“Hepatitis B and C: carrier to cancer — Asian perspectives”:
Pre-conference expert group deliberations

Hepatitis B

Terminology
The pre-conference deliberations between the invited faculty members from India and abroad were held on December 4 and 6, 1998 at New Delhi. The session was chaired by Prof. Kunio Okuda, Japan. The meeting started with Prof. SK Sarin giving background information on the term ‘carrier’ and then presenting the results of the Asian collaborative survey on ‘Hepatitis B and C carriers’.

The salient features of the discussion between the expert group, chairpersons of the various sessions, core group members, advisors and patrons are reproduced here. The issues on which consensus could be achieved have also been recorded.

Dr. SK Sarin: A ‘carrier’ is defined as a person who harbors a specific infectious agent in the absence of discernible clinical disease and serves as a potential source of infection for others. With reference to hepatitis B the proposed definition of HBV carrier is: i) an asymptomatic person with ii) HBsAg positive status for 6 months, iii) normal ALT and iv) normal histology (histological activity index [HAI] <3).

I invite your comments regarding this proposed definition.

Dr. NS Murthy: Why have you chosen the time limit of 6 months?

Dr. Sarin: A limit of 6 months is universally accepted.

Dr. SR Naik: I agree with clauses 1 and 2 of the definition, but disagree with clauses 3 and 4 because, if tested repeatedly (6 times), many of these patients will have elevated ALT.

Dr. Mobin Khazan: There are 20 million carriers of hepatitis B in Bangladesh. In my country there are three subgroups of these patients: (i) asymptomatic patients with normal ALT and persistently positive HBsAg; (ii) those with mildly increased ALT who will be detected only by clinical tests; and (iii) those with HBV mutant diseases. These three groups need to be differentiated.

Dr. G Hess: I disagree with the WHO definition mentioned by Dr Sarin since some patients with active liver disease will become asymptomatic and develop normal ALT when the disease goes into remission. Should they be called carriers as per the definition?

Dr. R Sharma: Carriers are of three types: (i) incubatory carriers, (ii) post disease carriers and (iii) healthy carriers. Where does the hepatitis B carrier fit in this classification?

Dr. Sarin: We need to discuss whether this definition fits hepatitis B.

Dr. K Chaudhary: The WHO definition does not apply here because it is not clear whether there are any patients at all with chronic HBV infection who truly do not have liver disease.

Dr. H Gatum: It must be appreciated that the chronic HBV infection is not a static disease; it is a dynamic disease, if followed over a period of time. A ‘carrier’ may change into active liver disease with elevation of ALT at any time.

Dr. Hess: What is the difference between chronic persistent hepatitis B virus infection and the carrier state?

Dr. Guma: No difference.

Dr. G McCaughan: The term ‘carrier’ should be deleted and replaced with ‘chronic hepatitis B infection’.

Dr. SJ Hadziyannis: The term ‘carrier’ was introduced in the 1960s when the hepatitis B surface antigen was first detected from the blood of a healthy person. Subsequently, an Austrian study showed that a subgroup of patients with HBsAg positivity and normal enzymes remained well over a follow-up of five years. However, several subsequent studies have revealed that this was not always true.

Dr. Sarin: A recent study from Alaska revealed that HBV carriers followed up for up to fifteen years developed hepatocellular carcinoma (HCC). Hence, a carrier state is not a benign state.

Dr. Okuda: The term ‘carrier’ is synonymous with chronic hepatitis B.

Dr. McCaughan: Some patients have hepatitis B viremia but do not have ‘itis’, i.e., they carry the virus but do not have hepatic inflammation. Hence, it is technically incorrect to label them as having chronic hepatitis B.

Dr. Hadziyannis: ‘Carrier’ is old and redundant terminology and should be deleted.

Dr. Sarin: I propose we should use the term ‘chronic virus B infection’ and not chronic hepatitis B infection for the reason mentioned by Dr. McCaughan. The word ‘chronic’ in chronic hepatitis B may be misunderstood.

Dr. McCaughan: Patients with chronic hepatic inflammation must be differentiated from those without inflammation. Therefore, chronic virus B infection should be grouped into two groups: (a) those with normal liver histology and (b) those with abnormal liver histology.

Dr. NK Arora: The term ‘carrier’ is misleading and should be changed.

Dr. YM Park: Patients with chronic hepatitis B infection need to be separated into two broad groups: (a) those with DNA positive and (b) those with DNA negative.

Dr. Naik: In our experience, when HBV carriers with normal ALT were given indomethacin, they showed increase in ALT, suggesting that even apparently healthy carriers do have some underlying liver pathology.
Dr. Roger Williams: The term ‘carrier’ means nothing. It should be replaced with ‘chronic hepatitis B virus infection’ because nearly every subject is HBV DNA positive.
Dr. Mark Thursz: I absolutely agree with deletion of the term ‘hepatitis B carrier’.

Thirty six of the 40 expert group members were in favor of deletion of the term ‘hepatitis B carrier’.
Dr. Sarin: What do you call somebody with normal ALT and normal histology?
Dr. Williams: Chronic HBV infection.
Dr. McCaughan: I agree with the term ‘chronic hepatitis B virus infection’ but would like to divide this into two groups: (a) with normal liver biopsy, and (b) with liver biopsy showing features of hepatitis.
Dr. HG Desai: Liver biopsy cannot be done routinely in high-endemicity countries.
Dr. Sarin: We should have clear guidelines regarding doing liver biopsy in apparently healthy individuals having chronic hepatitis B virus infection.
Dr. Park: I feel we should test for HBe antigen and DNA levels before doing liver biopsy.
Dr. Sarin: Prof. Okuda, what is your opinion?
Dr. Okuda: I agree with the term ‘chronic hepatitis B virus infection’. I think it should be divided into two groups: (a) those with no evidence of liver disease and (b) those with liver diseases. I prefer imaging modalities over liver biopsy to solve this question.
Dr. Hess: I would prefer HBV DNA and biochemistry over liver biopsy because of the invasive nature of the latter.
Dr. Williams: Liver tests are not reliable; therefore, in my opinion, liver biopsy is mandatory in every subject.

The unanimous consensus now was that the term ‘hepatitis B virus carrier’ is to be deleted, to be replaced by the broad term ‘chronic hepatitis B virus (HBV) infection’ with two subgroups: a) with normal liver histology, b) with abnormal liver histology. The classification can be done only on liver biopsy as ALT, HBeAg and HBV DNA do not correlate with histology.

Follow-up of patients with chronic hepatitis B infection

Frequency of follow-up

Dr. Hadziyannis: I feel the follow-up should be more frequent in patients with HBe antigen positive status to determine the time of seroconversion.
Dr. Park: I do not agree with this segregation into HBeAg positive and anti-HBe positive. The ‘c’ antigen is an unreliable marker for viral replication. I feel the anti-HBe positive group needs to be subdivided on the basis of HBV DNA status. The group with negative HBV DNA needs less frequent follow-up as compared to those with DNA positive.
Dr. Williams: I feel there should be no difference in the follow-up between the two groups as 60% of the patients in the UK today have HBV mutant infection. Both HBeAg positive and anti-HBe positive patients should be followed up at intervals of 6 months to 1 year.
Dr. Hess: The follow-up cannot be the same in patients with raised ALT versus those with normal ALT.
Dr. Sarin: Dr. Guan, what is your experience in the Asia Hep studies?
Dr. Guan: I think in Asia hepatitis B is more active. Therefore, subjects with chronic hepatitis B virus infection should be followed up every three to six months.

The consensus at this stage was that there should be no difference in the follow-up intervals between HBeAg positive and anti-HBe positive subjects and that follow-up should be at intervals of six months.

Status of DNA testing

Dr. Park: For reasons which I have earlier stated, DNA testing should be done in all patients on follow up at variable intervals.
Dr. McCaughan: DNA testing is to be done if a patient with chronic hepatitis B infection develops elevated AST/ALT and one wants to determine whether this is due to HBV reactivation or due to unrelated causes such as alcohol.
Dr. Hess: I agree that the DNA is the best test for assessing replication.
Dr. Williams: I do not think that HBV DNA test is needed in HBeAg positive patients routinely. Moreover, the methods for testing are not reliable enough.

The consensus was that HBV DNA test should be done in anti-HBe positive subjects. In those with normal ALT, only a baseline DNA needs to be done. However, in the subgroup with increased ALT, DNA test may be done more frequently to decide on therapy.

Status of ultrasonography

Dr. Hadziyannis: Ultrasound examination is not indicated in young persons and there is no need to do it routinely in countries with low endemicity. However, in older patients (>50 years) it may be done at regular intervals.
Dr. Guan: For Asians, we recommend ultrasonographic follow-up every six months in patients >50 years and annually for those <50 years.
Dr. Williams: I would do six monthly ultrasonography only in a patient who is male, aged >50 years, has cirrhosis and has actively replicating HBV infection. Else, it may be of little use.
Dr. Hadziyannis: Ultrasonography is popular only in Japan, but not in most other countries. The other problem with ultrasonography is that it is operator-dependent.
Dr. Okuda: We regularly do ultrasonography every 3 months. It is the most reliable and simple test.

Status of alpha fetoprotein (AFP)

Dr. Hess: Ninety percent of patients with hepatoma have increased alpha fetoprotein. Therefore, it should be done routinely and if it is increased, patients should be followed...
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up with ultrasound examination.
Dr. Okuda: I do not recommend serial alfa fetoprotein estimation. This should be deleted from the follow-up recommendations.

Dr. McCaughan: The Alaskan data have shown that alfa fetoprotein is useful in the early detection of hepatoma. Hence, this should not be deleted.

Dr. Park: Alfa fetoprotein levels are also age-dependent. I recommend six monthly estimations in patients >50 years and annual estimations in patients <50 years.

Dr. Sarin: Should we use both modalities for follow-up and, to save cost, one could suffice?

Dr. Hess: Use of both the modalities gives better pick-up for HCC.

The majority of experts were in favor of both serial ultrasonography and AFP estimations on follow-up. However, no consensus could be reached on the interval at which ultrasonography should be repeated.

Management

Dr. Sarin: Let us now discuss the management options for subjects with chronic hepatitis B virus infection. For this we would have to refer to our survey questionnaire where we have divided the subjects into four subgroups:

Group A (HBsAg positive, HBeAg positive, ALT normal)

Dr. Hadzlynnia: Regarding this group, I feel there is a desire to treat, but the modality is disputed since the results of interferon treatment are likely to be disappointing.

Dr. Williams: I would treat them if there is any evidence of liver disease on biopsy.

Dr. Sarin: This means that we would have to do a biopsy before starting therapy.

The consensus was that liver biopsy was mandatory to decide whether to treat or not to treat. The majority felt that if the histological activity index (HAI) is >3 this group should be treated in view of the ongoing viral replication, but if HAI is <3, a 'wait-and-watch policy' should be adopted. If this group (HAI >3) was to be treated, the majority preferred to use interferon.

Group B (HBsAg positive, HBeAg positive, ALT raised)

Dr. Hadzlynnia: These subjects have liver disease as the ALT levels are high. They should be treated without delay.

The consensus was that these subjects should be treated. The recommended modality for treatment is interferon.

Group C (HBsAg positive, HBeAg negative, ALT normal)

Dr. Sarin: We have discussed that HBV DNA should be done in these subjects. What about the treatment options?

Dr. Hess: Just DNA positivity has no meaning. You have to state by which method you would test for DNA.

Dr. Park: By PCR technique.

Dr. Williams: With current technology, positive or negative is difficult to define. There is no cut-off limit to define DNA negativity.

The consensus was that treatment decision was dependent on HBV DNA. Patients with DNA-negative status required no treatment. However, no consensus could be reached whether DNA-positive individuals should be treated.

Group D (HBsAg positive, HBeAg negative, ALT raised)

Dr. Sarin: Subjects belonging to this group constitute a disease group and hence, depending on HBV DNA results, should be considered for treatment.

Vaccination

Dr. Sarin: Horizontal spread is a major problem in developing countries. We need to have proper vaccination guidelines for contacts. Should we do a screening test before vaccination?

Dr. Guan: We recommend testing for HBsAg.

Dr. Okuda: I would recommend testing for anti-HBs before vaccination. What is the point of vaccinating someone who already has antibodies?

Dr. Sarin: A large majority of the Indian population has anti-HBc and also low levels of anti-HBs (<10 IU/L). These could be taken as markers of past exposure.

There was a consensus that all family members should be screened if there is an index case of chronic HBV infection in the family. The test of choice is HBsAg whereas anti-HBs and anti-HBc testing is optional. Vaccination should be suggested to family members who are HBsAg negative.

Hepatitis C

Terminology

Dr. Sarin: We have all agreed on changing the terminology for hepatitis B carrier. I think the literature is more clear for hepatitis C as a majority of investigators already believe that the term 'HCV carrier' is inappropriate. HCV infection is known to be more often chronic. I propose that we should drop the terms 'HCV carrier' or 'hepatitis C carrier' and call the state of infection 'chronic hepatitis C virus (HCV) infection'.

Dr. McCaughan: Yes. This would be correct.

Dr. Thurez: Yes, I agree. We should change the term as in hepatitis B.

Dr. Van Thiel: Yes. This is acceptable.

It was unanimously recommended that the term hepatitis C 'carrier' be dropped. This is to be replaced by the term 'chronic hepatitis C virus (HCV) infection'.

Dr. Dass: What should be the definition of 'chronic' in this case?

Dr. McCaughan: Six months is used internationally to differentiate acute from chronic liver disease. There cannot be any dispute over that.

Dr. RR Rai: But what should we take as the starting point?

Dr. McCaughan: This would vary from patient to patient. You cannot diagnose someone to have HCV infection in the absence of any identifiable risk factor.
Dr. Naik: For whom are we defining all these terms? Is it for the patient or for the purpose of clinical studies?

Dr. Sarin: For uniformity and global acceptance.

Dr. Van Thiel: If at presentation there is no identifiable risk factor/source of infection/evidence of chronic liver disease, then it is mandatory to wait for 6 months to establish chronicity. If there is an identifiable risk factor or source of infection or evidence of liver disease, then a single reading is enough.

Dr. RK Tandon: Yes. Liver disease due to HCV should be specified.

Dr. Sarin: These are very valid points and since there is unanimity on these issues they would be incorporated to define 'chronic' in reference to liver disease due to HCV.

Dr. Sameer Shah: We should include histology. The patient may come with a liver biopsy showing chronic liver disease. Then there is no need to wait for 6 months.

Dr. Van Thiel: That is acceptable.

The unanimous statement agreed upon reads as follows:

_If at presentation there is no identifiable risk factor/source of infection/evidence of chronic liver disease, it is mandatory to wait for 6 months to establish chronicity of HCV infection. If, however, there is a definite identifiable risk factor, source of infection (blood transfusion in the past, etc.), or discernible clinical, biochemical, histological or radiological evidence of liver disease due to hepatitis C, a single reading of anti-HCV positive is enough._

Classification

Dr. Sarin: I would now like to propose the classification of chronic hepatitis C infection into three groups on nearly similar lines as was suggested by Dr. Mark Thursz earlier. These groups could be:

- **Group I**: Anti-HCV positive, RNA negative, ALT normal
- **Group II**: Anti-HCV positive, RNA positive, ALT normal
- **Group III**: Anti-HCV positive, RNA positive, ALT elevated

Dr. McCaughan: There is no consensus whether the subjects in the first group really have evidence of persistent HCV infection. I am happy to include this group, but we should put an asterisk about whether there is any infection at all.

Dr. Thursz: It is possible that some subjects are in the process of clearing the infection and some become infective intermittently and show HCV infection from time to time. Some subjects may have HCV RNA in liver tissue.

Dr. Hubert Blum: Some patients in Group I may not have chronic infection. Their test results may simply reflect past infection. Should we call subjects in this group as having chronic hepatitis C virus infection? Why should we do a biopsy?

Dr. McCaughan: Let me put it the other way. Some patients in this group do not have HCV infection but they cannot be defined without liver RNA.

Dr. Khan: I feel Group I should be subdivided into two subgroups based on liver RNA: one group which is HCV RNA positive in liver tissue and the other which is negative.

Dr. Sarin: But we cannot include liver RNA for the purpose of definition.

Dr. McCaughan: I agree. To ask for liver RNA in the definition is asking for too much.

Dr. Thursz: We should certainly have this group included since it is important to learn about the natural history of these subjects.

Dr. Sarin: Yes, we agree. We should put an asterisk in the first group as advised by Dr. McCaughan and Dr. Blum.

_The statement was that the rider suggested by Dr. Blum and Dr. McCaughan for Group I should be included in the terminology. Further, it was unanimously agreed that there is no need for liver biopsy and HCV RNA test in liver tissue in these subjects._

Dr. Thursz: We should also include in the definition what we mean by 'normal ALT'. Three ALT readings should be normal at least up to 6 months. This would be true for both Groups I and II.

Dr. Blum: Yes. This would be fine.

_The suggestion to have ALT levels in the classification was agreed upon. It was unanimously accepted that a rider be put on what constitutes 'normal ALT '. There should be three normal ALT readings over a period of 6 months to conclude that ALT is normal._

Dr. Shah: The same should be true for HCV RNA. We should repeat RNA.

Dr. Thursz: This point needs to be clear. What do we mean by a negative HCV RNA? We know that the HCV RNA level could be quite low at times or it may fluctuate. Hence, I feel that at least two HCV RNA tests should be negative in Group I subjects before inclusion into the group.

Dr. McCaughan: Absolutely. We cannot rely on one HCV RNA report. We should have two HCV RNA reports for Group I.

Dr. Sarin: But two HCV RNA tests would add to the cost.

Dr. Leung: Yes. We should have two HCV RNA reports. Then we are more certain about negative RNA. The techniques for HCV RNA are not so well standardized.

Dr. Rai: What should we say to the patient in the meanwhile?

Dr. Thursz: We could say that he does not have any evidence of HCV infection at present, but would need a checkup after 12-24 months.

Dr. McCaughan: For Group II, we need not have two RNA values.

_For Group I, there was no consensus whether a repeat HCV RNA should be done for the purpose of definition. There was unanimous agreement that for defining group II, there is no need to repeat HCV RNA testing._

Dr. Naik: We should propose an algorithm. As for HBV, divide as ALT normal or raised. If the ALT values are
raised repeat an RNA testing.

Dr. Sarin: Here we are trying to define the groups of patients and not management issues.

Dr. Tandon: Yes. We are not discussing management. There is no need to have an algorithm for definition.

Dr. Okuda: I agree with the definitions for both the groups. They are all right.

Dr. Van Thiel: I would like to add another group. There are subjects who are anti-HCV negative but are HCV RNA positive. These are subjects with uremia, all the transplant patients, immuno-suppressed subjects.

Dr. Sarin: How do you find out such subjects? Is it a common problem? We rarely see these patients.

Dr. Van Thiel: Especially in the patient population I see, this is quite common. This situation is common in immune-compromised individuals.

Dr. Thursz: Yes. We could have a fourth group in our classification.

There was unanimous agreement that we should add the fourth group.

Dr. Sarin: Since in our definition and classification we have included anti-HCV positivity as a criterion, diagnosing individuals of Group IV would not be easy. Hence, we should add an asterisk to define this group:

*Group IV: Anti-HCV negative, HCV RNA positive, ALT normal

Diagnostic work-up

Dr. Sarin: What should be the diagnostic work-up of individuals with 'chronic hepatitis C virus (HCV) infection'. In my opinion, Group III is quite clear as subjects belonging to this group should be considered as patients belonging to the category of 'chronic hepatitis C'. As for hepatitis B, we should proceed in this group with assessment followed by specific therapy.

Dr. Van Thiel: We should definitely treat Group III, by a combination of interferon and ribavirin. I would, however, do a liver biopsy before starting therapy.

It was unanimously agreed that subjects in Group III should be considered as having chronic hepatitis C. They should be assessed and treated without further delay.

Dr. Sarin: Let us go back to the diagnostic work-up before discussing therapy. Should we do confirmatory tests like RIBA in our anti-HCV positive subjects?

Dr. Blum: No. RIBA does not confer any advantage. I always need an HCV RNA.

Dr. Tandon: No. RIBA is an expensive test. We do not use it.

Dr. Nalik: We should specify that RIBA should not be done. Otherwise, some people would keep on doing it.

Dr. McCaughan: Yes. I do not think RIBA is useful. But we should repeat anti-HCV test before doing HCV RNA.

Dr. Arora: Why should we test for anti-HCV twice?

Dr. McCaughan: Two anti-HCV tests are necessary. The thought of giving an anti-HCV positive report without confirmation is horrifying. It is done routinely all over the world. Repeating the test is a separate issue from classification. My suggestion is that two assays, which detect different antibodies, should be used. This may improve the sensitivity and specificity of HCV screening.

It was unanimously accepted that there is no advantage in doing a confirmatory RIBA test in an anti-HCV positive subject. Instead, an HCV RNA test could be done. A repeat anti-HCV test is recommended, preferably by another test kit.

Follow-up

Dr. Sarin: How should we follow-up these patients? Should we check ALT every 3 months?

Dr. McCaughan: This would be too soon. We should check it every 6-12 months.

Dr. Arora: It would be a good practice to check it every 6-12 months.

Dr. Nalik: This is only pretreatment assessment for Groups I and II. Once the decision for treating is taken the follow-up would change.

Dr. Sarin: Yes. We all agree that ALT should be checked every 6-12 months in Groups I and II. What about the alpha fetoprotein levels? Should we do a baseline study?

Dr. Van Thiel: Yes, that is fine.

Dr. Sarin: What about ultrasonography? Should that also be done at least at baseline?

Dr. Blum: Yes, that is right.

Dr. Sarin: What about endoscopy?

Dr. Van Thiel: No. If there is evidence of liver disease, only then should endoscopy be done. For example, if there is some ultrasound evidence.

Dr. Sarin: What about HCV RNA? Should we repeat it during follow-up?

Dr. Desai: How would it matter?

Dr. YK Chawla: No. I would not repeat an HCV RNA in Group II.

Dr. Sarin: I would like to repeat HCV RNA as the patient may have cleared the virus. Anyway, before therapy, HCV RNA should be repeated.

A majority supported the decision to repeat HCV RNA testing after 12-24 months in Group II patients.

Dr. Sarin: What about liver biopsy? Dr Thursz, you had suggested that we should repeat liver biopsy every three years in Group II. Would it be justified, as we have not even decided to treat these subjects?

Dr. Thursz: What I meant was that such patients should be followed up only under a research protocol and a repeat biopsy is done.

Dr. Sarin: Yes. Liver biopsy could help decide whether the subject needs treatment or not. However, I am not sure whether biopsy should be done since our treatment options are limited.
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Dr. Desai: If the ALT is normal, the issue of biopsy is debatable.

Dr. McCaughan: I personally feel that liver biopsy is justified since these subjects have good prognosis. Moreover, ultrasonography would almost always be normal in them.

Dr. Blum: I think if the ALT is persistently normal, only a minority would have disease, and that too, minimal. These patients should not be treated.

Dr. Thrusz: The data from the French study show that these subjects, in fact, may have disease. Moreover, the group with normal ALT could also progress.

Dr. Van Thiel: I agree with Mark and would do a biopsy. I would put an asterisk there. If there is any discernible evidence of liver disease – clinical, biochemical or radiological – a liver biopsy should be done.

Dr. Okuda: We do not do biopsy. Imaging as is good.

Dr. Sarin: Your point is valid. I think we should be cautious in deciding about biopsy. We should mention in the follow-up protocol of subjects belonging to Group II that biopsy should be done only if therapy is contemplated. We would add the asterisk for the sake of clarity.

There was unanimous agreement that the liver biopsy should not be done routinely in Group II subjects; biopsy should be done only if clinical, biochemical or imaging studies are abnormal.

Dr. Sarin: What about the follow-up of subjects in different groups?

The final proposals for follow-up which were unanimously approved by the expert group are shown in the Table.

Since subjects belonging to Group I have no evidence of current HCV infection, they could be followed up every 12-24 months. On the other hand, clinical and biochemical follow-up in Group II subjects should be done every 6-12 months.

Management

Dr. Sarin: Now, let us discuss the management. I do not think anybody would recommend therapy for Group I subjects since they do not have HCV RNA. We have already discussed about Group III subjects; they should be considered as suffering from chronic hepatitis C and treated accordingly. The main problem is of Group II subjects, the ones with HCV RNA positive status and normal ALT.

Dr. Van Thiel: We have already discussed that. The subjects in this group should be treated under a protocol. If the liver histology suggests evidence of disease (HAI > 3), we could assess for therapy.

Dr. Thrusz: I would like to treat these patients. Of course, more clinical trials are needed in this area.

No definite recommendations for therapy could be suggested. It was agreed that treatment should be given strictly under study protocols. If at any time the subject has raised ALT or some evidence of liver disease due to hepatitis C, specific antiviral therapies need to be instituted.

Dr. Sarin: What about Group IV subjects?

Dr. Van Thiel: I give them specific antiviral therapy. Of course liver biopsy is needed and the management of the underlying condition should be planned.

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<td>Anti-HCV (+)</td>
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<th>Approach</th>
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<th>Follow-up Clinical</th>
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* To be performed only if clinical, biochemical, radiological evidence of liver disease is present or under a research protocol, prior to therapy. # If therapy has to be instituted. Needs to be individualized. It is unsatisfactory in the post transplant scenario.

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