When the joint is open small fragments may be washed out by irrigating with saline, and this may bring to light others, which had disappeared from sight during the earlier stages of the operation.

The management of loose bodies depends on the underlying cause. In an osteoarthrotic knee loose bodies should be removed if they are interfering with joint movement; but only rarely do they cause symptoms. Most require no treatment. Small fragments derived from an osteochondral fracture should be removed, and large fragments replaced accurately to restore the joint surface.⁷ In patients with osteochondritis dissecans the fragment should be removed if it has separated from the underlying bone and cartilage. The crater from which it originated should be carefully inspected and any other loose pieces excised.³

The treatment of synovial osteochondromatosis poses more difficult problems. Milgram⁴ has postulated that there are three recognisable phases of the disease: active intrasynovial disease without loose bodies, intrasynovial disease with loose bodies, and multiple loose bodies with no evidence of synovial

disease. He suggests, therefore, that if gross examination of the synovium at the time of surgery shows it to be normal synovectomy may be unnecessary and removal of the loose bodies should be sufficient.

Patients with active synovial disease require synovectomy, and this may have to be done from both the front and the back of the joint. Even then, extrasynovial intra-articular cartilaginous lesions may continue to grow and cause the patient's symptoms to recur. In the absence of symptoms osteochondral or chondral loose bodies may either remain free in the joint or become reattached to the synovium and resorb—and many patients with synovial osteochondromatosis may, perhaps, remain asymptomatic and undetected.⁴

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Regular Review

Bile salt tests in clinical practice

K W HEATON

While the introduction of a new test into routine clinical practice is notoriously difficult, the rarity of tests of bile salt metabolism in district general hospitals requires some further explanation. Research in the last 12 years has shown not only that bile salts are important for the function of the liver and intestines but also that their metabolism or circulation is disturbed in a wide variety of diseases—including gall stones, all kinds of liver and biliary disease, gastric ulcer and gastritis, stagnant loop syndrome, ileal disease including Crohn's disease, and even some cases of "functional" diarrhoea which would otherwise be labelled as irritable bowel syndrome.¹⁻³

Why, then, are tests on bile salts unknown in the average hospital laboratory? Certainly there are technical problems, but these are not beyond the ingenuity of chemical pathologists. The reluctance lies not in the laboratory but in the ward. Most clinicians, even most gastroenterologists, seem to think that they do not need to measure bile salt concentrations to diagnose or manage their patients adequately. Are they right? Bile salt tests are not, it is true, absolutely necessary for the diagnosis of any important or common disease; but they can provide a simple screening test for one small bowel disorder, definitive proof of another, and an extremely sensitive test of liver function.

Four tests have been advocated as simple and reliable enough for routine clinical use: the radioactive glycocholate breath test; faecal radioactivity after an oral dose of labelled

bile salt; measurement of the serum bile salt concentration; and analysis of bile salts in duodenal aspirate.

Bile salt breath test—This is a simple non-invasive screening test for bacterial overgrowth in the small intestine or the stagnant loop syndrome. All the patient has to do is to swallow a test meal or a drink containing 5 or 10 microcuries of ¹⁴C-labelled glycocholate (also called cholyglycine); he then breathes down a tube for a few minutes every one or two hours for four to six hours. His expired air bubbles through a measured amount of base, which traps all the carbon dioxide, including any ¹⁴CO₂ derived from the labelled bile salt. The amount of this ¹⁴CO₂ depends on the extent to which intestinal bacteria have deconjugated ¹⁴C-glycocholate and released ¹⁴C-glycine for further metabolism. Patients with excessive numbers of bacteria in the small intestine expire abnormal amounts of ¹⁴CO₂.

Intellectually, the test is attractive because the deconjugating bacteria are the very anaerobes whose presence in the upper gut is the hallmark of the stagnant loop syndrome. It is also cheap and the radiation exposure is no more than that of routine x-ray examinations. Nevertheless, for a variety of reasons few academic gastrointestinal units, let alone general hospitals, use the bile salt breath test. Patients with the stagnant loop syndrome are rare. Breath tests of any kind are unfamiliar in most hospital laboratories, and are expensive in terms of technician time. Some laboratories do not have the

liquid scintillation counter required to measure radiocarbon. Complex calculations are needed to convert the raw data on $^{14}\text{CO}_2$ specific activity into something with physiological meaning, such as the proportion of the administered radioactivity excreted per hour. Collecting control data is difficult, since it entails radioactivity, yet each laboratory must establish its own normal range. Some gastroenterologists prefer other breath tests, such as the measurement of hydrogen in expired air after an oral glucose load.

Finally, the clinical utility of the bile salt breath test has not been proved. In the first large series to be published the results seemed promising, with no false-negatives in 89 patients and rare false-positives.⁴ Two recent reports, however, have suggested that the result of the bile salt breath test may be misleading in a discouragingly high proportion of patients. At the Mayo Clinic (where the test originated) seven out of 23 patients with bacteriologically proved small bowel contamination had negative results. Moreover, false-positive results were given by two out of 20 patients with negative bacteriological tests.⁵ Even worse results were reported from Glasgow, with false-negative and false-positive rates of 59% and 27% respectively.⁶ These findings are obviously worrying. Nevertheless, to the clinician the real question is not how the breath test correlates with the result of a single bacterial culture (which, after all, is valid only for the level of the intestine from which the juice was aspirated) but whether it can predict the effect of antibiotic treatment on a patient's symptoms and malabsorption. Some reports suggest that the correlation is good,^{4 7} but published data are too scanty for final conclusions to be drawn.

Faced with all this, the pragmatic clinician who does not have unlimited laboratory back-up may be excused for deciding that, until research has proved the clinical value of the bile salt breath test, he will continue to use conventional criteria for the diagnosis of the stagnant loop syndrome—namely, the correction of steatorrhoea and vitamin B₁₂ malabsorption by antibiotics in a patient with a structural abnormality of the small intestine.

Nevertheless, whatever its clinical limitations, the breath test has proved valuable in research, where it has shown, for example, that small bowel bacterial overgrowth can cause malnutrition and malabsorption in old people with structurally normal intestines,⁸ and that it may be a major factor in diabetic diarrhoea.⁹ The value of the test, however, in research is greatly enhanced by concurrent measurement of radioactivity in the faeces.

Faecal radioactivity—In this procedure a labelled bile salt is given by mouth, when it appears in the faeces at a rate determined by the efficiency of its absorption. Since bile salts are absorbed mainly in the terminal ileum, faecal counting should be a good measure of ileal function and so be useful in the early diagnosis of Crohn's disease. Some authors have, in fact, reported that faecal radioactivity is raised after ^{14}C -glycocholate by mouth in some patients negative on radiographic examination who are subsequently shown to have ileal Crohn's disease.⁴ Others, however, have found normal faecal radioactivity in the presence of radiologically obvious disease,^{10 11} even when the patient has diarrhoea.¹⁰ These disappointing results may be due to the use of an inappropriately labelled bile salt. The glycocholate used for the breath test has the ^{14}C label on the glycine moiety, and any labelled glycine split off in the colon by bacterial deconjugation may disappear from the faeces by being absorbed as such (or as $^{14}\text{CO}_2$ after bacterial degradation). This problem may be overcome by giving a bile salt labelled on the steroid nucleus

(as originally suggested by Fromm and Hofmann¹²)—ideally, accompanied by an unabsorbable marker such as ^{51}Cr ; but, even without this refinement, impressive results have been reported. Thus, van Blankenstein and his colleagues¹³ found abnormally fast excretion of nucleus-labelled taurocholate in 15 out of 18 patients with ileal Crohn's disease, several of whom had negative x-ray findings.

Unfortunately, this test is too cumbersome for general clinical use. Either collection of stools must be prolonged and fastidiously complete or a non-absorbable marker must be used. Next—and worse—the stools must be homogenised and a portion combusted in a special and expensive oxidiser, and the $^{14}\text{CO}_2$ produced is then adsorbed and counted in a liquid scintillation counter. So this is a test for the enthusiast and the research worker. The ordinary clinician must rely on a therapeutic trial of cholestyramine to decide if a patient's diarrhoea is due to malabsorption of bile salts and therefore to ileal dysfunction. This assessment could change, however, if a bile salt became commercially available with a gamma-emitting label, since the whole stool could then be counted in an ordinary well counter and no laboratory handling would be needed.

Again, the faecal radioactivity test has proved its worth in clinical research. When Hess Thaysen's group in Denmark applied it to patients with longstanding watery diarrhoea of unexplained origin (often blamed on psychoneurosis) they discovered some who had idiopathic malabsorption of bile salts, their diarrhoea being due to the cathartic effect of unabsorbed bile salts on the colon.⁴ In all these patients the diarrhoea subsided overnight with treatment with cholestyramine. The test has also been used to show that women who develop diarrhoea after pelvic irradiation usually have malabsorption of bile salts,¹³ presumably due to radiation ileitis.

Serum bile salts—The convention of measuring the concentration of serum bilirubin rather than that of the bile salts in patients with hepatobiliary disease is paradoxical. Altered bilirubin metabolism is clinically obvious but it has no important ill effects (after the neonatal period), whereas altered bile salt metabolism accounts for the major complications of cholestasis, including malabsorption of fat and vitamin K and probably pruritus. Moreover, a raised serum bile salt concentration, especially after a meal, is a much more sensitive indicator of liver cell dysfunction than is a raised bilirubin concentration: it is probably as sensitive as any liver function test^{14 15}—and has been technically possible for half a century. Why, then, are serum bile salts not measured routinely? One reason may be emotional rather than intellectual. Bilirubin is visible, often dramatically so, and cries out to be measured. Bile salts (being colourless) are unseen, and "what the eye does not see, the heart does not grieve over." Another reason is technical. The assay is more difficult than that of bilirubin, and normally it requires extraction of the serum, which is time-consuming even with modern resin techniques. Nevertheless, simplified methods are becoming available, including an enzyme kit and a rocket method, and even a technique which does not require extraction of serum.¹⁶

So will measurement of serum bile salt concentrations soon become popular after all? Probably not. Firstly, there are no diagnoses which cannot be made by other, more standard methods (except perhaps mild cases of benign recurrent cholestasis, a rare disease). Secondly, the place in routine clinical practice of an ultrasensitive liver function test is questionable. Action is seldom taken on borderline dysfunction of any organ. As an exception, Javitt¹⁵ has suggested that patients with suspected Gilbert's disease could be spared a liver biopsy if they have a normal postprandial serum bile salt

concentration. Other suggested uses are the early detection of drug hepatotoxicity and of relapse in chronic active hepatitis,¹⁷ and making the distinction between chronic active and chronic persistent hepatitis.

Many attempts have been made to identify patterns of abnormality among the individual serum bile salts and so to distinguish different causes of jaundice.¹⁵⁻¹⁸ Such studies have usually shown that in biliary obstruction on the one hand and in parenchymal liver disease on the other there are significant differences between the ratios of trihydroxy to dihydroxy bile salts and of cholate to chenodeoxycholate. Nevertheless, there is so much overlap that the ratios cannot be safely used in diagnosis; and, furthermore, the measurements are time-consuming, since they require gas-liquid chromatography or radioimmunoassay.

Disappointment has also followed attempts to introduce an intravenous bile salt tolerance test into clinical medicine. The concept of the test is attractive: measuring the clearance of bile salts from the blood is assessing one of the important functions of the hepatocyte, the uptake and transport of bile salts. Again, however, in practice there is considerable overlap in clearance rates between liver disease and normal and between mild and severe liver disease,¹⁹ probably owing to the large reserve capacity of the liver cell mass. Better discrimination may be obtainable with an oral bile salt tolerance test, but this has not been fully evaluated.

Measurement of bile salts in duodenal juice—Two clinically important questions can be answered by examining the bile salts in duodenal aspirates. The first is "Does the patient have bacterial deconjugation of bile salts in the upper small intestine?" In a patient with malabsorption finding unconjugated bile salts in duodenal or jejunal juice is strong evidence that the malabsorption is due to bacterial contamination of the

small intestine.²⁰ Unfortunately, this test requires thin-layer chromatography, and of course duodenal intubation, so it is probably too cumbersome for routine use. Even for a specialised gastroenterology unit it offers little advantage over a ¹⁴C-glycocholate breath test, especially if this is combined with anaerobic culture of small bowel aspirate.

The second question is: "Is the patient at risk of forming cholesterol-rich gall stones?" By measuring the bile salt concentration in duodenal aspirate while the gall bladder is emptying one can assess the degree to which bile is saturated with cholesterol. This information should be useful in deciding whether or not a patient with gall stones should be offered treatment with chenodeoxycholic acid,²¹ since stones are unlikely to dissolve if the bile is unsaturated (in which case they are presumably cholesterol-poor). It could also help in monitoring the dosage of chenodeoxycholic acid. In practice, however, bile varies so much from day to day that a single sample is probably not a safe basis for clinical decisions. Furthermore, assessing cholesterol saturation requires measurements not only of bile salts but also of phospholipids and cholesterol.

In conclusion, then, altered bile salt metabolism is now recognised to be important in several diseases, and its study has thrown much light on these diseases. Bile salt tests, and especially the breath test, are useful in specialised gastrointestinal units for the detailed study of patients; but their cost-benefit ratio is probably too high for everyday clinical practice.

K W HEATON

Consultant and senior lecturer in medicine,
university department of medicine,
Bristol Royal Infirmary

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