knows that water is what sustains life but many people seem to forget it. Here, caregivers should make sure that the older person has water by his side at all time. Frequent drinking in moderate amounts should be encouraged.

A good formula for how much water is needed everyday is to take one-third of the person's body weight in pounds and drink the equivalent number of ounces of water daily. For example, a 150-pound woman would need 50 ounces of water daily, or about six to eight glasses of water [6].

We should consider the following facts

If the elder's current intake is below the required amount, they should be instructed to increase the amount they drink gradually.

Encourage elders not to wait until thirsty to start drinking water; at that point, dehydration has already started.

One sign of proper hydration is the color of the urine – it should be clear or pale-yellow in color.

Minimize the number of beverages with caffeine because of its diuretic effect, causing the kidneys to excrete more water.

When you see early signs of dehydration, offer a sports drink to enable quick replenishment of water and electrolytes needed by the body.

Severe dehydration requires medical attention; if you see any signs or even just suspect it, call the doctor (Table 1).

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