Hepatitis and activity

DENNIS M. KRIKLER
F.R.C.P.E., M.R.C.P.

Consultant Physician
The Prince of Wales's Hospital, London, N.15

Summary

The effects of physical activity during an attack of infectious hepatitis are discussed.

There is no evidence that activity during convalescence produces any ill-effects.

On the other hand, strenuous physical activity in the acute stage may be dangerous, possibly because hepatic blood-flow is reduced.

My credentials for speaking to you about hepatitis are slight, certainly when compared with those of the others on this panel, for my main interest is in diseases of the cardiovascular system. It was together with a consultant paediatrician that I made observations on activity and hepatitis which I propose to discuss today (Krikler & Zilberg, 1966), but towards the end of this presentation I aim to bring out a few points about the hepatic circulation that may be relevant and that may provide justification for the impressions that we formed.

Convalescence and rest during the attack

The possibility that premature return to activity might delay recovery from acute infectious hepatitis was the subject of a number of observations made during the epidemics that were so frequent in the armies on both sides during the second world war, and it became customary to advise strict bed-rest, in the hope and expectation that this would ensure rapid recovery without the sequelae of either a fulminating course on the one hand or persistent activity and possibly the development of chronic hepatic disease, including cirrhosis, on the other. Anecdotes abound with regard to the effect of premature exercise causing relapse in soldiers who had apparently recovered. Whether they would have relapsed in any case remains unanswered, for few controlled trials were carried out at that time. The amount and type of exertion said to have produced relapse was extremely variable and I know that it was felt by physicians serving with the South African Medical Corps that a certain number of patients were adversely affected by bouncing around in the back of a troop carrier, over rough roads, on the trip back to camp from hospital. As far as I can establish,

there was no proof that such cases had fully recovered and they may indeed have had mild hyperbilirubinaemia at the time they were sent back to duty. This possibility is supported by a study conducted by Swift *et al.* (1950), who compared the course in patients who were put on an exercise programme while convalescent, with those who were allowed to continue to rest. If at the time the period of exercise was started the serum bilirubin was less than 3 mg/100 ml the subsequent course was no different in those who rested and those who exercised. On the other hand, in those whose bilirubin was above 3 mg/100 ml at the commencement of the exercise period, convalescence was prolonged by an average period of 2 weeks as compared with the controls; but subsequently recovery seemed to be quite complete. Clinical evidence of the onset of relapse was indicated by anorexia or hepatic tenderness, and of course at that time enzyme studies and liver biopsy were not available to corroborate or deny the impressions that were formed.

The careful follow-up studies conducted by Chalmers and his associates on American soldiers who suffered from hepatitis in Korea in 1950-51 have certainly provided no evidence for long-term ill-effects due to failure to rest completely during acute infectious hepatitis (Nefzger & Chalmers, 1963). When, 10 years later, they studied 460 cases who had been allowed to take exercise during the convalescent phase, and compared their course with those who had been kept at rest, there was no significant difference in the incidence of liver damage, nor indeed any real proof that any of the patients had come to permanent harm, whether or not they had rested. It seems very reasonable, on the basis of their work, as well as other reports and impressions, to permit patients to get out of bed just as soon as they are feeling well again, and at least to rest in a chair, though I must say that I see no advantage in encouraging any patient who has been ill to undertake vigorous exercise at such a time. On the other hand there seems absolutely no reason for the protracted bed-rest that was in vogue some years ago, and that is often still recommended and used.

There is also the recent report by Zaversnik & Petrovic (1970) on the Slovenian epidemic in 1966, in which they wondered whether the lack of facilities to permit adequate rest would lead to persistent liver damage. One year after the attack, thirty-eight of their 2778 patients were affected in this way; of course we do know that biochemical and histological changes can persist for quite a long time without there necessarily being a long-term risk of permanent damage. This low incidence of possible complications strengthens the case against the need for prolonged bed-rest.

Activity during the acute stage

Our small study of five cases of fulminant hepatitis in Salisbury, Southern Rhodesia, was a clinical one (Krikler & Zilberg, 1966), and it may well be that other factors remain to be discovered, to provide the explanation for what we saw. Table 1 summarizes our data. As you will see three died, and two recovered. Using conventional diagnostic criteria these were cases of severe acute infectious hepatitis. They had all undertaken vigorous physical exercise during the first day or two of the disease; we saw no other cases of fulminant hepatitis. Usually the patients were not quite well, and had a commitment to an athletic activity which they were encouraged to carry out, even though they did not feel like it. Case 1 was the son of a doctor who himself had been a great athlete and who thought his son should play rugby despite nausea, vomiting, anorexia and fever. This normally keen sportsman had been reluctant to do so, and became very much worse during the night after the match, was obviously jaundiced 2 days later, and was soon dead. Two others were also children in whom these circumstances applied. In Case 2, there was a strenuous day-long cricket match followed by the school dance that night, in both of which he participated, even though feeling ill; his recovery was a gratifying surprise. The third patient also took part in sports and became *victrix ludorum* despite feeling unwell, and Case 5 was an adult who went yachting in a gale, which required much more strenuous effort than usual.

There have been few other published reports, but it is interesting to see that Swift *et al.* (1950) commented that the disease was more severe and protracted in soldiers who were exhausted at the onset than in others, and that right upper quadrant distress had been worsened by exercise during the pre-icteric phase (Barker, Capps & Allen, 1945). In this connection I might perhaps mention unpublished observations that have been made by several medical officers in the Israeli army (Sheba, personal communication). They have seen a number of cases of fulminant hepatitis in soldiers who had been on route marches, and had correlated this with electrolyte changes, having thought that the intense sweating produced during a stiff march under hot conditions had been responsible; I wonder whether the activity *per se* was not the real factor.

How might this work? I would like to throw in some highly theoretical suggestions that might be relevant, and who knows, it might be possible to support the point experimentally. One would guess that the liver needs all the oxygen it can get during infectious hepatitis, at least during the early stages, and that anoxia might be a factor in producing the necrosis or in increasing its severity. One of the body's mechanisms of redistributing blood flow during exercise is, of course, to cut down on the splanchnic circulation, the active muscle mass deriving its necessary extra share in this way. That this does happen has been shown in normal human subjects by a number of workers including Wade *et al.* (1956), who also demonstrated that splanchnic oxygen consumption diminished in proportion to the fall in blood flow. These studies were done in supine subjects, and in them the decrease in splanchnic blood flow was of the order of 30–50%. This work was further extended by Rowell, Blackmon & Bruce (1964), who found that exercise produced an even greater decrease of splanchnic blood flow if it was undertaken in the upright posture; this was of the order of 80% or more. It seems to me very plausible that great damage could be done to the liver if such very great circulatory changes took place during a period of viral invasion with damage to cells. This

TABLE 1. Clinical data on five cases of fulminant hepatitis (reprinted from Krikler & Zilberg (1966) *Lancet*, ii, 1046. With kind permission of the Editor)

Patient number	Age (years)	Sex	Date	Highest levels		Outcome
				Serum-bilirubin (mg/100 ml)	Serum-glutamic-pyruvic-transaminase (Frankel units)	
1	11	M	May 1961	7.0	6800	Died four days after onset
2	12	M	March 1964	8.8	3200	Recovered; liver biopsy—? fibrosis
3	11	F	April 1965	5.0	2800	Died fourteen days after onset
4	45	F	November 1965	10.5	44	Died sixteen days after onset
5	32	M	March 1966	8.2	5400	Recovered

may be amenable to demonstration in the experimental animal, e.g. murine hepatitis, which is analogous in some ways to human hepatitis (Piazza, 1969). Perhaps some-one could try the effect of a treadmill on mice infected with murine hepatitis and compare the outcome with that in others allowed to take their ease. I do not know how practical this is, but it does seem to me to be a reasonable thought to consider.

Wider enquiry about the history of strenuous exercise during the pre-icteric phase may be useful in enabling us to understand why some patients develop severe hepatitis and others do not, but this may well be only one of a whole host of factors.

In conclusion, I would like to cite as a justification for drawing attention to the possible role of strenuous activity during the early stages of hepatitis, the following extract from Trey *et al.* (1968): 'Fulminant hepatic failure is rare, but because of its grave prognosis, any factor that could lead to its prevention should be critically examined.' It may prove difficult to do anything about it, but I think we should at least have a better look at the facts and see whether intense activity during the early stages of hepatitis is a potentially lethal situation.

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