The Diagnosis of Disease of the Bovine Liver - A Clinician's View

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The diagnosis of disease of the liver is a vague and unsatisfactory, confusing and difficult, subject from the clinician's point of view.

It is, of course, very difficult, in fact practically impossible, to examine the liver properly by traditional clinical methods. One cannot see it: one cannot feel it: it is to all intents and purposes entirely within the costal arch unless it is grossly enlarged. It is, in fact, very easy to examine a cow without even considering the liver.

The liver is involved in many physiological processes: it has many functions. This implies that liver failure or disease may produce a diversity of symptoms according (1) to the function involved and (2) to the lesion produced e.g. pus, fat, fibre and so on. We have only to remember some of the many clinical symptoms which we have seen associated with various forms of liver disease to understand the complexity which may confuse the diagnostic process.

For example lethargy, slow weight loss, anaemia, failure to thrive, lowgrade abdominal pain, acute abdominal pain, massive abdominal haemorrhage, abdominal distention, ascites, chronic venous congestion, ataxia, skin conditions i.e. photosensitisation, meningitis, endocarditis, encephalopathy due to hyperammonaemia; dyspnoea with pulmonary thrombosis and massive nasal haemorrhage and even, occasionally, jaundice, may be signs pointing to liver disease, not to mention the diverse problems of the high yielding cow calving down with a grossly fatty liver, where even such mundane syndromes as metritis, coliform mastitis, ketosis, low solids, milk fever, and infertility may all stem from, and point to, a primary liver condition.

This list leads one directly to the idea that very often the liver is not the immediate cause of the disease syndrome exhibited, but the background factor which encourage and predisposes to disease in other organs and systems.

It is also important that the huge tissue reserve present in the liver may well mean that a disease process is irreparably advanced by the time clinical signs of liver pathology become even reasonably obvious.

We must also accept that even at post-mortem examination the liver may prove difficult.

1. postmortem decomposition is very rapid because of the ease with which putrefactive organisms enter from the gut via the portal system.
2. the liver may well show a developing and coincidental cirrhosis, fatty change, or even abscessation which is NOT in fact the cause of the fatal illness of the animal concerned. Assessment of the significance of post-mortem liver changes is a task which can confuse even the experienced pathologist.

There are, of course, many laboratory tests for hepatic damage, and liver biopsy is always possible. But these tests themselves may be misleading. We have already spoken of the huge tissue reserve and made the point that there may be quite extensive liver lesions which are, not as yet, causing disease. So, when liver tests are suggestive, one must decide on clinical grounds whether the liver lesions indicated are part of the present ill health, or not.

Also, one must admit that none of the so-called liver tests are completely selective for liver. Even biopsy can pick out a relatively normal portion of a severely diseased liver, or vice versa.

What hepatic function tests, or tests otherwise indicative of hepatic disease, are there available.

1. *Haematology*—anaemia is often the result of hepatic disease. But, anaemia per se may be present in many other conditions.
   —the white cell picture is of little if any value in hepatic disease.
2. *Proteins*—chronic liver damage tends to produce lowered serum albumin, whilst if the process is inflammatory globulins may be raised. But similar changes may occur in gut or kidney damage.
3. *Serum enzymes*
   a) SGOT (AST) is not specific for liver damage—it rises in acute liver damage : sometimes in chronic : but may show a far greater rise in muscle damage.
   b) SAP (serum alkaline phosphatase) may rise very markedly in any liver lesions causing severe biliary obstruction, but such biliary obstruction may be due not only to cirrhosis, but sometimes to fat, or acute inflammatory change. SAP may also rise in disease processess not involving liver.
   c) SDH (sorbitol dehydrogenase) is not completely selective, but nearly so. A raised level indicates acute cellular breakdown. The level tends to fall as soon as the irritating factor is overcome, even though there is still unresolved liver damage, and this makes it a very useful test.
   d) Gamma GT—gamma glutamyl transferase is a most useful test in cattle liver disease. Basically, it is elevated in chronic damage e.g. liver fluke, but sometimes massive fatty change will provoke a

raised level. Nevertheless it tends to be fairly selective for cirrhosis.

SDH rises in acute phases and drops as Gamma GT rises. Gamma GT's usefulness in prognosis is undeniable and may be used extensively in groups of cattle, particularly to check for fluke.

We do need, however, very badly, a simple and reliable test for fatty change in the liver, but so far none is available.

4. *Bilirubin* levels may be useful? One must remember that jaundice may not indicate primary hepatic cellular damage : it may be obstructive. One needs to know this.

   In fact very many cases of liver disease in cattle do **not** show jaundice whilst some of the most severe cases showing jaundice are haemolytic in nature e.g. piroplasmosis or even the haemolysis of kale toxicity.

Liver biopsy should be considered. The writer does not find liver biopsy as easy in cattle as in horses, even using a needle biopsy instrument rather than the apple corer device traditionally used for copper estimation. He uses the method established by Loosmore and Allcroft (1951) thirty years ago, but finds the technique difficult (second to last right intercostal space i.e. between ribs 11 and 12, at an average distance of 7 inches from the dorsal mid line).

One problem is that the procedure inevitably takes time in interpretation and costs a fair amount of money, and few farmers are prepared to accept any time consuming or expensive procedure unless the animal is particularly valuable. The butcher is generally preferred to the veterinarian.

Laparotomy— when the animal does merit complete investigation it may be preferable to open behind the last rib in the right sub lumbar fossa—inspect, palpate, and if necessary take biopsy material all in the same procedure.

Paracentesis—a simple and easy procedure which will always be useful if abdominal fluid is obviously present in quantity; for abdominal transudate is likely to indicate hepatic disease, whilst the presence of gallons of thin, foul smelling purulent material will indicate a diffuse peritonitis from one of a number of reasons, including unfortunately, for the diagnostician, a liver abscess.

But, again, it must be stressed that the farmer will, by and large, no longer tolerate expensive laboratory and diagnostic procedures on any but the most valuable individual cows.

So what is the formula for successful diagnosis of liver disease?

As far as the writer is concerned there is one rigid rule. Just as one must never examine a cow without checking the udder, so one must never examine a cow, particularly a dairy cow, without considering the liver.

But even when it has been decided that the liver is involved, one must remember that no diagnosis has yet been made. One has only established the part of the body, the system involved. Before a true diagnosis is made the lesion must be specified.

A mental list of the syndromes involved in liver disease in cattle helps in differential diagnosis.

1) *Abscessation*—abscessation is a common finding at post mortem examination or in the slaughter house. Abscesses may be single and large, or numerous and smaller. It is obvious that they are often well walled off and do very little harm, but there is evidence that even if no obvious clinical illness is present, affected cattle may be in a state of sub-optimal health and production.

   Most such abscesses are caused by organisms arriving from the rumen via the portal system. Fusiformus necrophorus is common: so of course is *C. pyogenes.* Obviously conditions damaging the rumen mucosa, as for example, cereal overeating and other conditions producing rumen acidosis, will predispose to liver abscesses.

They are difficult to diagnose, for usually pain is minimal, white cell reaction is limited, and liver function relatively unimpaired. Occasionally there is sufficient reaction to produce a "wire" like syndrome with neutrophilia, pain and temperature, plus abnormal liver function tests. Sometimes, in fact, a reticular foreign body moving in an unusual direction may set up a huge liver abscess and may produce a somewhat muted "wire" like syndrome—muted because visceral peritoneal lesions are not painful.

It is, in fact, not the presence of hepatic abscesses per se which causes significant illness, but the sequelae which may occur.

(a) rupture of an abscess into the peritoneal cavity, leading to an acute diffuse peritonitis.
(b) rupture of an abscess into a major vessel leading to shock, pyaemia, and rapid death OR to major haemorrhage and sudden death.
(c) thrombosis of the vena cava usually near the point, where it passes through the diaphragm. If it affects the hepatic protal system to a marked degree one may get abdominal distention and ascites, as well as enlargement and congestion of the liver itself with progressive weight loss and malaise. If pulmonary thrombosis and embolism occur, embolic pulmonary abscesses form and a thoracic syndrome emerges, with rupture of abscesses into bloodvessels and bronchi producing severe and often recurrent haemorrhage through the nose and mouth. There will be a painful cough and dyspnoea.

It is, in fact, true that most cases of significant epistaxis in the cow are due to lung abscesses secondary to liver abscesses.

2) *Hepatic Necrosis*—necrosis of liver tissue occurs following most liver lesions, and there is frequently considerable necrosis associated with Fusiformus abscessation of the liver following cereal engorgement, but it is interesting that a specific, or nearly specific clinical syndrome, bacillary necrosis, occurs due to

Fusiformus necrophorus invasion of the liver of the individual adult cow, reminding one of the similar syndrome in the 10 day old lamb.

The picture is of pyrexia, with inappetence, lethargy, and rapid pulse rate, loss of flesh and weakness, followed by ataxia and recumbency. There is grunting and grinding of the teeth with, sometimes, localisation of pain in the anterior abdomen. Fortunately for the clinician jaundice occasionally occurs.

Post mortem examination reveals a number of well circumscribed greyish hard areas of encapsulated necrosis, with enlargement of the liver and some ascites.

3) *Cholecystitis* is rare in cattle, although one suspects that the difficulty in diagnosis makes it easy to miss. It was well described by Professor E.J. Ford in 1955. The present writer has seen two cases only—both were diagnosed by the pathologist and not the clinician—both followed Ford's description. There was a slightly raised temperature with lowered appetite and milk yield. Rumen movement was absent: there was ataxia, jaundice and, eventually anterior abdominal pain. It is interesting that these cases support the contention that jaundice is much more likely to occur in obstructive hepatic conditions than in parenchymatous change within the liver itself.
4) *Cirrhosis* - in cattle, for all practical purposes, means liver fluke infestation. All veterinarians are aware of fascioliasis and yet there are many misconceptions. How often, still, do we hear it said that it only affects young cattle; that it causes diarrhoea; that the clinical signs must include wasting; submaxillary oedema, and marked anaemia. It may well be that many veterinary surgeons have practically forgotten about fluke after these last few dry summers; caution is necessary. There have been a number of herd outbreaks during this last winter; and it only requires two or three consecutive wet summers and calamitous outbreaks like those of the early 1970's may well re-occur.

Several points need re-iteration

(a) "Fluke" must always be high, along with nutritional energy deficit (the two often occurring together, and both requiring attention) on the differential list for suboptimal yield in the winter months, usually with suboptimal bodily condition between parturition and peak yield. One does not need the dramatic clinical signs of the text books to draw one's attention to "fluke" infestation.
Incidentally, in very severe clinical disease, obstinate constipation is much more likely than diarrhoea, but this should be a matter of historical interest only.
(b) if one "fluke" egg is found in a dozen faeces samples from a hundred cow herd, the herd must be regarded as "fluke" infested, and dosed. The results may be quite spectacular.
(c) The Gamma GT is a good general test for "fluke" infestation in cattle. Once cirrhotic changes have occurred the Gamma GT will be high and will stay high until long after clinical improvement.
(d) Obviously prophylactic dosing should be regarded as obligatory in most herds in most years, even allowing for the value of the Ministry forecasts, of routine sampling for eggs, and of Gamma GT tests, but farmers nowadays are loathe to dose a herd of adult cattle because of the fairly lengthy milk withdrawal times necessary following the use of the more efficient "flukicides".

One should remember that liver fluke infestation can well lead to infertility (possibly by virtue of weight loss) low solids not fat, salmonellosis, and endocarditis (due to the passage of streptococcus faecalis into the liver and on into the circulation with the young liver fluke).

Remember also the occasional subacute abdominal pain syndrome, closely resembling the "wired cow" syndrome, which is occasionally seen in the Autumn during the migratory stage of the young fluke.

And, finally, let us remember that fluke infestation accentuates energy deficit (starvation) and energy deficit accentuates liver fluke damage. It may be useful to give 'fluky' cows more food, but it is decidedly not useful to give starved cows flukicides. The correct diagnosis must be made.

Cirrhosis also results from ragwort poisoning, which although the most common form of chronic liver damage in horses, and still seen in young cattle on rough pasture, or grazing hay off rough pasture, should never, today, be seen in milking herds, for ragwort should never appear on ley pastures. The signs of loss of weight, terminal tenesmus, ataxia, and encephalopathy, along with raised Gamma GT, and sometimes jaundice in a group of youngsters should give one a lead.

Occasionally, however, the onset may be sudden in animals in good condition, there may be a scant, sticky, black diarrhoea in a very sick animal, making it only too easy to diagnose intussusception, especially if there is some straining, but as yet the nervous signs have not begun.

These signs, with blindness, headpressing, and dragging of hind fetlocks may make one think of lead poisoning.

Photosensitisation may also occur.

5) *Photosensitisation* is worth mention in its own right. Quite apart from ragwort, there are very many relatively benign pasture and hedgerow plants which under certain circumstances produce hepatotoxins leading to hepatic damage producing the phylloerythrin type of photosensitisation.
In passing it is worth suggesting that the acute skin and mucous membrane signs of photosensitisation can resemble malignant catarrhal fever, or even the severe head forms of mucosal disease, so closely that before diagnosing one of these two diseases it is worth running one's hand over the white areas for signs of the leathery necrosis that confirms photosensitisation and therefore

liver damage.

But more relevant to our present theme is the fact that there may be a period of up to 36 hours before skin and mucus membrane lesions appear when the clinical picture is related to acute liver damage alone, producing depression, gut atony, and fairly acute abdominal pain which can easily lead to a false diagnosis of intestinal obstruction.

Incidentally the pain associated with the early development of photosensitisation lesions of the udder and teats may provoke such an energetic display of kicking at the belly, and looking at the flanks, that one can hardly be restrained from immediate laparotomy.

6) *Neoplasia of the liver* is relatively infrequent, usually involves lymphosarcoma, sometimes adenocarcinoma, and is difficult to diagnose, particularly as it may also involve other sites. Basically the picture is one of loss of weight.
7) *Tuberculosis of the liver,* of course, occurs. The younger generation regard it as an admission of senility to talk about clinical tuberculosis, but tuberculosis of cattle, in these years of the badger, is far from being a matter of history. The liver lesions per se are, of course, unlikely to be diagnosed: it is much more likely that lesions deriving from liver infection, for example, meningitis in young stock, will provide a recognisable syndrome.
8) *Chemical poisons* - it is probably still worth remembering that certain drugs, now more or less obsolete, could cause severe liver damage, and in particular, one remembers the serious fatty change often associated with the use of chloroform as an anaesthetic, and of carbon tetra chloride and hexachlorethane as flukicides. Many chemical and bacterial toxins may produce severe fatty change of the liver.

But, of course, any discussion regarding fatty change in the bovine liver leads immediately to discussion of the most common and most important hepatic syndrome of the modern intensively fed dairy cow.

9) *The Fatty Liver Syndrome* which is also spoken of as the Fat Cow Syndrome, though it is of course the degree of fatness of the liver, rather than of the cow, which is all important. Morrow's (1976) description of the syndrome was followed by several years of work at Compton by Reid and his colleagues (1979: 1980: 1981) which has revolutionised thinking about the nutrition of the immediately pre and post parturient cow.

We are now all aware of the dangers of excessive weight gain in the preparturient period, and of the association of excess fatty change in the liver at this time, not only with herd ketosis in the period of relative energy deficit after calving, but also with the occurrence of milk fever, metritis and retained membranes, coliform mastitis, abomasal disorders and infertility in the post parturient animal. A problem in any of these areas now merits an investigation into nutrition and liver function within the herd.

Although it is only in the last few years that we have attained reasonably full understanding of the causes and effects of this fat liver syndrome, it is not a new condition. It has occurred before, in times when the economics of milk production made it apparently profitable to feed a preparturient dairy cow almost to the point of producing pate de fois gras in an effort, however misguided, to improve already spectacular milk yields. Wright (1949) described the so-called "preparturient inability to rise" syndrome of the Cheshire Ayrshire which, heavily steamed up and grossly fat, not uncommonly became recumbent in the last weeks of pregnancy and never regained her feet. The spectacularly fatty state of the livers of these unfortunate cows was a striking feature of the condition.

Holmes (1950) made us aware of the widespread incidence of sub-clinical ketosis in intensive dairy herds at that time. Not infrequently one met herds heavily "steamed up" and fed a high protein level after calving, in which nearly every cow from 2 to 6 weeks calved smelt of ketone bodies: gave a positive result, refused to eat the last pound or so of concentrates, and gave a yield approx. 1 gall. below expectation at peak. The clinical cases were merely the tip of the iceberg.

But then, of course, came lean years when it was almost more economic not to produce milk than to produce it, and it is only recently with the spectacular swing back towards the intensively fed high production herd that these fat liver syndromes have become of universal importance to the industry.

References

1. Ford, E. J., 1955, Vet. Rec., 67, 634. - 2. Loosmore R. M., and Allcroft R., 1951, Vet. Rec., 63, 414. - 3. Wright J. G., 1949. Personal communication. - 4. Holmes J. R., 1950. Subclinical Ketosis in a Dairy Herd. Brit. Vet. Journal 106, 365. - 5. Morrow, D. A., 1976. Fat Cow Syndrome. Journal of Dairy Science 59, 1625. - 6. Reid I. M., 1980. Incidence and severity of fatty liver in dairy cows. Vet. Rec. 107, 281. - 7. Reid I. M., Roberts C. J. and Manston R., 1979. Reduced fertility associated with fatty liver in high yielding dairy cows. Vet. Science Communications 3, 321. - 8. Roberts, C. J., Reid I. M., Rowlands C. J. and Patterson A., 1981. A fat mobilisation syndrome in dairy cows in early lactation. Vet. Rec. 108. 7.