CHAPTER SEVEN

TREATING AND MANAGING HEPATITIS C:

THE CURRENT SITUATION

The Inquiry's Terms of Reference ask the Committee to look at treatment services available to those with Hepatitis C and the adequacy of policies directing these services. The following discussion identifies and examines treatment policies and currently available treatment regimes and services.

7.1 CURRENT TREATMENT POLICIES

Currently there is only one approved treatment available for those with chronic Hepatitis C and that is drug therapy using interferon alpha (the drug is referred to as interferon throughout this report). Two drug companies currently market interferon in Australia: Roche (under the brand name of Roferon) and Schering-Plough (under the brand name of Intron).

Strict federal policies regulate the administration of this drug in terms of who can receive it, how much can be administered and for how long, and which hospitals can dispense and manage the therapy.

Intron was first approved for the treatment of chronic Hepatitis C by the Therapeutic Goods Administration (TGA) on 9 December 1992 for a treatment duration of six months (Schering-Plough submission). Following evaluations of both clinical and cost effectiveness data by the Pharmaceutical Benefits Advisory Committee (PBAC), the Federal Government released Intron for use in a specific group of Hepatitis C patients, under Section 100 (S100) of the *Commonwealth National Health Act, 1953* scheme for highly specialised drugs on 1 October 1994. The Pharmaceutical Benefits Scheme (PBS) listing was conditional upon adherence to a list of S100 criteria determined by the PBAC and based on advice from the former NHMRC/AHMAC Taskforce on Hepatitis C.

In June 1996 Schering-Plough was successful in gaining TGA approval to extend the duration of treatment with Intron A from six months to up to 18 months. Subsequently the duration of treatment under S100 was extended to 12 months with the new conditions of listing starting from 1 May 1997. The Committee understands that Intron A is the only form of interferon to have both TGA and PBAC approvals for the treatment of chronic Hepatitis C (Schering-Plough submission).

The Highly Specialised Drugs Program is currently under review. In its submission to this Inquiry, ANCARD provided their submission to this review.

The current course of treatment is 3 million units (MU) of interferon administered subcutaneously three times a week for 12 months. In its review of the management of Hepatitis C, the NHMRC considered this dosage to be the optimal schedule (1997:34). It is also the recommended dosage in the United States (National Institutes of Health, 1997:5S) and Canada (Sherman, 1996).

During the course of this Inquiry, the eligibility criteria under the S100 program has altered. At the commencement of the Inquiry, interferon was available to patients who:

- had chronic hepatitis proven by liver biopsy (except patients with inherited coagulation disorder);
- had positive anti-HCV antibody, tested twice over six months with an interval of at least 16 weeks;
- had an ALT level (Alanine Aminotransferase - a commonly cited liver function test) higher than 1.5 times the upper limit of the laboratory reference range on three occasions over a period of six months;
- did not have cirrhosis or other liver disease;
- did not have HIV infection;
- were not pregnant, lactating or exposed to the risk of pregnancy;
- did not have a history of significant psychiatric illness;
- would be likely to attend regularly for treatment and follow-up;
- consumed no more than seven standard drinks a week; and
- had not used illicit injectable drugs within the previous 12 months (PBAC Secretariat, 1997).

At the December 1997 meeting of the PBAC the criteria referring to illicit injectable drug usage and HIV-HCV coinfection were deleted from the criteria listing. The current criteria and its appropriateness will be discussed in further detail in Section 8.1.

Before May 1995 persons under the age of 18 years were excluded from receiving interferon under the S100 program. At that time the criteria were modified and children are now able to receive interferon.

If, after 12 weeks of treatment, the ALT remains higher than the upper limit of the laboratory reference range, treatment ceases to be freely available under PBS. Patients are able to continue therapy but at their own expense.

The course of treatment must be continuous and excludes retreatment of non-responders or patients who relapse (PBAC Secretariat, 1997). Patients eligible for the twelve months' course are therefore new patients and current responding patients who have not completed six months' treatment (PBAC Secretariat, 1997).

Hospitals that have received approval to prescribe and administer interferon are known as Interferon Prescribing Centres. The Health Departments of each state/territory develop the criteria used in approving these centres. The NSW criteria includes:

- physician with adequate experience in the management of Hepatitis C;
- establishment of links between the physician and a teaching hospital with a specialised unit involved in the management of Hepatitis C;
- 24 hour access to medical care (via 24 hour Accident and Emergency Centre);
- facilities for safe liver biopsy;
- a nurse educator/counsellor with some expertise in the management of Hepatitis C; and
- a dedicated outpatient liver clinic (NSW Health submission).

All Interferon Prescribing Centres must undertake to provide data to the National Interferon Data Base based at the John Hunter Hospital, Newcastle.

7.1.1 The National Interferon Data Base

In its 1994 report on Hepatitis C, the NHMRC/AHMAC recommended that a centralised data base of all patients receiving interferon therapy be established. It was envisaged that such a resource would allow ongoing monitoring and evaluation of treatment outcomes and:

> *provide a sound clinical basis for the modification of patient selection criteria, treatment schedules and monitoring as appropriate. It would also provide valuable prospective data on the safety and efficacy of interferon* (NHMRC, 1994:70).

The Hepatitis C National Data Base (NDB) was established by the Gastroenterological Society of Australia in October 1994. The initial financial commitment came from the Commonwealth and Schering-Plough, each contributing $37,000 (Schering-Plough submission). When Roche received reimbursement approval for their product the Commonwealth withdrew from the program and Roche "picked up" the Commonwealth's share of the contribution (Schering-Plough submission). In commenting on the establishment of the Data Base, Schering-Plough noted that:

> *a unique aspect of the PBS listing of Intron A for the treatment of chronic Hepatitis C was that the company was required by the Federal Government to support financially the setting up and maintenance of a National Hepatitis C Database under the auspices of the Gastroenterological Society of Australia. The supposed primary function of the Database was to collect data on treatment response* (Schering-Plough submission).

The Data Base currently gathers data from the 2700 patients receiving interferon under the S100 Highly Specialised Drug Program both at entry to treatment and in follow-up. The project comes to an end in October 1999. Issues pertaining to the Data Base that have been raised during the course of this Inquiry are discussed in Section 8.1.1.

7.2 AVAILABLE TREATMENT OPTIONS AND MEDICAL PROCEDURES

7.2.1 INTERFERON

Interferon is a protein made by the immune system which acts to fight viral infections. For unknown reasons, Hepatitis C does not stimulate the body to make interferon (Hollinger, 1997:7). Interferon is a global antiviral agent that can affect the life cycle of both RNA and DNA viruses (Hollinger 1997:7).

During the course of this Inquiry, people with Hepatitis C expressed a range of views on the usefulness of interferon therapy and its capacity to improve their health. For some considering treatment, interferon has too many side effects and a low success rate. Others consider that it is the only option they have. For many, however, it has not been an option because of the strict eligibility criteria (Hepatitis C Council submission).

- **Location of Interferon Prescribing Centres**

At the commencement of this Inquiry, there were 22 centres in NSW authorised to prescribe interferon to treat patients with Hepatitis C. The 15 centres based in Sydney metropolitan region included:

- Blacktown Hospital
- Bankstown-Lidcombe Hospital
- Campbelltown Hospital
- Concord Hospital
- Corrections Health Service
- Liverpool Hospital
- Mount Druitt Hospital
- Nepean Hospital
- Prince of Wales Hospital
- Royal North Shore Hospital
- Royal Prince Alfred Hospital
- St George Hospital
- St Vincent's Hospital
- Sutherland Hospital
- Westmead Hospital

(NSW Health submission).

A further seven Interferon Prescribing Centres were in regional and base hospitals across the state. These included:

- Bega District Hospital
- Bathurst Base Hospital
- Illawarra Area Health Service
- John Hunter Hospital.
- Lismore Base Hospital
- Orange Base Hospital
- Wagga Wagga Base Hospital

At the time of making its submission to the Inquiry NSW Health informed the Committee that applications for Interferon Prescribing Centres received from two Rural Areas were under consideration. During the course of the Inquiry these hospitals received approval and interferon is now able to be prescribed at the Dubbo and Port Macquarie hospitals bringing to 24 the number of Interferon Prescribing Centres in the state.

- **Utilisation of Interferon Therapy**

As of October 1997 approximately 1500 of the state's 40,000 known cases of HCV, or 3.75% of identified cases, have accessed interferon treatment (NSW Health tabled document, 3 October 1997). Across the nation almost 3,000 have commenced treatment (Federal Parliamentary Liaison Group on HIV/AIDS and Related Diseases, 1998:3). The breakdown according to year is reported in Table Twenty-four.

TABLE TWENTY-FOUR
NUMBERS COMMENCING INTERFERON THERAPY
1994 - 1997

YEAR	TOTAL NUMBER COMMENCING THERAPY
1994	151
1995	929
1996	1005
1997	892
TOTAL	**2977**

Source: Federal Parliamentary Liaison Group on HIV/AIDS and Related Diseases, 1998:3.

There are several reasons why the numbers of those on drug therapy relative to the number with the disease are so low. These include:

- the strict eligibility criteria which excludes a large number of people;
- the side effects of the therapy, which for many are quite unpleasant; and

- the relatively low efficacy of the therapy.

The significance of these last two factors is such that NSW Health observed:

> *It is clear that the 40,000 known infected individuals in NSW would not seek interferon treatment even if they were eligible for it* (NSW Health, tabled document).

- **Efficacy of Interferon Therapy**

An individual's response to interferon depends on a number of factors including the amount of virus in the blood, the speed with which it replicates and other factors such as the virus' genotype with some strains being very sensitive and disappearing immediately while others are more resistant to interferon. An individual's response can be measured in one of two ways: end-of-treatment response, and sustained response. Not all studies discussing the effectiveness of interferon therapy identify the type of response under consideration.

Data received by the Committee on the efficacy of interferon therapy varied somewhat and included:

- Roche suggested that 30 per cent of patients will be considered sustained responders at the end of a 12 month treatment (Roche submission);

- in evidence given by NSW Health officials it was suggested that interferon is effective for approximately one in four of those treated (Wilson evidence, 3 October 1997);

- the Hepatitis C Council's submission cited recent studies showing the overall long term response for 12 months of treatment to be between 20-40 per cent (Hepatitis C Council submission);

- Hepatitis C expert, Dr Farrell, suggested to the Committee that the response to interferon ranges from 30 to 60 per cent for genotypes 2 and 3 to less than 10 per cent for genotypes 1 and 4 (Farrell submission);

- data provided by the National Interferon Data Base suggested that after a standard course of six months 14 per cent of those treated achieve a long term benefit (National Interferon Database, 1997, cited in the Hepatitis C Council submission);

- the NHMRC noted that the six month therapy regime was providing a 15 per cent sustained remission rate (NHMRC, 1997:page no);

- the Panel Statement arising from the US-based National Institutes of Health's Consensus Development Conference on Hepatitis C Management suggested a

biochemical end-of-treatment response of 40 - 50 per cent after six months of treatment and a biochemical sustained response of 15 - 20 per cent. In terms of virological response, the six month course of treatment has produced an end-of-treatment response of 30 - 40 per cent and a sustained response of 10 - 20 per cent. In the Panel's opinion, increasing the duration of treatment to 12 months is not associated with higher biochemical or virological end-of-treatment response although the biochemical sustained response is increased to 20 - 30 per cent (NIH, 1997:5S). They caution that:

> *although interferon treatment may be associated with favourable effects on biochemical and virological markers, its effects on important clinical outcomes such as quality of life and disease progression remain undetermined* (NIH, 1997:5S).

As the above suggests, expert opinion on the efficacy of interferon ranges from 0 - 40 per cent. It would appear, from the literature, that the rate of one in four cases is the standard 'rule of thumb' in discussing the efficacy of interferon therapy. This is the figure adopted by the Committee. While it may not be possible to cite the exact rate at which people on interferon clear the virus, the rate is clearly unsatisfactory.

In submissions received, the Committee heard from those for whom interferon had been successful:

> *The change in my health was amazing. Several weeks after I started the program I noticed I felt better and I just got better and better. Finally I had energy again and could play with my children, do the house work, gardening etc. Most of my aches and pains were gone; the nausea which I lived with for years had stopped. I felt alive again - as though I had been given a second chance. I was so sure that the interferon was working* (Submission 73).

On the other hand, there were those with less positive experiences:

> *interferon was a dreadful experience and in the end didn't work for me, in fact since the end of the course 18 months ago I have experienced pain in my liver which wasn't there before* (Submission 37).

- **Side Effects of Interferon Therapy**

A major issue relating to interferon is the side effects, both physical and emotional, which, for many, can be debilitating and severe, particularly in the first few months of commencing therapy. Date collected by the National Data Base show that 63 per cent of patients experienced side effects during the first month on interferon. As a person's body develops a natural tolerance to the drug, the severity and number of side effects

lessens over time. Data collected from the NDB show that the number of patients experiencing side effects declined from 63 per cent to 21 per cent within a six month period (Hepatitis C National Data Base, 1997:4).

Common side effects experienced include:

Influenza-like: fatigue, fever, mayalgia, malaise, poor appetite, tachycardia, chills, headache, arthralgias;

Neuropsychiatric: apathy, irritability, mood changes, insomnia, cognitive changes;

Miscellaneous: diarrhea, nausea, abdominal pain, back pain, pruritus, alopecia, rhinorrhea; and

Laboratory: decrease in granulocytes, platelet counts, and red blood cell counts, increase in serum triglyceride concentrations, proteinuira, increases in serum alanine and ALT levels (Dusheiko, 1997:113S).

Data provided by the National Data Base show the twelve main side effects reported to be:

- flu like symptoms (21%);
- lethargy (19%);
- gastrointestinal disturbances (14%);
- headaches (12%);
- emotional disturbances (8%);
- depression (4%);
- hair loss (4%);
- skin changes (3%);
- sleep disorders (2%);
- decreased platelet levels (2%);
- neutropenia (2%); and
- local injection site reaction (1.2%) (Hepatitis C National Data Base, 1997:4).

While depression is reported by only 4% of patients registered with the National Data Base, a Clinical Nurse Specialist working with Hepatitis C patients at St. George Hospital suggested to the Committee that:

> *approximately 99% of [Hepatitis C] patients have exhibited flu like symptoms which appear to abate over time . . . However, from my observation, I contend that an under-estimated number of patients experience depression related to the use of interferon, rather than depression stemming from their diagnosis* (Looby submission).

Many of the submissions made by HCV+ people included comments on the side effects they had experienced with interferon. Comments included:

> *The interferon really made me sick . . . After four months I was withdrawn from the programme due to severe side effects. I suffered mainly depression and suicidal tendencies* (Submission 61);
>
> *I have suffered quite horrific side-effects . . I have suffered hair loss, mood swings and a worsening of my general health* (Submission 52);

and

> *The side effects made it difficult for me to work in my role as a clinical nurse specialist. My sick leave and recreation leave ran out. I began using my long service leave* (Submission 82).

For many of those who contacted the Committee, their response to interferon is complicated by the fact that their general practitioners were insufficiently informed about these side effects:

> *I have just checked with my local general practitioner about his knowledge of the side effects of interferon because one of his patients is now on Interferon. He said that his knowledge was from a Department of Health book, which he could not find, and he was looking around the room. He said, "The standard effect is flu-like symptoms". I said, "Do you know about diarrhoea and hives?". He said, "No, no one has ever told me that." He is a reasonable doctor, but knowledge is still not easily available to doctors to support people who are on Interferon* (Lamb evidence, 30 March 1998).

The issue of general practitioner education on this and other Hepatitis C related issues is considered in Section 8.4.1.

- **Contraindications to Interferon Therapy**

There are important contraindications to interferon therapy. These contraindications are based largely on the known side effects of the drug and include:

- severe depression;
- decompensated cirrhosis;
- cirrhosis and hypersplenism;
- autoimmune hepatitis;
- hyperthyroidism;
- coronary artery disease;
- renal transplant;
- pregnancy;
- seizures;
- drugs: herbal remedies;
- diabetes/hypertension and retinopathy; and

- laboratory - thrombocytopenia
  leukopenia
  anaemia
  high titers of autoantibodies
  hyperthyroidism (Dusheiko, 19987:118S).

- **The Cost of Interferon Therapy**

Shiell, Briggs and Farrell (1994:269) document the treatment costs (in $1994) of a six month course of interferon as:

Pathology Services	$920
(anti-HCV serology, liver function tests, liver biopsy, full blood count, ultrasound)	
Hospital Services	$1,990
Interferon	$3,425
(dose 3 x 10^6 IU thrice weekly for 24 weeks)	
Total Cost, per patient per course	**$6,335**

Shiell *et al's* figures demonstrate advice received by the Committee concerning the extent of indirect costs of therapy. Wodak suggested that the indirect costs of interferon for the considerable work up and monitoring involved with a course of interferon therapy are probably as much again as the direct costs of the drug although much harder to compute (Wodak submission). In addition to monetary costs of the treatment are also those costs borne by the patient including, as has been discussed, the side-effects frequently experienced.

The Federal Government funds the cost of the interferon used on receipt of requests from state and territory governments for eligible patients under the S100 Highly Specialised Drug Scheme, except, as will be discussed in Section 8.4, in the case of prisoners.

Hepatitis currently accounts for a relatively small proportion of expenditure under the Highly Specialised Drugs Program. Of the $143,239,374 spent on all drugs under the program in 1996/97 interferon accounted for only 4.4 per cent of expenditure - $6,286,696 (ANCARD submission to the Review of the Highly Specialised Drugs Program - attachment to their submission). ANCARD's submission to the Review of the Highly Specialised Drugs Program suggests that the supply of interferon under the Highly Specialised Drugs Program has cost approximately 50 per cent of the amount originally predicted. The low uptake is due, the submission suggests, to the restrictive guidelines, the toxicities experienced by many patients and the comparatively low efficacy of the drugs (ANCARD submission to the Review of the Highly Specialised Drugs Program - attachment to their submission).

- **The Cost Effectiveness of Interferon Therapy**

A British study (based on a six month course of treatment) calculated that the discounted cost per year of life saved ranged from £2,142 to £17,128 (Dusheiko, 1995). The study concludes that:

> *the potential usefulness of interferon alpha on the clinical and economic outcome of treatment is indicated from the model. These findings together with the benefits that are likely to accrue from the reduction in infectious individuals, suggest that this therapy has a role to play in public health policy to contain the impact of hepatitis* (Dusheiko, 1995).

An Australian study conducted in the early 1990s looked at the cost effectiveness of interferon in the treatment of Hepatitis C. The results, which are recorded in Table Twenty-five, show that interferon treatment of chronic Hepatitis C patients resulted in a discounted cost per life-year saved of $33,230 in patients with cirrhosis at the start of treatment and $71,950 in patients without advanced liver disease (Shiell, Briggs and Farrell, 1994:268).

TABLE TWENTY-FIVE
COST EFFECTIVENESS OF INTERFERON THERAPY

	CIRRHOSIS AT DIAGNOSIS (N=300)	NO CIRRHOSIS AT DIAGNOSIS (N=700)	ALL PATIENTS (N=1000)
Total Cost	$1,488,500	$4,374,100	$5,862,600
Lives Saved	3.6	7.1	10.7
Cost Per Life Saved	$419,865	$615,755	$550,480
Life-Years Gained	44.8	60.8	105.6
Cost Per Life-Year	$33,230	$71,950	$55,515

Source: Shiell, Briggs and Farrell, 1994:270.

The study's authors are cautious in commenting on the cost effectiveness of interferon noting that:

> *whether or not this is considered cost effective depends on comparisons with other health care interventions with which interferon might compete for resources. Results from published evaluations suggest that interferon is a more expensive way to improve health than many health care interventions or health promotion strategies. However, differences in the methods adopted by*

> *such studies mean that comparisons should be made with care* (Shiell, Briggs and Farrell, 1994:271).

In its submission to the Inquiry, NSW Health confidently claimed that:

> *interferon treatment of people with HCV offers long term savings to the health system by reducing the number of people who progress to serious liver disease requiring liver transplant. Liver failure was estimated to require between $75,000 and $129,000 associated health costs per episode in 1994* (NSW Health submission).

However, Briggs and Shiell are more cautions. They suggested that:

> *Although there may be a role for interferon in reducing the rate of progression from acute to chronic infection commentators agree that more evidence is required before firm conclusions can be drawn* (Briggs and Shiell, 1996:205).

Interferon is expensive, its effectiveness is limited and it can have significant adverse effects. Clearly its cost effectiveness is, as Briggs and Shiell (1996:208) observe, "open to question".

- **Factors Predictive of a Beneficial Response to Interferon Therapy**

Because most patients do not experience a sustained response to interferon, attempts have been made to identify those individuals who are more likely to respond to therapy. The strongest predictors of response are viral in nature: a low concentration of virus and genotypes other than genotype 1 are more often associated with a favourable response (Hollinger, 1997:7). A number of studies have identified pretreatment patient characteristics that are associated with a greater or lesser likelihood of response to interferon. These have been identified by Davis and Lau as including:

Drug:	dose 3 million units
Demographics:	female sex younger age history of injecting drug use unknown source of infection (sporadic) short duration of infection
Histology:	mild chronic hepatitis absence of fibrosis or cirrhosis
Biochemical:	low serum ALT low gamma glutamyl transpeptidase low serum iron or ferritin

Virologic:	low HCV RNA level genotype 2 or 3 low number of quasispecies multiple mutations in the interferon sensitivity determining region
Interferon Response:	early normalisation of serum ALT early loss of serum HCV RNA (Davis and Lau, 1997:123S).

The identification of such factors has led the National Institutes of Health (NIH) to suggest that:

> *treatment is clearly recommended only in a selected group of patients. In others, treatment decisions are less clear and should be made on an individual basis or in the context of clinical trials* (NIH, 1997:6S).

The NIH's Statement on Hepatitis C management recommends treatment for the group of patients with chronic Hepatitis C who are at the greatest risk of progressing to cirrhosis. These patients are characterised by:

- persistently elevated ALT;
- positive HCV RNA; and
- a liver biopsy with either portal or bridging fibrosis and at least moderate degrees of inflammation and necrosis (NIH, 1997:6S).

In patients with persistent ALT elevations, but with less severe histological changes progression to cirrhosis is likely to be slow, if at all. It is suggested that for this group, observation and serial measurements of ALT and a liver biopsy every three to five years is an acceptable alternative to treatment with interferon (NIH, 1997:6S).

- **Counselling on Interferon Therapy**

The NHMRC have identified a range of issues which should be addressed when counselling a patient on interferon treatment. These include:

- the nature of interferon;
- the mode of action of interferon;
- the effectiveness of interferon in the treatment of Hepatitis C;
- the meaning of "response";

- adverse reaction to interferon;
- duration of therapy;
- action to be taken if the patient relapses;
- predictors of response to interferon;
- administration of interferon;
- liver biopsy;
- pregnancy contraindicated; and
- alcohol consumption (NHMRC, 1997:41).

As will be discussed in Chapter Eight there is often insufficient time in the state's overcrowded liver clinics for these issues to be discussed adequately with patients and their families.

- **Monitoring and Assessing the Efficacy of Interferon Therapy**

The efficacy of interferon therapy currently is defined biochemically as normalisation of serum ALT and virologically as loss of serum HCV RNA. In the Panel Statement arising from the 1997 Consensus Development Conference of the National Institutes of Health, serial ALT testing was recommended for monitoring patients during treatment to document biochemical responses and testing for HCV RNA by qualitative PCR recommended at selected times to document the level and activity of the virus (National Institutes of Health, 1997:5S). PCR testing is therefore being used not only as a confirmatory test for HCV, but also an important tool in the assessment of a person's response to interferon and in the predication of treatment outcomes.

In the main, funding for these tests is provided through pharmaceutical companies and is restricted to certain sites. NSW Health has provided time limited funding for HCV testing, specifically PCR testing but as the Committee was advised "this funding . . . is clearly inadequate for future testing requirements" (Hepatitis C Council submission).

The Panel Statement from the NIH's Consensus Development Conference on the management of Hepatitis C suggests monitoring during therapy at two to four week intervals with serum ALT and complete blood count. Both serum ALT and serum HCV RNA testing should be performed after three months to assess whether the patient is responding to therapy. This should be repeated at the end of therapy to document end-of-treatment response. Follow-up testing, with serum ALT and serum HCV RNA should be performed six months after therapy is stopped to determine whether there has been a sustained response. In the Institutes' opinion, follow-up liver biopsy is not necessary (NIH, 1997:6S).

7.2.2 OTHER MEDICATIONS

- **Ribavirin**

Ribavirin is an oral antiviral agent, discovered in the 1970s, that is effective against some RNA viruses like HCV. It is a nucleoside analogue which inhibits the replication of many different viruses including some related to HCV. Nucleosides are the building blocks of RNA and ribavirin resembles these nucleosides. The virus will mistakenly use it in its life cycle and become defective so that it is no longer infectious (Hollinger, 1997:7).

When used alone ribavirin reduces serum ALT levels in approximately 50 per cent of patients (NIH, 1997:6S). However ribavirin does not lower serum HCV RNA levels, and relapses occur in virtually all patients when therapy is stopped (NIH, 1997:6S). Combining ribavirin and interferon has resulted in virological sustained response rates 40 - 50 per cent higher than interferon alone in six month trials (NIH, 1997:6S).

The drug ribavirin which is currently being used in clinical trials with interferon costs $14,000 to $18,000 for one year of treatment. The cost of one year of treatment with the combination of the two drugs would currently cost approximately $20,000 to $24,000 excluding the salaries of the medical, nursing and laboratory staff supporting the treatment regime (NSW Health tabled document, 3 October 1997).

A randomised, double-blind, placebo-controlled trial study conducted in Norway which combined interferon and ribavirin found that 36% of those on the combined therapy had a sustained virological response compared with 9% in the interferon and placebo group (Reichard, Norkrans, Fryden, Braconier, Sonnerborg, Weiland, 1998:83). At the one year follow-up, the proportion of patients with a virological response was greater in the combined therapy group than the interferon and placebo group. The study concluded that:

> *more patients with chronic Hepatitis C have a sustained virological response with interferon α-2b and ribavirin than with only interferon α-2b treatment. We suggest that patients with high HCV-RNA loads should be treated with interferon α-2b and ribavirin* (Reichard, Norkrans, Fryden, Braconier, Sonnerborg, Weiland, 1998:83).

Farrell suggested that for those who had tried interferon and relapsed, the combination of interferon and ribarivin is about 50 per cent curative (Farrell evidence, 26 November 1997). However the Hepatitis C Council advised the Committee that people receiving combination therapy report a greater number of side effects.

Given the initial promising results of combining interferon and ribavirin, the drug company Schering-Plough has received TGA approval for a ribavirin compassionate use protocol under its Special Access Scheme (Schering-Plough submission).

- **Protease Inhibitor Drugs**

The Committee understands that research into the use of protease inhibitor drug therapies in Europe has commenced. It will, however be four to five years before any meaningful results are available (Hepatitis C Council submission). The Norwegian study cited above recognised that, despite the improved response to combination therapy "many" patients still do not respond. The study called for the development and evaluation of new antiviral drugs such as the protease inhibitors for the treatment of chronic Hepatitis C (Reichard, Norkrans, Fryden, Braconier, Sonnerborg, Weiland, 1998:83).

- **Ursodeoxycholic Acid**

Ursodeoxycholic acid has been used in a number of liver diseases and has been shown to improve liver function tests in some Hepatitis C patients (NHMRC, 1997:37). The mode of action for Hepatitis C remains uncertain and its long-term benefits are unproven (NHMRC, 1997:37).

- **Corticosteroids**

While the use of corticosteroids alone tends to worsen the prognosis for Hepatitis C by facilitating viral replication, the NHMRC suggests there may be some benefit in giving steroids as a "priming" dose in conjunction with interferon (NHMRC, 1997:37).

7.2.3 LIVER BIOPSIES

A liver biopsy is a very accurate method of determining the condition of liver cells. The procedure involves a needle being passed between the ribs into the liver and a small sample of the liver being taken for examination. The procedure is performed under local anaesthetic. Most people with HCV undergo at least one liver biopsy, often as part of the process of being considered for interferon therapy. A biopsy is always performed before commencing interferon therapy, except in those patients with inherited clotting disorder, such as haemophilia. A further liver biopsy may be performed after therapy.

7.2.4 LIVER TRANSPLANTS

Committee Members were repeatedly told during the course of this Inquiry that Hepatitis C is now the most common indication for liver transplantation in Australia. Transplantation is carried out usually for end-stage liver disease and the transplanted organ often becomes infected with Hepatitis C. However, as the NHMRC report notes,

> *The fact that the disease recurs in the transplanted liver has not been a major problem for transplant units as many of these patients are young and the provision of an additional ten years of life for a productive 30 to 40 year old adult appears most appropriate* (NHMRC, 1997:38).

7.2.5 HEPATOCELLULAR CARCINOMA

Those with end stage liver disease are most at risk of developing hepatocellular carcinoma. The Committee was advised that 15 to 20 per cent of people with cirrhosis will get hepatocellular carcinoma (Rallings evidence, 27 October 1997). This particular form of cancer is, as the Committee was told, "a very serious cancer" and "very little is known about the treatment of it and it is very difficult to treat once you get it" (Rallings evidence, 27 October 1997).

As was discussed in Section 2.2.3 there is no accurate statistical information in Australia on the frequency of Hepatitis C related hepatocellular carcinoma. Until this is known, it will be impossible to predict cost savings that might be achieved by transplanting patients with end-stage liver disease before hepatocellular carcinoma develops (NHMRC, 1997:38).

Shiells, Briggs and Farrell (1994:269) have costed (based on $1994) the treatment protocols for hepatocellular carcinoma as:

Without Surgery (67% of patients), cost per patient	$117,895
With Surgery (33% of patients), cost per patient	$28,290
Expected Cost Per Episode	**$88,325**

7.2.6 COMPLEMENTARY TREATMENTS AND THERAPIES

Given the limited efficacy of interferon and its wide range of side effects, many people with HCV use complementary therapies to relieve symptoms and increase their wellbeing. Some people use these therapies regularly as an alternative to conventional medicine while others may use them to treat specific aspects of their illness. For example, some people who have used interferon report taking specific vitamins and herbal treatments to counteract the side effects. Others may choose to use a number of stress reduction techniques such as massage and meditation to assist them with the disease. As the Hepatitis C Council's submission noted:

> *some people have reported that in the absence of any conventional treatment for HCV, the practice and philosophies of a number of complementary and alternative therapies have provided effective ways of living with HCV* (Hepatitis C Council submission).

According to the National Hepatitis C Councils' Education Reference Group, the most commonly used therapies are:

- Chinese herbs;
- other herbal treatments (particularly St Mary's thistle);

- vitamins, minerals and nutritional supplements; and
- acupuncture and homeopathy (National Hepatitis C Councils' Education Reference Group, 1996:27).

Other therapy used include acupuncture, homoeopathy and oxygen drops (National Hepatitis C Councils' Education Reference Group, 1996:27).

In the study by Sladden *et al* a range of complementary therapies were trialed by those participating in the study (1998:510). The types of therapies and frequencies are reported in Table Twenty-Six. Percentages presented in the Table tally to more than 100 due to multiple treatments.

TABLE TWENTY-SIX
COMPLEMENTARY HVC TREATMENTS

TREATMENT	FREQUENCY (%)
Naturopathy	48 (10.3)
Anti-nausea	37 (7.9)
Analgesia	34 (7.3)
Homoeopathy	22 (4.7)
Dandelion Root	21 (4.5)
St Mary's Thistle	16 (3.4)
Acupressure	8 (1.7)
IV Vitamin C	7 (1.5)
Ozone	5 (1.1)
Chinese Herbs	3 (0.6)
Rest	3 (0.6)
Other Treatment	22 (4.7)
No Treatment	337 (72.4)

Source: Sladden *et al*, 1998:510

Clinical trials have been conducted on the role of Chinese herbs in liver inflammation. The initial placebo controlled trial of a tablet form of Chinese herbal medicine (CH100) was conducted at the John Hunter Hospital, Newcastle. Patients were evaluated

monthly during the six month treatment by a hepatologist and a traditional Chinese medical practitioner (Hossain, Batey and Bollipo, 1996). At commencement ALT was higher in the active than the placebo group (133 ± 21 sem vs 109 ± 16) and at completion it was lower (82 ± 12 vs 101 ± 13) (Hossain, Batey and Bollipo, 1996). The percentage fall in ALT was 38% in the active and 8.5% in the placebo group ($p = 0.048$). Six patients, all on active treatment, normalised their ALT during treatment, but in two it was not maintained despite therapy (Hossain, Batey and Bollipo, 1996). A second, larger study using the same tablet formula as used at John Hunter, is currently being conducted in the Northern Rivers Area Health Service (Sladden evidence, 30 March 1998). Assessment of participants was expected to commence in September 1998 with a rolling enrollment over a one year period. Subject to funding approval testing of PCR viral genotype, PCR viral load and PCR viral detection will be undertaken.

Many of the available complementary therapies receive little support from the medical profession. Despite this, the NHMRC recommends a "watching brief" be kept on the use of natural therapies in the treatment of Hepatitis C (NHMRC, 1997:37).

For many the costs of alternative and complementary therapies is an issue. It is not possible to claim a rebate from Medicare for purchases of items such as milk thistle or vitamins or for attending a natural therapist although some private health insurance schemes do cover certain natural therapies. Many people on middle to low incomes find the cost factor simply prohibitive.

A number of those who made submissions to this Inquiry spoke of their experience with using complimentary therapies:

> *I went to a Chinese herbalist who treats quite a few HIV and Hepatitis people. I began on two infusions a day, dropping down to one, then one every second day. I abstained from alcohol, rested, exercised, used a bit of heroin. My health returned rapidly* (Submission 15);
>
> *I use homoeopathic remedies to treat my symptoms. I have found that my liver function tests are effected positively when I do this, so I continue to research and self-treat carefully* (Submission 88); and
>
> *As I have had little help or feedback from conventional medicine I resort to alternative therapies (herbalist and homeopathy) when the hepatitis virus rears its ugly head and I get crook* (Submission 71).

7.2.5 SUMMARY

The current state and future direction of treatment for Hepatitis C was summarised by Wodak as:

> *Treatment is expensive, far less effective than we would like it to be and, unfortunately, accompanied by very significant side effects. The encouraging news is that very effective treatment is on the horizon. The same advances that have occurred recently in HIV treatment - namely the development of protease inhibitors which have really brought about a remarkable difference in the way HIV is now managed and the results we achieve from HIV - are going to become available to people with Hepatitis C within the next few years. It is confidently expected that this will change the picture* (Wodak evidence, 2 October 1997).

However, he noted that, the negative side is that:

> *the treatment will almost certainly be unaffordable, particularly for an epidemic which involves 150,000 Australians. We have a treatment at the moment which is pretty well unaffordable and not very effective. When we have a much better treatment, which will be undoubtedly even more expensive, we are going to have a real problem knowing how to deal with that* (Wodak evidence, 2 October 1997).

7.3 TREATING AND MANAGING HEPATITIS C POSITIVE INMATES IN THE STATE'S CORRECTIONS SYSTEM

7.3.1 TREATING HEPATITIS C POSITIVE INMATES

The process of screening inmates for Hepatitis C was outlined in Section 6.5. Once identified as Hepatitis C positive inmates are able to access specialist medical services for the treatment and management of their Hepatitis C. As Corrections Health Service Acting Clinical Nurse Consultant informed the Committee:

> *We have policies in place for someone who is Hepatitis C positive and is unwell. His history is taken and his liver function tests are monitored according to that policy. People have to meet certain criteria and they are referred to the specialist clinics for a consultation with the specialist. They may go for liver biopsy, if deemed appropriate, and then on to interferon if that is the course of action for that person* (Harper evidence, 23 March 1998).

The Hepatitis C medical needs, including specialist clinics and treatment, of the entire corrections system are based at the Long Bay Corrections Centre. Specialist Hepatitis C clinics are held at the Long Bay complex twice a month staffed by two attending specialists. As one of the specialists told the Committee: "We see 20 or so individuals a month, which is a couple of hundred a year of the many thousands who are infected" (Lloyd evidence, 30 March 1998). Inmates from non-metropolitan centres and females at Mulawa requiring treatment or consultations with the specialists are required to find their way to Long Bay. With reference to female Hepatitis C positive inmates Lloyd informed the Committee, "we do not seek them out" (Lloyd evidence, 30 March 1998).

The Committee heard that these two doctors are “marvellous” because:

> *they will come to the Metropolitan Reception Remand Centre and see people if they can or they will come in on a one-off visit. If a prisoner comes for another appointment Sandra [the Clinical Nurse Specialist responsible for co-ordinating the Hepatitis C specialist clinic] will co-ordinate that and the doctors will pop in. It is very good even though they are so busy. The clients will tell you that they have never had such a good service in that respect* (Harper evidence, 23 March 1998).

- **Liver Biopsies**

All liver biopsies are performed at the Long Bay prison hospital. When asked to comment on the use of pre- and post-medication Lloyd (who performs the biopsies) informed the Committee that:

> *We do offer good amounts of local anaesthetic and pain relief afterwards . . . It is a vexed problem within the prison system generally, probably more than anywhere else, where there is much concern about potential drug misuse of narcotic analgesics, Valium, and benzodiazepine . . . and people are anxious about prescribing often or even at all for any of those things. We usually negotiate carefully for a limited supply and set the time lines for how long it could be available* (Lloyd evidence, 30 March 1998).

- **Interferon Therapy**

Interferon therapy is available to inmates in the NSW corrections system. The Committee was advised that NSW is the only state within Australia with approval to prescribe interferon to prison inmates. Further, NSW is one of the very few prison systems worldwide where interferon therapy is available to Hepatitis C positive inmates (Lloyd evidence, 30 March 1998).

To be eligible to receive interferon, inmates must meet the s100 criteria outlined earlier in this chapter. The Committee was advised that additional criteria are applied to inmates:

> *From our point of view we very carefully select individuals who meet the S100 criteria for interferon therapy, plus some extra criteria that we add to it: not too much psychiatric pathology, a length of sentence that covers the time to biopsy and treatment and not currently using [drugs]* (Lloyd evidence, 30 March 1998).

The Committee was advised that 22 inmates have completed interferon therapy (Parsons evidence, 23 March 1998). Two people had came to gaol on treatment and it was monitored, however one was withdrawn from therapy due to a psychiatric illness and noncompliance with his medication (Parsons evidence, 23 March 1998). The

Committee also heard that, as of March 1998, five male inmates were on interferon therapy and one was awaiting treatment (Parsons evidence, 23 March 1998).

- **Inmates with Established Hepatitis C Related Diseases**

Given the prevalence of Hepatitis C in the state's corrections system, a number of inmates have already progressed to advanced stages of Hepatitis C-related liver damage. The Committee heard that:

> *Individuals within the prison system who have established cirrhosis and have some degree of liver failure I suspect come to our attention or come to medical attention in the centres. I would be surprised if that did not happen. Already a small number of individuals are in overt liver failure and probably have a pre-terminal condition. We have debated whether they should have an early release on medical grounds because of their limited life expectance, but that is pretty rare. That far end of the spectrum is probably well catered for* (Lloyd evidence, 30 March 1998).

7.3.2 MANAGING HEPATITIS C POSITIVE INMATES

It would appear that the primary mechanism available to Hepatitis C positive inmates to manage their illness is the Lifestyle Unit. This Unit is located in the Special Care Correctional Centre at the Long Bay Correctional Centre. It was opened in late 1992 and accommodates up to eight inmates who have voluntarily applied and been accepted to take part in the program provided by the Unit (Taylor, 1997:9).

While in the Unit inmates are able to cook for themselves, and access (free of charge) vitamins, diet supplements and herbal tonics such as milk thistle (Vumbaca evidence, 23 March 1998).

Opportunity to participate in the program is, the Committee heard, "very limited":

> *probably four to six beds are available at any one time for Hepatitis C inmates and they have to be referred through the hepatitis clinic because of the number of inmates that could seek to access that residential lifestyle program* (Christensen evidence, 23 March 1998).

7.4 CONCLUSION

This chapter's discussion has highlighted the limited range of treatment options available to those with Hepatitis C. Not only are there few options available, but those that are available are not particularly effective and often result in a range of debilitating side effects.

Treating and managing Hepatitis C is currently quite unsatisfactory. The Committee therefore agrees with the state's Chief Health Officer who concluded that "the focus has to be on prevention of the disease" (Wilson evidence, 3 October 1997).