Chronic Hepatitis C Treatment with A4^{+}

Controlled Clinical Test

Authors:

- **José Cabanillas MD**
- **Joseph w. Nystrom MD**
- **Luis Zambrano MD**
- **Gerardo Chiclote MD**

Lima – Peru
May - June 2004

CHRONIC HEPATITIS C TREATMENT WITH A4+ CONTROLLED CLINICAL TEST

INTRODUCTION

According to the **World Health Organization,** the prevalence of hepatitis C (HCV) infection worldwide is approximately 170,000,000 people. **The Centers for Viral Disease Control and Prevention in North America** (CDC) estimate that at least4,000,000 people in the U.S. (1.8% of the population) have been infected by the HCV, according to positive results in VHC antibody tests, and 100,000 new cases are reported each year in this country[1-2].

In most people with HCV, the immune system is unable to eradicate the virus. According to the CDC's most recently collected data, 70% of people infected with HCV will develop chronic hepatitis, which is defined as the presence of detectable HCV RNA for six months or longer[3]. Many of this people will develop liver conditions as a result of the disease; the course of progression and the manifestation of symptoms may occur only decades later. Between 20 % and 30% of chronically infected patients are at risk of developing **hepatic cirrhosis** or even **hepatocellular carcinoma** [4-5], since it has proven to be oncogenic in humans[6]. Chronic hepatitis may result in end-stage liver failure, which is the most frequent cause for liver transplant in most of the countries where it is performed.[7].

The course of chronic hepatitis C progression varies among individuals and, therefore, it is not possible to accurately predict which HCV-infected patients will go on to develop cirrhosis, liver cancer or end-stage liver disease. However, several cofactors appear to affect the severity of the disease. In some, but not in all studies, HCV subtypes **1a** y **1b del VHC** have been associated with more rapid progression, more extensive liver damage, and reduced response to treatment.[8].

Alcohol consumption is likely to be the most important external factor. Excessive alcohol use alone can damage the liver, in conjunction with HCV; and the additive effects of the virus can lead to a more severe disease. The person's **age** can also affect disease progression; people over the age of 50 tend to have more rapid progression and develop more severe symptoms. Research indicates that children's immune systems can fight better and eradicate the virus more frequently that those of the adults. **Gender** also seems to have an effect on progression; men tend to develop more severe liver disease. Finally, individuals who are **immunologically compromised**, due to HIV, to the use of drugs that suppress the immune system or to any other cause, tend to experience rapid HCV disease progression[9].

Over time, while liver cells are infected and destroyed, individuals may develop progressive liver damage. This process begins with persistent inflammation, and proceeds to fibrosis or fibrinogenesis, steatosis, and cirrhosis of the liver. When normal liver cells are replaced with fibrous tissue, fat and scar tissue, they are unable to carry out their functions of metabolism.

According to these data, HCV infection is a **worldwide health problem** and there is a need for effective therapy. Hepatitis C treatments are not perfect and there is still a lot of research to be conducted. Recent progress has improved the chances of maintaining the highest viral suppression.

It is known that Interferon (IFN) is the only drug that has shown some efficacy in the inhibition of viral replication and, therefore, in the clinical and histological progression of chronic HCV infection. Many therapeutic schemes were tested since the first original work by Hoofnagle in 1986 [10] until the introduction in May of 1999 of **Pegylated Interferon alpha-PEG** [11]. Standard doses of 3,000,000 units 3 times a week, as well as high doses have been tested both by induction and by escalation schemes.[12-13]. Combined therapy with **Ribavirin** was approved in the year 2,000 by the FDA, for treatment-naive patients as well as for non-responders and relapsers Clinical trials for this kind of patients had already been conducted before. [14-15] Compared with Interferon, the combined therapy reduced the risk of not having a sustained virological negativization, in 28% of the patients with a previous treatment; 33% in relapsers and 11% in those that had not responded before. Regardless of previous treatment, the combined therapy reduced the risk of not obtaining a sustained normalization of biochemical tests or an histological improvement; but it significantly increased the risk of discontinuing treatment due to various adverse side effects.[16].

The observations of **Dr. José Cabanillas**, on positive and encouraging results about the clinical manifestations of HCV (chronic hepatitis C) patients treated with "**active organic ingredients** (**A4**$^{+}$), motivated us to conduct a 30-day controlled clinical test that would allow us to asses the clinical, hematological, biochemical, ultrasound and anatomic manifestations in a group of 9 voluntary patients who carry chronic hepatitis C and one control patient with cirrohosis.

Methods

We conducted a controlled clinical test in 10 Caucasian adult patients with a confirmed diagnosis of chronic hepatitis C except for one control patient who had been cured of Hepatitis B and C but had severe cirrhosis (Susan White). Some of them had been treated before without satisfactory results. They were patients with chronic hepatopaty symptomatology who voluntarily underwent the **therapy with A4^{+}.**

Out of the10 patients included in the study, 5 were men and 5, women, and their ages ranged from 37 to 58 years. The estimated period, by anamnesis, of **time of virus inoculation** was 30 years for those with the longest time and 4 years for those with the shortest period. The duration **of the disease** observed in the patients was established by the means of the appearance of symptoms and serologic diagnosis from 12 to 1 year. **Table 1**

Table 1

Chronic Hepatitis C (HCV)

Possible Inoculation Period and Disease Duration

CASES	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
PATIENTS	**S.R**	**S.T.**	**O.P.**	**L.R.H.**	**Ch.D.**	**W.S.**	**F.S.**	**D.S.**	**H.G.**	**S.L.**
Sex	M	M	M	M	M	F	F	F	F	F
Age (years)	51	37	46	52	46	58	46	47	56	53
Inoculation Period (y)	34	18	21	6	28	32	4	15	26	33
Disease Duration (y)	7	7	5	3	12	5	1	5	10	12

Source: Dr. José Cabanillas & Colleagues
Lima – Peru

To assess the current state of the disease, clinical, serological, biochemical, ultrasound and histo-pathological tests were conducted.

A second generation ELISA system was used to confirm the presence of seric **anti–VHC**. Moreover, we conducted an investigation of **Hepatitis B**, by the means of investigating surface **antigen (HBs Ag) and core antigen (HBc Ag.).** Results are shown in **Table 2.**

Table 2
Chronic Hepatitis C (HCV)
Serologic Evaluation

CASES	1	2	3	4	5	6	7	8	9	10
PATIENTS	S.R	S.T.	O.P.	L.R.H.	Ch.D.	W.S.	F.S.	D.S.	H.G.	S.L.
Anti-HCV	+	+	+	+	+	+	+	+	+	+
Antigen HBs Ag	-	-	-	-	-	-	-	-	-	-
Antigen HBc Ag	-	-	-	+	-	+	+	-	-	-

Source: Dr. José Cabanillas & Colleagues
Lima – Peru

HCV FIBROSURE (550123) was used to determine the state of **histo-pathological lesions** in patients. The HCV FIBROSURE is a noninvasive blood test for assessing liver state in hepatitis C patients. Developed by hepatologists at the **PITIE–SALPETRIERE HOSPITAL and BIO PREDICTIVE** in Paris (France), it is only available in the United States through LAB–CORP.

The HCV FIBROSURE provides an easily accessible alternative to liver biopsy, which is used to assess **liver fibrosis and necroinflammatory activity** in HCV patients, while liver biopsies have been traditionally used in hepatitis C patients to provide important information on disease prognosis, as well as potential lateral response, they are considered an invasive procedure that can cause complications and frequently accompanied by transitory pain.

The HCV FIBROSURE combines the quantitative results of six serum biochemical markers**: Alpha2-Macroglobulin, Haptoglobulin, Apolipoprotein A1, Bilirubin, Gamma Glutamyl Transpeptidase (GGT) and Glutamic Piruvic Transaminase (GPT)** with age and gender, in a patented artificial algorithm to determine the degree of liver fibrosis and the level of ongoing necroinflammatory activity.

Results obtained with HCV FIBROSURE constitute a reliable quantitative assessment of fibrogenetic and inflammatory liver activity in HCV patients.

The results of the HCV FIBROSURE are shown in **Table 3** and **Table 4**

Table 3
Chronic Hepatitis C (HCV)
HCV FIBROSURE-Biochemical Indicators

Biochemical Indicator	Alpha2 Macroglobulin	Hapto Globulin	Apo-lipo Proteein A1	Total bilirubin	Gama glutamyl Transpeptidase	Piruvic Transaminase
Normal Value	**110-276 mg/dl.**	**34-200 mg/dl.**	**110-205mg/dl.**	**0.1-1.2mg/dl**	**0.0-60 IU/L.**	**0.0-40 IU/L.**
PATIENTS						
Stad, Raymond	437	16	125	1.20.	191	330
Smith, Troy	293	102	120	1.20	91	61
O'Connor, Patrick	424	107	99	0.40	53	71
Langen, Ron Harry	337	60	116	0.60	71	54
Charron, Daniel	312	124	110	0.50	32	34
White, Susan	291	<15	83	1.70	34	21
Fetterroll, Susan	149	180	116	0.30	57	49
Doyle, Susan	236	138	165	0.30	27	37
Hutchines, Geraldine	185	138	152	0.50	26	40
Stockert, Linda	437	67	106	0.90	36	181

Source: Dr. José Cabanillas & Colleagues
Lima – Peru

Table 4
Chronic Hepatitis C (HCV)
HCV FIBROSURE-Histopatologic Evaluation

	Fibrosis Score	Necrosis Score	Fibrosis Score	Inflammatory Necrosis Score
Normal Value	**0.0-0.21**	**0.0-0.17**	**Diagnosis**	**Diagnosis**
PATIENTS				
Stad, Raymond	0.96	0.96	**F4** cirrhosis	**A3** Severe Activity
Smith, Troy	0.67	0.50	**F3** fibrous bridges w/ numerous septa	**A1-2** Minimal Activity
O'Connor, Patrick	0.70	0.58	**F3** fibrous bridges w/ numerous septa	**A2** Moderate Activity
Langen, Ron Harry	0.50	0.22	**F2** fibrous bridges w/ numerous septa	**A0-1** No Activity
Charron, Daniel	0.76	0.48	**F4** cirrhosis	**A1-2** Minimal Activity
White, Susan	0.90	0.20	**F4** cirrhosis	**A0-1** No Activity
Fetterroll, Susan	0.10	0.23	**F0** no fibrosis	**A0-1** No Activity
Doyle, Susan	0.12	0.16	**F0** no fibrosis	**A0** No Activity
Hutchines, Geraldine	0.16	0.18	**F0** no fibrosis	**A0-1** No Activity
Stockert, Linda	0.81	0.89	**F4** cirrhosis	**A3** Severe Activity

Source: Dr. José Cabanillas & Colleagues
Lima – Peru

We conducted a study using THREE-DIMENSIONAL ULTRASOUND to determine liver volumetry, the characteristics of its borders and the ultrasound alterations of the liver parenchyma. The assessment of characteristics of the portal vein, the spleen and the presence of ascites are included in the study. **Table 5**

Table 5
Chronic Hepatitis C (HCV)
Three-dimensional ultrasound

	Stad, Raymond	Smith, Troy	O'Connor, Patrick	Langen, Ron Harry	Charron, Daniel
Liver	Hepatomegaly	Hepatomegaly	normal	Hepatomegaly	Hepatomegaly
Size of right lobe	165 mm.	153 – 156 mm.	138 mm.	168 mm.	151-153 mm.
Size of left lobe	114 – 116 mm.	103 – 116 mm.	92 mm.	121 mm.	113-122 mm.
Borders	Regular	Regular	Regular	Regular	Regular
Diffuse echogenicity	Slight Increase	Moderate Increase	Moderate Increase	Moderate Increase	Moderate Increase
Types of echos	Low-amplitude	High-amplitude	Medium-amplitude	Medium-amplitude	Medium-amplitude
Focal Injuries	no signs observed.	no signs observed.	no signs observed.	no signs observed.	no signs observed.
Portal Vein	Normal Appearance	Brightness in portal wall	Normal	Portal hypertension	Normal
Measurements	12mm.	11 – 13 mm.	12-13 mm.	16 mm.	13 mm.
Spleen	Splenomegaly	Splenomegaly	Normal	Splenomegaly	Normal
Measurements	132 x 66 mm.	157 x 81 mm.	92 x 41mm.	135 x 45 mm.	91 x 45 mm.
Splenic vein	8 mm.	8 mm.		4 mm.	
Ascites	Not present	Not present	Not present	Not present	Not present

Source: Dr. José Cabanillas & Colleagues
Lima – Peru

Table 5 (Cont.)
Chronic Hepatitis C (HCV)
Three-dimensional ultrasound

	White, Susan *	Fetterroll, Susan	Doyle, Susan	Hutchines, Geraldine	Stockert, Linda
Liver	Decreased	Hepatomegaly	Normal	Normal	Hepatomegaly
Size of right lobe	108 mm.	186mm.	133 mm.	130 mm.	146-149 mm.
Size of left lobe	83 mm.	142mm.	104 mm.	104 mm.	105-124 mm.
Borders	Regular	Regular	Regular	Regular	Regular
Diffuse echogenicity	High Increase	Slight Increase	Slight Increase	Slight Increase	Moderate Increase
Types of echos	High-amplit = cirrhosis	Low-amplitude	Low-amplitude	Low-amplitude	Medium and High
Focal Injuries	no signs observed.	no signs observed.	no signs observed.	no signs observed.	no signs observed.
Portal vein	Hypertension Signs	Hypertension Signs	Normal	Normal	Brightness in portal wall
Measurements	13mm.	11 – 14 mm.	11 mm.	10 mm.	15 mm.
Spleen	Splenomegaly	normal	Normal	Normal	Splenomegaly
Measurements	121 x 51 mm.	106 x 62 mm.	87 x 45mm.	97 x 51 mm.	112 x 58 mm.
Splenic vein					
Ascites	present	Not present	Not present	Not present	Not present

Source: Dr. José Cabanillas & Colleagues
Lima – Peru
***Control Patient**

The biochemical study of the alterations produced by chronic hepatitis C (HCV) is based on 4 criteria. First: tests to measure liver synthesis capacity. Second: tests to measure alterations due to architectural disorders caused by fibrosis that lead to intrahepatic obstruction. Third: tests to measure necroinflammatory activity in the hepatocytes where it was present, a test to assess focal alterations due to possible hepatocarcinoma. And fourth: tests to measure liver purifying function.

Tests to measure liver synthesis capacity are considered as the study of liver function reserve, once **CHOLINESTERASE** has been determined, since there is evidence[20] that it is produced in the liver and that it decreases with chronic hepatitis, having an average life of 28 days; the assessment of **PREALBUMIN** that indicates the nutritional state of chronic hepatitis patients; and **PROTHROMBIN TIME**, considering that they did not present a deficit of vitamin K and that we did not find, in any case, obstruction of extrahepatic biliary tracts that could inhibit absorption, resulting in a synthesis function of the hepatocyte. See **Table 6**

Table 6
Chronic Hepatitis C (HCV)
Hepatic Synthesis Activity

	Cholinesterase	Prealbumin	Prothrombin time	Concentr. of Prothrombin
Normal Values	**<5,500 U/L**	**<20 mgr/dl**	**11 sec.**	**100%**
PATIENTS				
Stad, Raymond	3,742	16.0	15.0 sec.	65.0
Smith, Troy	8,018	13.0	15.0 sec.	65.0
O'Connor, Patrick	6,241	20.0	13.0 sec.	80.0
Langen, R. Harry	4,631	15.0	14.0 sec.	75.0
Charron, Daniel	4,390	28.0	14.0 sec.	75.0
White, Susan	2,321	7.0	18.0 sec.	51.0
Fetterroll, Susan	5,408	27.0	13.0 sec.	80.0
Doyle, Susan	5,408	25.0	13.0 sec.	80.0
Hutchines, Geraldine	6,696	20.0	14.0 sec.	75.0
Stockert, Linda	5,086	14.6	13.0 sec.	80.0

Source: Dr. José Cabanillas & Colleagues
Lima - Peru

In order to assess liver structural alterations caused by fibrosis and hepatocyte degeneration, both the determination of bilirubin and alkaline phosphatase dosage were taken into consideration. It had already been determined by the means of ultrasound that there was no obstruction of the extrahepatic biliary ducts and, therefore, any increase could be interpreted as intrahepatic alterations in the structure. See **Table 7**.

Table 7
Chronic Hepatitis C (HCV)
Evaluation of intrahepatic structure

	Total bilirubin	Direct bilirubin	Indirect bilirubin	Alkaline phosphatase
Normal Values	**0.3 - 1.0 mgl./ dl**	**0.0 – 0.3 mgl/dl**	**0.3 – 1.0 mgl/dl**	**40 – 129 U/L**
PATIENTS				
Stad, Raymond	1.90	0.60	1.30	97
Smith, Troy	7.2.2.	0.60	1.60	116
O'Connor, Patrick	0.70	0.30	0.40	70
Langen, R. Harry	1.00	0.40	0.60	99
Charron, Daniel	1.00	0.20	0.80	78
White, Susan	3.00	1.20	1.80	196
Fetterroll, Susan	0.60	0.20	0.40	72
Doyle, Susan	0.70	0.20	0.50	58
Hutchines, Geraldine	0.80	0.20	0.60	77
Stockert, Linda	1.30	0.40	0.90	76

Source: Dr. José Cabanillas & Colleagues
Lima - Peru

Tests that measure alterations in the hepatocyte due to viral damage in its membrane are considered as the study of hepatocyte injury and the necroinflammatory activity it can lead to, once the **GLUTAMIC PIRUVIC TRANSAMINASES (GPT) and the GLUTAMIC OXALOACETIC TRANSAMINASES (GOT)** have been determined., as well as the determination of **TRANSFERRIN,** knowing that an increase is due to the release of iron stored in liver cells when they suffer necrosis. The determination of **GAMMA GLUTAMYL TRANSPEPTIDASE,** whose activity in serum increases moderately when there is diffuse liver damage, but it is a guiding enzyme in hepatic toxic lesions due to alcohol 21. And finally, a tumor maker was determined, the **ALPHA-FETOPROTEIN** (AFP), since it increases with chronic and acute liver disease such as cirrhosis and hepatitis, although it rarely exceeds 50-75 ng/ml. Most authors agree that values over 100ng/ml. correlate with primitive hepatocellular cancer[22, 23]. See **Table 8**

TABLE 8
Chronic Hepatitis C (HCV)
Necro-Inflammatory Activity Evaluation

	GPT	GOT	GGT	Transferrin	AFP
Normal Values	**0.0 – 38.0 UI**	**0.0 – 40.0 UI**	**9.0 – 35.0 U/L**	**300 – 360 ug/dl**	**0.8 – 8.5 ng/ml**
PATIENTS					
Stad, Raymond	546	340	186	295	231.0
Smith, Troy	97	62	108	330	7.7
O'Connor, Patrick	93	65	60	331	4.3
Langen, R. Harry	113	96	70	404	6.0
Charron, Daniel	22	21	27	310	1.4
White, Susan	28	48	36	243	3.1
Fetterroll, Susan	71	55	72	410	2.5
Doyle, Susan	50	41	27	377	5.4
Hutchines, Geraldine	48	29	24	306	4.4
Stockert, Linda	306	214	33	347	3.0

Source: Dr. José Cabanillas & Colleagues
Lima - Peru

Finally, we conducted a study of the liver purifying function, by the means of determining AMMONIA IN BLOOD SERUM.

The TNF-ALPHA test was added (tumor necrosis factor), with the intention of measuring hepatic necrosis.

We also included a PLATELET COUNT since an increase in of portal circulation pression and splenomegaly (checked via ultrasound) could be leading to platelet deficiency. See **Table Nº 9**

Table 9
Chronic Hepatitis C (HCV)
Evaluation of Hepatic Alterations

	Ammonia	TNF-alpha	Platelet count
Normal values	**25 – 80 ug/dl**	**0.0 – 8.1 pg/ml**	**140,000 – 440,000 x mm**
PATIENTS			
Stad, Raymond	36	10.0	85,000
Smith, Troy	56	7.5	216,000
O'Connor, Patrick	25	7.1	257,000
Langen, R. Harry	27	8.0	130,000
Charron, Daniel	79	4.5	243,000
White, Susan*	122	7.5	125,00
Fetterroll, Susan	39	6.4	381,000
Doyle, Susan	47	4.9	319,000
Hutchines, Geraldine	44	5.2	200,000
Stockert, Linda	33	11.1	196,000

Source: Dr. José Cabanillas & Colleagues
Lima – Peru
*Control Patient

To complement the study, **chest x-rays** were performed in all patients to rule out lung pathology; they were negative in all cases; we calculated the value of **blood sugar** with the purpose of investigating **Diabetes Mellitus**; a study of **renal function** by the means of serum dosage of urea and creatinine; an evaluation of the **nutritional state** through dosage of **total and fractioned proteins** and finally we determined **thyroid-stimulating hormone** (TSH) to rule out the presence of **thyroid** pathology. The results are shown in **Table 10** and **11**.

Table 10
Chronic Hepatitis C (HCV)
Hematologic Evaluation

	Count	Count	Formula						Constant Values			Hemoglobin	Hematocrit
	Erythrocytes	Leukocytes	E	B	A	S	M	L	Corpusculars				
			%	%	%	%	%	%	VCM	HbCM	CHbCM	gr/dl	%
PATIENTS													
Stad, Raymond'	4,610,000	4,140	3	1	0	62	5	29	102.0	34.6	33.6	15.8	47.1
Smith, Troy	5,420,000	9,150	3	0	1	64	7	25	93.0	31.6	33.9	17.1	50.4
O'Connor, Patrick	4,780,000	14,800	0	0	2	69	3	26	93.7	32.1	34.3	15.4	44.8
Langen, R. Harry	4'330,000	4,100	4	0	4	50	5	37	91.6	30.4	33.2	13.2	39.6
Charron, Daniel	5,220,000	11,600	4	1	1	67	5	22	90.7	30.5	33.6	15.9	47.3
White, Susan	3,980,000	6,420	0	0	0	64	6	30	95.4	31.9	33.4	12.7	37.9
Fetterroll, Susan	4,200,000	8,110	0	0	0	8	5	27	84.8	28.5	33.6	12.0	35.6
Doyle, Susan	3,900,000	5,480	2	0	0	54	6	38	89.8	31.0	34.6	12.1	35.0
Hutchines, Geraldine	4,530,000	7,620	0	0	0	71	6	23	94.9	31.2	32.8	14.1	43.0
Stockert, Linda	4,910,000	4,340	1	0	2	44	4	49	90.3	29.6	32.8	14.5	44.3

Source: Dr. José Cabanillas & Colleagues
Lima – Peru

Table 11
Chronic Hepatitis C (HCV)
General Biochemical Evaluation

	Basal glucose	Total proteins	Sero albumin	Sero globulin	Serum urea	Serum creatinine	Thyroid- stimulating hormone
Normal values	**75-110 mg/dl**	**6.0-8.0 gr/dl**	**3.5-5.0 gr/dl**	**2.0-3.0 gr/dl**	**15.0-40.0 mg/dl**	**0.7-1.4 mg/dl**	**0.2-6.8 m UI/ml**
PATIENTS							
Stad, Raymond	93.0	7.60	4.10	3.50	35.0	1.1	5.0
Smith, Troy	210	8.20	3,4,5.	3.70	38.0	1.0	1.3
O'Connor, Patrick	84.0	7.50	4.40	3.10	28.0	1.0	0.8
Langen, R. Harry	88.0	7.10	4.40	2.70	27.0	1.0	1.5
Charron, Daniel	90.0	7.60	4.70	2.90	37.0	0.9	1.2
White, Susan	77.0	6.10	3.0	3.10	14.0	0.8	1.6
Fetterroll, Susan	119.0	7.40	4.50	2.90	15.0	0.8	5.0
Doyle, Susan	82.0	7.90	4.60	3.30	16.0	0.9	6.4
Hutchines, Geraldine	77.0	6.10	3.0	3.10	14.0	0.8	1.5
Stockert, Linda	78.0	9.0	4.90	4.10	20.0	0.90	2.3

Source: Dr. José Cabanillas & Colleagues
Lima – Peru

CLINIC HISTORIES

CASE PRESENTATION

1. **STAD , RAYMOND**
2. **SMITH, TROY**
3. **O'CONNOR, PATRICK**
4. **LANGEN, R. HARRY**
5. **CHARRON, DANIEL**
6. **WHITE, SUSAN – CONTROL PATIENT ***
7. **FETTERROLL, SUSAN**
8. **DOYLE, SUSAN**
9. **HUTCHINES, GERALDINE**
10. **STOCKERT, LINDA**

Clinic History 1

Date: 16-05-2004

.- Personal Information

Name_____	**Raymond Stad**
Date of birth _____	February 12, 1953
Age_____	51
Place of birth_____	Vancouver – Canada
Address_____	2913 Panorama Drive North Vancover B.C. V7G 2A4
Telephone number_____	604 -290 -7373
Marital Status_____	common-law
Occupation_____	worker in shipping terminal

II- Medical Record:

1.- Family Medical Record:

Mother with congestive heart failure.
Others unknown. He denies any family history of hepatitis.

2.- Personal Pathological Record:

Pneumonia in adolescence.
Renal lithiasis at age 44.
He reports diagnosis of portal hypertension and lack of platelets.
He denies any blood transfusion.
He denies surgical history.

3.- Hepatitis C Record:

Estimated date of contact_____1970
Reason of exposure_____possibly due to the use of drugs

4.- Allergy Record:

Drugs_____ sulfas
Food_____he doesn't report any
Other_____he doesn't report any

5.- Harmful Habits Record:

Tobacco_____	smoked until 1974
Marihuana_____	from 1974 until 2003
Alcohol _____	he doesn't consume
Coffee_____	until 6 years ago
Drugs_____	he doesn't report any

6.- Treatment Record:

He used Interferon and Ribavirin for 2 months in 2002.
Other: cat's claw, timosin, vitamin B, garlic, vera Reishi.

III.- Present Disease:

Duration of disease	7 years
Onset	insidious
Course	progressive

Symptoms and Signs:

Symptoms: feeling of general discomfort, exhaustion, severe fatigue, extreme weakness, depression. General muscular aching and arthralgia, difficulty sleeping, increased urinary frequency at night. He doesn't report digestive problems: abdominal swelling, constipation, diarrhea, nausea, vomiting, blood in stools or abdominal pain.

He doesn't report headaches, dizziness, blurred vision, shortness of breath or any other pain.

Signs: mild jaundice.

Physical Examination:

Height	1.80 m. (5'8´´)
Weight	97 Kg. (215 pounds)
Body mass index	33
Blood pressure	148/90 mm. Hg.
Heart rate	78 beats per minute
Respiratory rate	18 breaths per minute
Temperature	36.5º C

The patient is a well developed and well nourished Caucasian male, with no feeling of fatigue, that walks without apparent difficulty.

Physical Examination- Preferential.

Patient with mild conjunctival icterus.

Soft, tender, non-sensitive abdomen. No presence of collateral circulation or hernia. Deep palpation revealed a small increase of liver size. Normal intestinal sounds. No presence of ascites. The spleen can't be palpated.

Further Clinical Examination.

Warm, dry, non-turgid skin. No rashes or skin lesions are observed.
Pearl ears, nose and throat. Pinkish and moist oral mucus. Normal oropharynx.

Flexible neck. No adenopathies in neck, axilla and inguinal regions.

RESPIRATORY.- clear lungs. No abnormal sounds.

CARDIOVASCULAR.- regular rate and rhythm, without abnormal sounds or murmurs.

MUSCULOSKELETAL.- no weakness or atrophy, no limitation to articular movement. He walks normally.

EXTREMITIES.- no deformities, cyanosis or edema.

NEUROPSYCHIATRIC.- awake, alert and well oriented.

Normal state of mind. Symmetric reflexes.

IV.- Other Data:

4/10/04 LIVER BIOPSY.- fibrosis in phase 4/4 according to LUDWING's criteria. (Cirrhosis) focal iron stains classified as 1/4 inside Kupffer cells.

7/6/02 ABDOMINAL ULTRASOUND.- 19 cm. increase in liver size, fat infiltration. Mild hepatosplenomegaly.

10/1/00 viral load 2,106,111 copies/ml.

12/2/02	GPT (ALT)	545 U/L
	GOT (AST)	321 U/L
	GGT	164 U/L
	Ferritin	1783 ug/

Clinic History 2

Date: 16-05-2004

I.- Personal Information:

Name_____ **Troy D. Smith**
Date of birth _____ January 27, 1967
Age_____ 37
Place of birth_____ Penticton – Canada
Address_____ 1202 Penticton Av. Penticton, B.C.V2A 2N4
Telephone number_____ 250-490 -8049
Marital Status_____married
Occupation_____truck driver

II- Medical Record:

1.- Family Medical Record:

Father with arterial hypertension.
Mother with coronary disease and psoriasis.

2.- Personal Pathological Record:

History of hypertension.
Peptic ulcer.
Pneumonia.
Renal calculus.
Fractures due to accident.

3.- Hepatitis C Record:

In 1986, truck accident, multiple reconstructive surgeries are performed on him (face and skull, as well as fractured leg). He received blood transfusion.
Reason of exposure: possibly due to blood transfusion.

4.- Allergy Record:

Food_____peanuts
Drugs_____ he doesn't report any
Other_____he doesn't report any

5.- Harmful Habits Record:

Tobacco	he doesn't smoke
Alcohol	he doesn't consume
Coffee	occasionally
Drugs	he doesn't consume

6.- Treatment Record:

ADVIL, calcium, magnesium and tylenol.

III.- Present Disease:

Duration of disease	8 years
Onset	insidious
Course	progressive

Symptoms and Signs:

Symptoms: feeling of fatigue, "I always have to fight to stay awake", light-headed, he frequently forgets things. He reports acidity, chronic abdominal pain, nausea. Perennial articular pain, depression and mood changes.

Signs: no signs have been observed.

Physical Examination:

Height	1.80 m. (5'8´´)
Weight	97 Kg. (215 pounds)
Body mass index	32
Blood pressure	140/100 mm. Hg.
Heart rate	72 beats per minute
Respiratory rate	18 breaths per minute
Temperature	36.5º C

The patient is a well developed and well nourished Caucasian male.

Physical Examination- Preferential

Tenderness in abdomen, with mild sensitivity in right superior quandrant. No organomegaly, masses or liquids upon deep palpation. Normal intestinal sounds.

Further Clinical Examination.

Warm, dry skin Normal turgency with some scarring.

Ears, nose and throat: facial surgery scarring.

Equal pupils, reactive to light, with mild conjunctival icterus. Pinkish and moist oral mucus. No erythema.

Flexible neck.. No adenopathies in neck, axilla and inguinal regions.

RESPIRATORY.- clear lungs upon auscultation. No abnormal noises, rhonchi or wheezing.
CARDIOVASCULAR.- regular rate and rhythm. No abnormal acceleration, sounds or murmurs. Tracheotomy scarring.

MUSCULOSKELETAL.- no weakness or atrophy, intact articular movement. He walks normally.

EXTREMITIES.- scarring in right thigh and back of the hip. No deformities, cyanosis or edema.

NEUROPSYCHIATRIC.- awake, alert and oriented 3. Normal state of mind. Deep symmetric reflexes in tendons. No trembling. Craneal nerves from II to XII are intact.

IV.- Other Data:

12/2/96 LIVER BIOPSY.- he presents mild fibrosis in portal triad. Mild fat infiltration. Moderate iron stains.

10/8/96 GPT (ALT) = 297UI/L
Iron 36 Umd/L

4/18/00 GOT (AST) = 97 UI/L
GPT (ALT) = 163 UI/L

Clinic History 3

Date: 16-05-2004

.- Personal Information

Name_____ **Patrick O'connor**
Birth Date_____ November 19, 1957
Age_____ 47
Place of birth_____Vancouver – Canada
Address_____Apt. 103 2407 Wall Street Vancouver British.
Telephone_____604 – 562 - 0570
Marital Status_____single
Occupation_____carpenter

II- Medical Record:

1.- Family Medical Record:

Father with arteriosclerotic disease
Mother with con arthritis
Brother with hepatitis C
Sister with hepatitis B and asthma

2.- Personal Pathological Record:

Appendectomy in 1970
Aneurysm repair in 1991
He denies any blood transfusion

3.- Hepatitis C Record:

Estimated date of contact_____1983
Reason of exposure_____possibly due to the use of drugs

4.- Allergy Record:

Medicaments_____he doesn't report any
Food_____he doesn't report any
Other_____he doesn't report any

5.- Harmful Habits Record:

Tobacco_____consumes up to date
Marihuana_____since 1974 to date
Alcohol _____quit in 1999
Coffee_____occasionally
Drugs_____valium from 1979 to 1987
Cocaine_____from 1979 until 1987
Heroine _____ in 1983

6.- Treatment Record:

He used Interferon for 6 months in 2000
He used Dialanton 1992

III.- Present Disease:

Duration of disease_____ 5 years
Onset_____ insidious
Course_____ progressive

Symptoms and Signs:

Symptoms: chronic fatigue, mild headache, back pain and mild shoulder pain. He presents pain around the thoracic box, chronic pain in articulations, myalgia, nauseas and heartburn on occasion. He doesn't report constipation or diarrhea. He does not present fever, stinging or lack of oxygen.

Signs: no signs have been observed.

Physical Examination:

Height_____ 1.80 m.
Weight_____72.3 Kg. (159 libras)
Body mass index_____ 26
Blood pressure_____ 144/80 mm. Hg.
Heart rate_____ 56 beats per minute
Respiratory rate_____ 18 breaths per minute
Temperature_____ 36.7º C

The patient is a well developed and well nourished Caucasian male, without acute exhaustion.

Physical Examination- Preferential.

Soft, tender, non-sensitive abdomen. No presence of collateral circulation or hernia upon deep palpation. No hepatosplenomegaly. Normal intestinal sounds. No presence of ascites.

Further Clinical Examination.

Warm, dry, non-turgid skin. No rashes or skin lesions are observed. He presents craniotomy scar.

Pearl ears, nose and throat. Pinkish and moist oral mucus. Normal oropharynx. Equal pupils, reactive to light, clear sclerotic, no jaundice, mild facial angioma.

Flexible neck. No adenopathies in neck, axilla and inguinal regions.

RESPIRATORY.- clear lungs. No abnormal sounds.

CARDIOVASCULAR.- regular rate and rhythm, without abnormal sounds or murmurs.

MUSCULOSKELETAL.- no weakness or atrophy, no limitation to articular movement. He walks normally.

EXTREMITIES.- no deformities, cyanosis or edema. Scar on right knee.

NEUROPSYCHIATRIC.- awake, alert and oriented 3.

Normal state of mind. Deep symmetric reflexes in tendons.

IV.- Other Data:

11/4/99 LIVER BIOPSY.- mild chronic hepatitic with slight fibrosis, with portal inflammation in phase 2 according to LUDWING's criteria, globular inflammation in phase 1, fibrosis in phase 1-2.

4/22/04	GPT (ALT)	105 U/L
	GOT (AST)	321 U/L

Clinic History 4

Date: 16-05-2004

I.- Personal Information:

Name_____ **Ron Harry Lagen**
Date of birth _____ August 06,, 1953
Age_____ 51
Place of birth_____ Casteglar – Canada
Address_____ # B, 105 – 7th Av. Casteglar
Telephone number_____ 250-354-9683
Marital Status_____single
Occupation_____writer, journalist

II Medical Record:

1.- Family Medical Record:

Father with chronic alcoholism
Mother with arterial hypertension

2.- Personal Pathological Record:

Pneumonia in 1992
Non- specified sexual transmitted disease
Bone fracture in 1980
Chronic alcoholism
Hepatitis B at 25 years old
Bronchial asthma for the past 10 years
Foot cyst extirpation in 1974

3.- Hepatitis C Record:

Estimated date of contact_____1998
Reason of exposure_____possibly due to the use of drugs

4.- Allergy Record:

Medicaments_____aspirin
Food_____he doesn't report any
Other_____cats

5.- Harmful Habits Record:

Tobacco	consumes with moderation
Marihuana	occasionally
Alcohol	frequently until 2 years ago
Coffee	little
Drugs	Ativan

6.- Treatment Record:

He used Pegasys – Interferón until April 2004
Ventolin and other bronchodilator up to date
Vitamins C and D

III.- Present Disease:

Duration of disease	3 years
Onset	insidious
Course	progressive

Signs and Symptoms

Symptoms: fatigue, weight loss, stinging (pruritus), congestion, abdominal pain, heartburn, diarrhea, general pain in articulations, myalgia, weakness, depression and anxiety.

Signs: no signs have been observed.

Physical Examination:

Height	1.76 m. (5'9´´)
Weight	88 Kg. (166 pounds)
Body mass index	25
Blood pressure	110/60 mm. Hg.
Heart rate	88 beats per minute
Respiratory rate	18 breaths per minute
Temperature	36.5º C

The patient is a well developed and well nourished Caucasian male, without acute exhaustion.

Physical Examination- Preferential.

Tender abdomen, pain on epigastry upon palpation and painful sensitivity in right superior quandrant. Liver left lobe palpable at 7 cm under of costal rim.

Further Clinical Examination.

Warm, dry, non-turgid skin. No rashes or skin lesions are observed.

Pearl ears, nose and throat. Equal pupils, reactive to light, clear sclerotic. Some facial angiomas are observed. Clear tympanic membranes, pinkish and moist oral mucus with mild sublingual varicose veins, normal oropharynx.

Flexible neck, no jugular ingurgitation.

No adenopathies in cervix, axilla and inguinal regions. He shows mild gynecomastia in chest.

RESPIRATORY.- clear lungs upon auscultation. No abnormal noises, rhonchi or wheezing.

CARDIOVASCULAR.- regular rate and rhythm, without abnormal cardiac sounds, systolic ejection sound grade1/6 at right sternal border, without irradiation.

EXTREMITIES.- no deformities, cyanosis or edema, no bruises.

NEUROPSYCHIATRIC.- no motor sensory deficiency.
Craneal nerves from II to XII are intact.
The patient is alert and well oriented.

IV.- Other Data:

Negative chest X ray.

4/10/04	GOT (AST)	145 U/L
	GPT (ALT)	181 U/L
	Viral load	1 Million
	Platelets	127,000/mm^3

Clinic History 5

Date: 16-05-2004

I.- Personal Information:

Name_____	**Daniel Charron**
Date of birth _____	March 16, 1958
Age_____	46
Place of birth_____	Quebec – Canada
Address_____	3022 – CH du pont, vals des ronte San
Telephone number_____	819-457-1737
Marital Status_____	single
Occupation_____	social worker

II Medical Record:

1.- Family Medical Record:

Father died of heart disease at 53
Mother died of multiple sclerosis at 53
Brother died of lung cancer at 44

2.- Personal Pathological Record:

Fracture of tibia in 1976

3.- Hepatitis C Record:

Estimated date of contact_____1998
Reason of exposure_____possibly due to tatoo

4.- Allergy Record:

Medicaments_____he doesn't report any
Food_____he doesn't report any
Other_____he doesn't report any

5.- Harmful Habits Record:

Tobacco	consumes regularly up to date
Marihuana	yes
Alcohol	little
Coffee	with moderation
Drugs	he doesn't report any

6.- Treatment Record:

He used Rebetron - Interferon from July 2001 until June 2002

III.- Present Disease:

Duration of disease	14 years
Onset	insidious
Course	progressive

Signs and Symptoms

Symptoms: general discomfort, fatigue, lack of concentration, muscular pain and arthralgia, difficulty to sleep, dizziness, alterations in digestion, nausea, semi-liquid stools, bloating after eating, depression.

Signs: no signs have been observed.

Physical Examination:

Height	1.72 m. (5'6'')
Weight	76 Kg. (170 pounds)
Body mass index	27
Blood pressure	120/70 mm. Hg.
Heart rate	76 beats per minute
Respiratory rate	18 breaths per minute
Temperature	36.5º C

The patient is a well developed and well nourished Caucasian male, without acute exhaustion.

Physical Examination- Preferential.

Tender abdomen, slight pain upon superficial and deep contact in right superior quadrant. The spleen and liver can't be palpated.

Further Clinical Examination.

Tattoos on right arm and chest, with mild erythema on chest possibly due to sun exposure.

Equal pupils, reactive to light, with mild conjunctival icterus. Pinkish and moist oral mucus. Normal tympanic membranes. No erythema.

Flexible neck, no jugular ingurgitation.
No adenopathies in cervix, axilla and inguinal regions. He shows mild gynecomastia in chest.

RESPIRATORY.- clear lungs upon auscultation. No abnormal noises, rhonchi or wheezing.

CARDIOVASCULAR.- regular rate and rhythm, regular sounds, no acceleration.

EXTREMITIES.- no deformities, cyanosis or edema, no bruises.

NEUROPSYCHIATRIC.- no motor sensory deficiency.
Craneal nerves from II to XII are intact.
The patient is alert and well oriented.

IV.- Other Data:

Negative chest X rays.

6/13/01 LIVER BIOPSY.- periportal inflammation with necrosis grade 4, moderate intralobular degeneration grade 3, significant portal inflammation grade 4, compatible with moderate fibrosis.

3/7/01 Viral Count 545,000 c/UI

12/4/01 Viral Count <600,000

4/5/03	GOT (AST)	19U/L
	GPT(ALT)	27U/L

Clinic History 6

Date: 16-05-2004

I.- Personal Information:

Name_____ **Susan White – CONTROL PATIENT**
Date of birth _____ November 10, 1945
Age_____ 58
Place of birth_____ Martella – Canada
Address_____ 1373 – 8 Martella Rd. Ladysmith B.C. V 9 G
Telephone number_____ 250-245-7654
Marital Status_____ divorced
Occupation_____ nursing assistant

II Medical Record:

1.- Family Medical Record:

Father with congestive heart disease and Diabetes Mellitus.
Mother with non-specified liver disease.
Brother with non-specified cancer.

2.- Personal Pathological Record:

Gastric ulcers
Non-specified fractures
Thyroid disorders (hipotiroidismo)
Rheumathoid arthritis
Pneumonia in 2004
Hepatorenal syndrome
Appendectomy in 1964
Hysterectomy in 1972

3.- Hepatitis C Record:

Estimated date of contact_____ 1962
Reason of exposure_____ blood transfusion

4.- Allergy Record:

Medicaments_____ she doesn't report any
Food_____ she doesn't report any
Other_____ she doesn't report any

5.- Harmful Habits Record:

Tobacco_____quit 2 years ago
Marihuana_____no
Alcohol _____no
Coffee_____no
Drugs_____antidepressants daily

6.- Treatment Record:

She used Pegasys - Interferon from July 2002 until January 2003
She used Rivavirin in combination with treatment above
Cured of Hepatitis B and C but has severe cirrhosis
Folic acid 5mg. daily
Raberazole 10 mg.
Wellbutrin 150 mg. daily
Espironolactone 40 mg daily
Furosemine 40 mg daily
Conjugated estrogens 80 mg daily
Atrovent 4 puff per day
QVAR 2 puff per day
Salbutamol 2 puff per day
Tylenol for pain

III.- Present Disease:

Duration of disease_____ 30 years
Onset_____ insidious
Course_____ progressive

Signs and Symptoms

Symptoms: feeling of general discomfort, exhaustion, severe fatigue, extreme weakness, depression. Muscular pain, arthralgia, chronic back pain, difficulty to sleep, digestive problems such as chronic abdominal discomfort, heartburn and nausea.

Signs: Mild conjuctival jaundice
Edema in lower extremities
Ecchymosis and petechies in body

Physical Examination:

Height	1.72 m. (5'3´´)
Weight	80 Kg. (177 pounds)
Body mass index	30.5
Blood pressure	114/80 mm. Hg.
Heart rate	104 beats per minute
Respiratory rate	18 breaths per minute
Temperature	36.5º C

Patient with low energy, extreme fatigue, no fever or shivering.

Physical Examination- Preferential.

Tenderness in abdomen, with mild sensitivity in right superior quandrant. Normal intestinal sounds. Spleen and liver cannot be palpated.

Further Clinical Examination.

Normal ears, nose and throat. Equal pupils, reactive to light, with mild conjunctival icterus. Pinkish and moist oral mucus. Pinkish and moist oral mucus with sublingual varicose veins. Facial angioma.

Flexible neck, no jugular ingurgitation. No adenopathies in cervix, axilla and inguinal regions. She shows mild gynecomastia in chest.

RESPIRATORY.- clear lungs upon auscultation. No abnormal noises, rhonchi or wheezing.

CARDIOVASCULAR.- regular rate and rhythm, regular sounds, no acceleration.

EXTREMITIES.- marked edema found within 10 cm under tibia. Presence of circular bruise with a 2.8 cm de diameter in calf. Good irrigation, intact pulses.

NEUROPSYCHIATRIC.- no motor sensory deficiency.
Craneal nerves from II to XII are intact.
Difficulty to concentrate.

IV.- Other Data:

8/3/99 LIVER BIOPSY.- fibrous bands, with moderate chronic inflammatory infiltrations, normal iron deposits, ludwing's criteria, portal inflammation 3, lobular inflammation 2, fibrosis 4, cirrhosis stadium.

3/31/04	Platelet	134,000 mm^3
	Total bilirubin	65 mol/ L
	GOT (AST)	321 U/L
	GPT (ALT)	49 U/L

4/21/04 Bilirubin 37 Umol/L
GALLBLADDER X RAY.- Gallstone.

Clinic History 7

Date: 16-05-2004

I.- Personal Information:

Name_____ **Susan Fetterroll**
Date of birth _____ August 22, 1957
Age_____ 46
Place of birth_____ New Jersey – USA
Address_____ 2692 Hayes Ropad. Shuy Lerville, NJ 12871
Telephone number_____ 518-695-5659
Marital Status_____single
Occupation_____gardener and elder caregiver

II Medical Record:

1.- Family Medical Record:

Mother died at 69 of unknown causes
Ignores information about fahter

2.- Personal Pathological Record:

Vocal cord surgery in 1992
Tubal ligation in 1988
Extirpation of benign breast tumor in 1990
She reports history of phlebitis and eczema

3.- Hepatitis C Record:

Estimated date of contact_____she doesn't report
Reason of exposure_____possibly due to the use of drugs

4.- Allergy Record:

Medicaments_____she doesn't report any
Food_____she doesn't report any
Other_____she doesn't report any

5.- Harmful Habits Record:

Tobacco_____no
Drugs _____all kinds
Alcohol _____yes
Coffee_____no
Medicine_____Xanax 0.25 mg Lexapro 10 mg

6.- Treatment Record:

She doesn't report treatment for hepatitis.

III.- Present Disease:

Duration of disease_____ 1 year
Onset_____ insidious
Course_____ progressive

Signs and Symptoms

Symptoms: fatigue, nasal congestion, general pain, depression, sleep alteration, heartburn, articular pain, general myalgia and anxiety.

Signs: no signs have been observed.

Physical Examination:

Height_____ 1.72 m. (5'4'')
Weight_____ 88 Kg. (193 pounds)
Body mass index_____ 43
Blood pressure_____ 134/84 mm. Hg.
Heart rate_____ 88 beats per minute
Respiratory rate_____ 16 breaths per minute
Temperature_____ 36.5º C

The patient is a well developed and well nourished Caucasian female that does not present exhaustion.

Physical Examination- Preferential.

Tenderness in abdomen, with mild sensitivity in right superior quandrant. Normal intestinal sounds. No hernia. Normal liver and spleen size.

Further Clinical Examination.

Warm, dry skin with mild angioma. No rashes or lesions.

Normal ears, nose and throat. Equal pupils, reactive to light, clear, white sclerotic. Normal tympanic membranes. Pinkish and moist oral mucus.

Flexible neck, no jugular ingurgitation. No adenopathies in cervix, axilla and inguinal regions. She shows mild gynecomastia in chest.

RESPIRATORY.- clear lungs upon auscultation, no rhonchi or wheezing.

CARDIOVASCULAR.- regular rate and rhythm, regular sounds, no acceleration or abnormal noises.

EXTREMITIES.- no deformities, cyanosis or edema, no bruises.

NEUROPSYCHIATRIC.- no motor sensory deficiency.
Craneal nerves from II to XII are intact.
The patient is alert and well oriented.

IV.- Other Data:

Negative chest X rays.

1/8/04	Viral load	33, 600,000 UI/ml
	GOT (AST)	321 U/L
	GPT (ASP)	79 U/L
	Total bilirubin	1 mg/dl
	AFP	3, 4 ng/ml
	Creatinine	0.7 mg/dl

Clinic History 8

Date: 16-05-2004

I.- Personal Information:

Name_____ **Susan Doyle**
Date of birth _____ September 26, 1956
Age_____ 47
Place of birth_____ Belmont - Canada
Address_____ 2712 Belmont Av. Victoria B.C.
Telephone number_____ 250-595-9944
Marital Status_____single
Occupation_____rehabilitation therapist

II Medical Record:

1.- Family Medical Record:

Doesn't know info about father
Mother with arthritis and thyroid disease

2.-Personal Pathological Record:

Rheumatic fever at 11
Vertebral fracture in 1996
Hypothyroidism
Extirpation of ovarian cyst
Gallbladder surgery in 1979

3.- Hepatitis C Record:

Estimated date of contact_____1979
Reason of exposure_____surgery

4.- Allergy Record:

Medicaments_____sulfas
Food_____she doesn't report any
Other_____she doesn't report any

5.- Harmful Habits Record:

Tobacco_____quit 6 years ago
Marihuana_____yes
Alcohol _____twice a week
Coffee_____yes
Drugs____ _____she doesn't report any

6.- Treatment Record:

She doesn't report treatment for hepatitis.

III.- Present Disease:

Duration of disease_____ 5 years
Onset_____ insidious
Course_____ progressive

Signs and Symptoms

Symptoms: general discomfort, exhaustion, lack of concentration, difficulty to sleep, irritability and depression. Digestive alterations, nausea in the morning, semi-liquid stools, muscular pain and arthralgia, headaches.

Signs: no signs have been observed.

Physical Examination:

Height_____ 1.60 m (5'1'')
Weight_____ 50 Kg. (110 pounds)
Body mass index_____ 21
Blood pressure_____ 114/74 mm. Hg.
Heart rate_____ 72 beats per minute
Respiratory rate_____ 16 breaths per minute
Temperature_____ 36.5º C

The patient is a well developed and well nourished Caucasian female that does not present exhaustion.

Physical Examination- Preferential.

Sensitivity in right superior and left inferior quandrans. No visceromegaly.

Further Clinical Examination.

Warm, dry, non-turgid skin.

Normal ears, nose and throat. Equal pupils, reactive to light, clear sclerotic. Pinkish and moist oral mucus with mild sublingual varicose veins. Normal oropharynx.

Flexible neck, no jugular ingurgitation. No adenopathies in cervix, axilla and inguinal regions. She shows mild gynecomastia in chest.

RESPIRATORY.- clear lungs upon auscultation, no rhonchi or wheezing.

CARDIOVASCULAR.- regular rate and rhythm, regular sounds, no acceleration or abnormal noises.

EXTREMITIES.- no deformities, cyanosis or edema, no bruises.

NEUROPSYCHIATRIC.- no motor sensory deficiency.
Craneal nerves from II to XII are intact.
The patient is alert and well oriented.

IV.- Other Data:

Negative chest X rays.

8/6/99 LIVER BIOPSY.- chronic hepatitis, with activity grade 1 to 2, fibrosis grade 1 to 2. No coloration due to iron.

4/1/04	Negative serologic hepatitis A and B	
	GOT (AST)	321 U/L
	GPT (ASL)	57U/L
	Total bilirubin	5 Mol/L

Clinic History 9

Date: 16-05-2004

I.- Personal Information:

Name_____ **Geraldine Hutchings**
Date of birth _____ June 19, 1947
Age_____ 56
Place of birth_____ Vancouver - Canada
Address_____ 1313-1030 Burnaby St. Vancouver B.C. VGE
Telephone number_____ 604-632-9699
Marital Status_____divorced
Occupation_____transportation worker

II Medical Record:

1.- Family Medical Record:

Mother with hypertension
Brother with liver disease

2.- Personal Pathological Record:

Scarlet fever
Repetitive urinary infections
Traffic accident 30 years ago

3.- Hepatitis C Record:

Estimated date of contact_____30 years
Reason of exposure_____use of needles

4.- Allergy Record:

Medicaments_____she doesn't report any
Food_____she doesn't report any
Other_____she doesn't report any

5.- Harmful Habits Record:

Tobacco_____no
Marihuana_____yes
Alcohol _____yes
Coffee_____no
Drugs_____she doesn't report any

6.- Treatment Record:

She reports Interferon for 1 month and Pegasys.
Progestagens, antidepressants

III.- Present Disease:

Duration of disease_____ 5 years
Onset_____ insidious
Course_____ progresivo

Signs and Symptoms

Symptoms: articular general pain, moderate fatigue, chronic liquid stools, loss of shor-term memory, back pain, weakness and depression.

Signs: no signs have been observed.

Physical Examination:

Height_____ 1.80 m (6'0´´)
Weight_____ 65 Kg. (142 pounds)
Body mass index_____ 24
Blood pressure_____ 136/80 mm. Hg.
Heart rate_____ 78 beats per minute
Respiratory rate_____ 14 breaths per minute
Temperature_____ 36.5º C

The patient is a well developed and well nourished Caucasian female that does not present exhaustion.

Physical Examination- Preferential.

Tender abdomen suave, so sensitivity.
No visceromegaly. Positive intestinal sounds.

Further Clinical Examination.

Warm, dry, turgid skin.

Normal ears, nose and throat. Equal pupils, reactive to light, clear sclerotic, no jaundice, slightly injected. Clear tympanic membranes. Pinkish and moist oral mucus. Normal oropharynx.

Flexible neck, no jugular ingurgitation. No adenopathies in cervix, axilla and inguinal regions. She shows mild gynecomastia in chest.

RESPIRATORY.- clear lungs upon auscultation, no rhonchi or wheezing or other noises.

CARDIOVASCULAR.- regular rate and rhythm, regular sounds, no acceleration.

EXTREMITIES.- no deformities, cyanosis or edema, no bruises.

NEUROPSYCHIATRIC.- no motor sensory deficiency.
Craneal nerves from II to XII are intact.
The patient is alert and well oriented.

IV.- Other Data:

20/03/ 2004

GOT (AST)	321 U/L
GPT (ALT)	46 U/L

1/20/04

Viral load	444,023 copies/ml

19 /07/2001 LIVER BIOPSY.- macrovesicular steatosis with mild non-specific portal and lobular inflammation. No fibrosis, cirrhosis or negative iron staining.

Clinic History 10

Date: 16-05-2004

I.- Personal Information:

Name_____ **Linda Stockert**
Date of birth _____ December 28, 1950
Age_____ 53
Place of birth_____ Vancouver - Canada
Address_____ 115-2200 Highbury Street Vancouver. B.C.
Telephone number_____ 604-876-7487
Marital Status_____single
Occupation_____sales representative

II Medical Record:

1.- Family Medical Record:

Father with hypertension and Gillian Barre Syndrome
Mother with arterial hypertension.

2.- Personal Pathological Record:

Sexually transmitted disease
Curettage in 1988
Uterine neck biopsy in 1974
Extirpation of benign urethral polyp in 1980
Breast surgery in 1981and 1999
Total abdominal hysterectomy in 2000

3.- Hepatitis C Record:

Estimated date of contact_____1971
Reason of exposure_____surgery

4.- Allergy Record:

Medicaments_____sulfas and andanesthetics
Food_____dairy products and eggs
Other_____dust, dog hair

5.- Harmful Habits Record:

Tobacco_____no
Marihuana_____no
Alcohol _____no
Coffee_____no
Drugs_____she doesn't report any

6.- Treatment Record:

Korean herbs in 2000

III.- Present Disease:

Duration of disease_____ 12 years
Onset_____ insidious
Course_____ progressive

Signs and Symptoms

Symptoms: fatigue, abdominal pain, heartburn, bloating after eating with gas production and painful discomfort in right superior quadrant of abdomen. Back, neck and articular pain. General pain, rigidity, headaches, weakness and difficulty to think clearly.

Signs: no signs have been observed.

Physical Examination:

Height_____ 1.72 m (5'9'')
Weight_____ 62 Kg. (140 pounds)
Body mass index_____ 21
Blood pressure_____ 118/80 mm. Hg.
Heart rate_____ 84 beats per minute
Respiratory rate_____ 16 breaths per minute
Temperature_____ 36.5º C

The patient is a well developed and well nourished Caucasian female that does not present acute exhaustion.

Physical Examination- Preferential.

Tenderness in abdomen, with mild epigastric sensitivity in right superior quandrant. No visceromegaly. Normal intestinal sounds.

Further Clinical Examination.

Warm, dry, turgid skin.

Normal ears, nose and throat. . Equal pupils, reactive to light, clear sclerotic, no jaundice, slightly injected. Clear tympanic membranes. Pinkish and moist oral mucus. Normal oropharynx.

Flexible neck, no jugular ingurgitation. No adenopathies in cervix, axilla and inguinal regions. She shows mild gynecomastia in chest.

RESPIRATORY.- clear lungs upon auscultation, no rhonchi or wheezing or other noises.

CARDIOVASCULAR.- regular rate and rhythm, regular sounds.

EXTREMITIES.- no deformities, cyanosis or edema, no bruises.

NEUROPSYCHIATRIC.- no motor sensory deficiency.
Craneal nerves from II to XII are intact.
The patient is alert and well oriented.

IV.- Other Data:

Negative chest X rays.

12/4/00 LIVER BIOPSY.- slightly active chronic hepatitis C, no cirrhosis. No iron staining.

4/1/04 Negative serologic hepatitis A and B

3/26/04	GOT (AST)	107 U/L
	GPT (ALT)	35 U/L
	Viral load	63,700 copies/ml

EVALUATION OF CLINIC HISTORIES

1. DEFINITION OF TERMS

2. RESULTS

Definition of symptoms

To evaluate and tabulate the discomforts presented by patients, expressed in different manners, we made two lists of symptoms : general and gastrointestinal. We also made a group of signs related to chronic hepatitis found in the clinical examinations of patients. They are cited below:

General symptoms:

1.- General discomfort.- expressed as upset feeling, feeling uncomfortable or feeling of being sick.

2.- Severe fatigue.- expressed as feeling of exhaustion, difficulty to walk or climb stairs, feeling of weakness.

3.- Lack of concentration.- expressed as difficulty to carry out work, feeling light headed, feeling of decreased abilities.

4.- Sleep disorders.- expressed as difficulty to fall asleep, awaken in the middle of the night, interrupted sleep, having to sleep some hours during the afternoon.

5.- Depression.- expressed as feeling diminished, discouraged, depressed almost all the time.

6.- Articular pain.- expressed as pain in articulations, with or without movement, erratic and of varied intensity.

7.- Muscular pain.- expressed as general pain in different muscular masses along the body.

8.- Headaches.- expressed as cephalalgia and dizziness.

Gastrointestinal symptoms:

1.- Indigestion.- expressed as abdominal discomfort and heartburn.

2.- Dyspepsia.- expressed as feeling full, abdominal bloating, slow digestion or failure to digest food.

3.- Nausea.-expressed as feeling nauseous.

4.- Abdominal pain.- in relation to food or not.

5.- Intestinal dysfunction.- expressed as presence of semi-liquid stools, occasional diarrhea or constipation.

A summary of the 10 clinic histories allows us to establish a table of symptoms and signs that were present in patients in relation to Chronic hepatitis, and that we classified as follows:

General symptoms: general discomfort, severe fatigue, lack of concentration, sleep disorders, depression, articular pain, muscular pain and headache.

Gastrointestinal: indigestion with heartburn, dyspepsia with abdominal bloating, nausea, abdominal pain and intestinal dysfunction.

Signs: jaundice, ascites, collateral circulation, pain upon palpation, palpable spleen, presence of ecchymosis and edema in lower extremities.

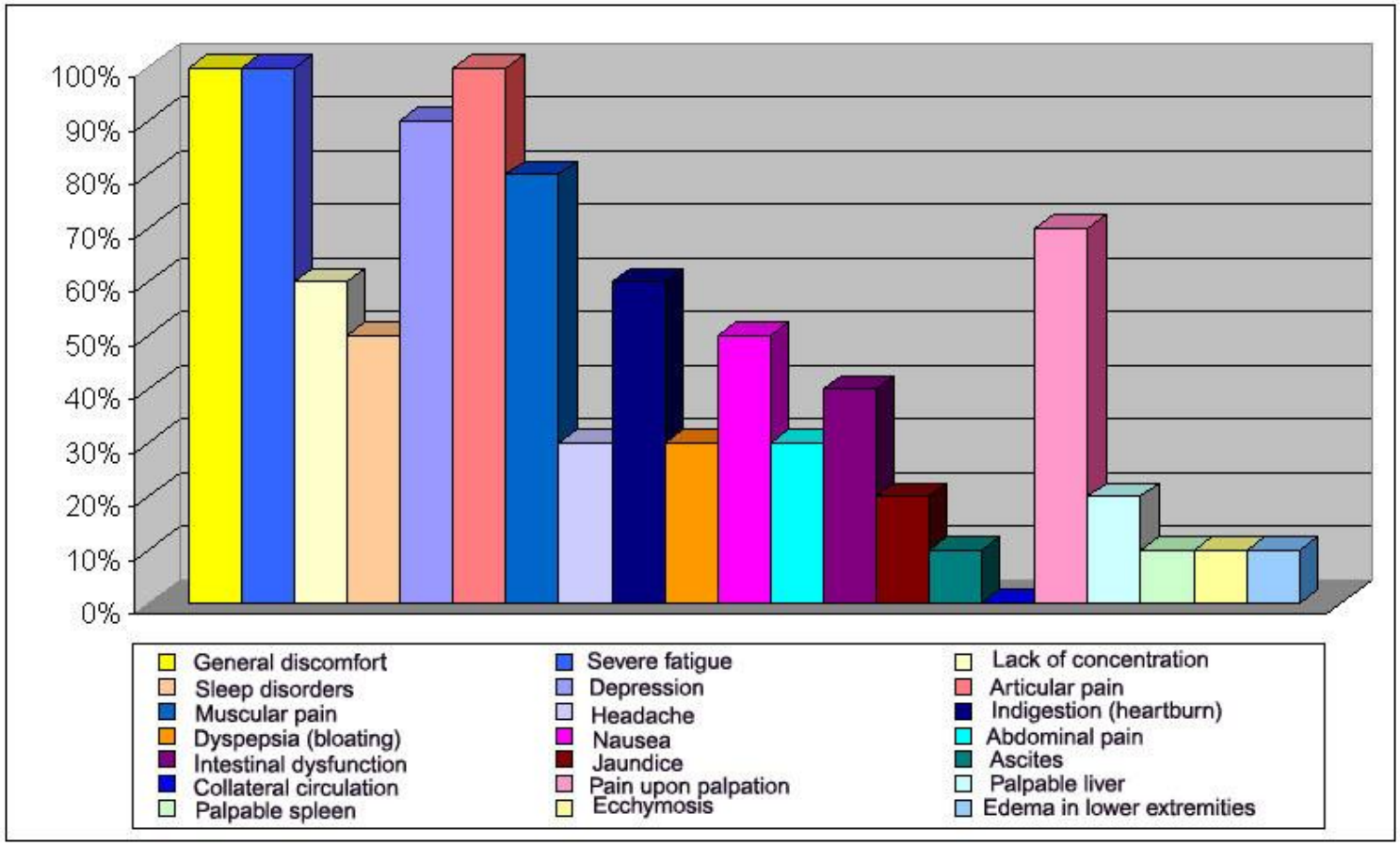
The results are shown in **Table 12 and Figure 1.**

Table 12
Chronic Hepatitis C (HCV)
Symptoms and signs

Síntomas	Stad, R.	Troy, S.	O'Connor	Langen	Charron	White	Fetterroll	Doyle	Hutchines	Stockert	
I) General											
1.- General discomfort	+	+	+	+	+	+	+	+	+	+	**100%**
2.- Severe fatigue	+	+	+	+	+	+	+	+	+	+	**100%**
3.- Lack of concentration	-	+	-	-	+	+	-	+	+	+	**60%**
4.- Sleep disorder	+	-	-	-	+	+	+	+	-	-	**50%**
5.- Depression	+	+	+	+	+	+	+	+	+	-	**90%**
6.- Articular pain	+	+	+	+	+	+	+	+	+	+	**100%**
7.- Muscular pain	+	-	+	+	+	+	+	+	-	+	**80%**
8.- Headache	-	-	+	-	-	-	-	+	-	+	**30%**
II) Gastrointestinal											
1.- Indigestion (heartburn)	-	+	+	+	+	+	+	-	-	-	**60%**
2.- Dyspepsia (bloating)	-	-	-	-	+	+	-	-	-	+	**30%**
3.- Nausea	-	+	+	-	+	+	-	+	-	-	**50%**
4.- Abdominal pain	-	+	-	+	+	-	-	-	-	+	**30%**
5.- Intestinal dysfunction	-	-	-	+	+	+	-	+	+	-	**40%**
Signs											
1.- Jaundice	+	-	-	-	-	+	-	-	-	-	**20%**
2.- Ascites	-	-	-	-	-	+	-	-	-	-	**10%**
3.- Collateral circulation	-	-	-	-	-	-	-	-	-	-	**0%**
4.- Pain upon palpation	-	+	-	+	+	+	+	+	-	+	**70%**
5.- Palpable liver	+	-	-	+	-	-	-	-	-	-	**20%**
6.- Palpable spleen	-	-	-	+	-	-	-	-	-	-	**10%**
7.- Ecchymosis	-	-	-	-	-	+	-	-	-	-	**10%**
8.- Edema in lower extremities	-	-	-	-	-	+	-	-	-	-	**10%**

Source: Dr. José Cabanillas & Colleagues
Lima – Peru

Figure 01
Chronic Hepatitis C (HCV)
Symptoms and Signs:

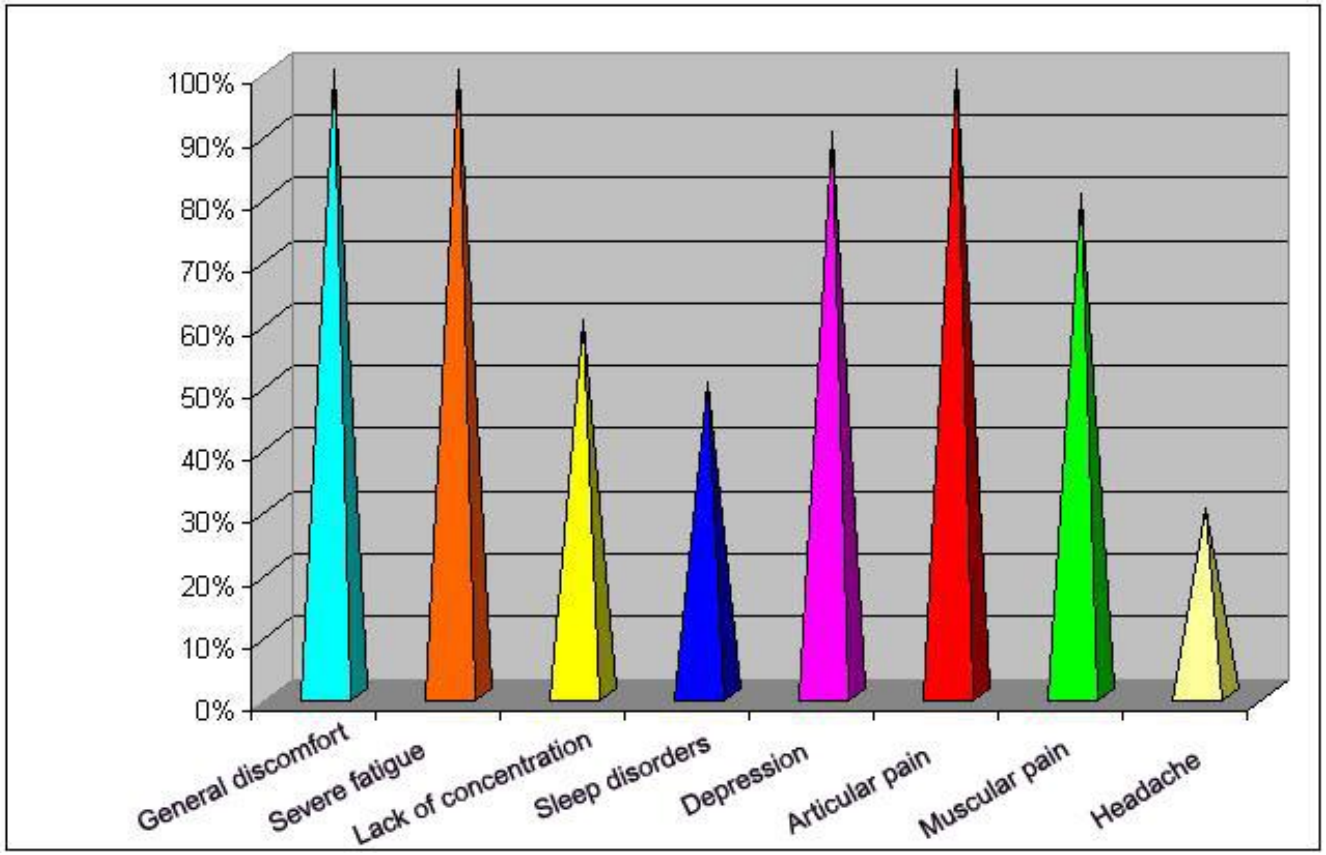


Source: Dr. José Cabanillas & Colleagues
Lima – Peru

The study of clinical histories allows us to establish that in the **general symptoms** group; a feeling of general discomfort, of fatigue, and osteoarticular pain was present in all ten patients, what constitutes 100%; depression was present in 90%; muscular pain attained a frequency of 80%; while lack of concentration and sleep problems were present in 60 and 50% respectively; and headache attained 30%.

See Table 12 and Figure 02

Figure 02
Chronic Hepatitis C (HCV)
General symptoms:

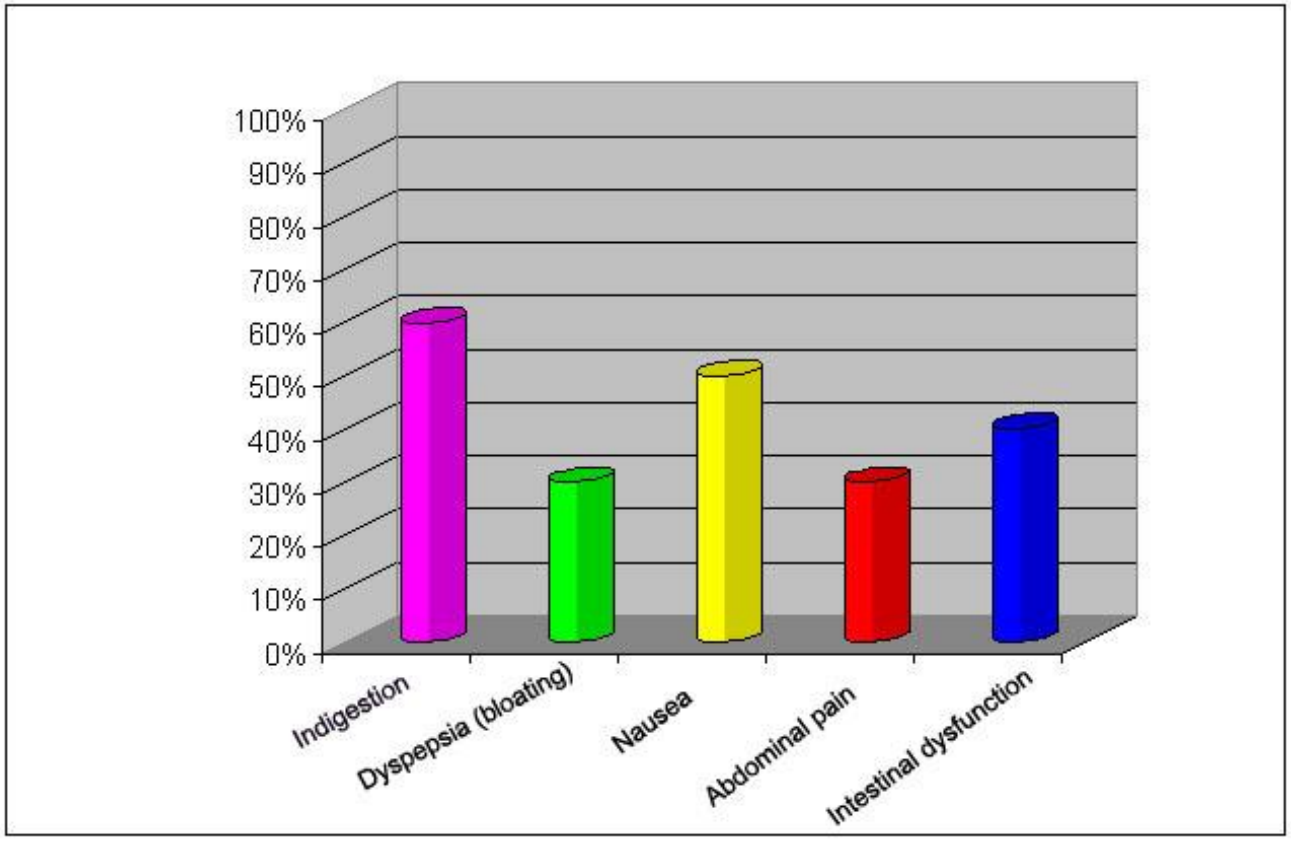


Source: Dr. José Cabanillas & Colleagues
Lima – Peru

In the group of **gastro-intestinal symptoms**: indigestion, referred to as abdominal discomfort and/or heartburn was present in 60% of the cases; nausea was present in 50%, intestinal dysfunction attained 40%; while dyspepsia, stomach bloating and abdominal pain were present in 30% of the cases.

See Table 12 and Figure 3

Figure 3
Chronic Hepatitis C (HCV)
Gastrointestinal symptoms:

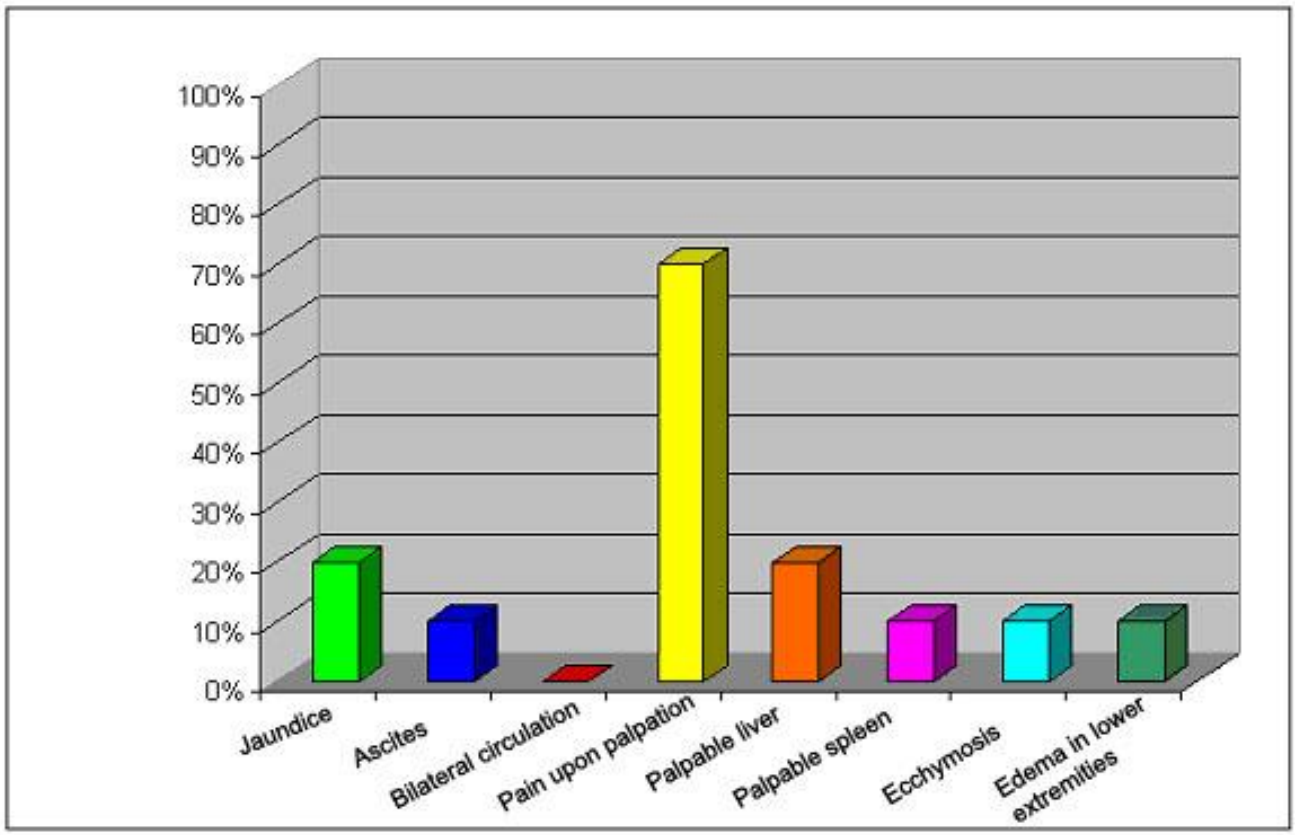


Source: Dr. José Cabanillas & Colleagues
Lima – Peru

In the clinical findings collected through clinical examination, the most frequent **sign** were abdominal pain, palpitation primarily at the level of the right hypochondrio and epigastrium, which was present in 70% of the cases; jaundice and palpable liver were found in 20%; while the presence of ascites, palpable spleen, ecchymosis, and edema in lower extremities were present in only one case representing 10%; no patient showed collateral circulation, 0%.

See Table 12 and Figure 4

Figure 04
Chronic Hepatitis C (HCV)
Signs



Source: Dr. José Cabanillas & Colleagues
Lima – Peru

Diagnosis

The assessment of the clinical records, as well as the information obtained with the HCV Fibrosure, the ultrasounds and the laboratory analysis, allowed us to establish the diagnosis and stadium of each patient.

Stad, Raymond

Chronic Hepatitis C (HCV)
Stadium: cirrhosis
Arterial Hypertension
Low platelet count

Smith, Troy

Chronic Hepatitis C (HCV)
Stadium: fibrosis 3
Diabetes mellitus

O'Connor, Patrick

Chronic Hepatitis C (HCV)
Stadium: fibrosis 3

Langen, R. Harry

Chronic Hepatitis C (HCV)
Chronic Hepatitis B
Stadium: fibrosis 2
Low platelet count

Charron, Daniel

Chronic Hepatitis C (HCV)
Stadium: cirrhosis

White, Susan
Control Patient

Cured Hepatitis C
Cured Hepatitis B
Stadium: cirrhosis
Low platelet count
Hepatorenal synd.

Fetterroll, Susan

Chronic Hepatitis C (HCV)
Chronic Hepatitis B
F0 no fibrosis

Doyle, Susan

Chronic Hepatitis C (HCV)
F0 no fibrosis

Hutchines, Geraldine

Chronic Hepatitis C (HCV)
F0 no fibrosis

Stockert, Linda

Chronic Hepatitis C (HCV)
Stadium: cirrhosis

Treatment

All patients underwent treatment with **Active Organic Ingredients: A4+**; 40 ml. orally, three times a day for 28 days, that was complemented with phototherapy by exposure of chest, arms and legs to sun rays during some hours a day.

There was no controlled diet; fat intake was low but there was no quantity restriction; different fruits were administered. Alcohol intake was not permitted.

Carbohydrate or salt intake was restricted for those patients that also suffer from other pathologies (diabetes mellitus, arterial hypertension) who also received regular treatment for their pathologies.

Patients that were taking other drugs, such as sedatives or tranquilizers, did not discontinue their previous treatment.

Evolution

After **14 days**, the clinical symptomatology of patients was controlled and they underwent biochemical analysis; a new evaluation was performed after **28 days**. It included the clinical examination, evolution of symptomatology, ultrasound control and laboratory tests, to be compared to those performed at the beginning of the study.

We will now present the results obtained in the control evaluation 28 after the **ULTRASOUND**, which are: in **six cases** a **favorable** evolution shown by a lower increase of diffuse Echogenicity in comparison with the first evaluation or a decrease in liver and spleen size; in **three cases** the ultrasound showed **stable** sings when compared to the first evaluation and in **one case**, the evolution was **unfavorable** with an increase of **Echogenicity** and an increase in volume of liquid of ascites. **Table 13**

Table 13
Chronic Hepatitis C (HCV)
Three-dimensional ultrasound (control after 28 days)

	Stad, Raymond	Smith, Troy	O'Connor, Patrick	Langen, Ron Harry	Charron, Daniel
	Favorable Evol.	**Stable Evol.**	**Stable Evol.**	**Stable Evol.**	**Stable Evol.**
Decrease	Echogenicity	Remained the same	Remained the same	Remained the same	Echogenicity
Liver	Hepatomegaly	Hepatomegaly	normal	Hepatomegaly	Hepatomegaly
Left lobe size	165 mm.	153 – 156 mm.	138 mm.	168 mm.	151-153 mm.
Right lobe size	114 – 116 mm.	103 – 116 mm.	92 mm.	121 mm.	113-122 mm.
Borders	Regular	Regular	Regular	Regular	Regular
Diffuse echogenicity	Slight Increase	Moderate Increase	Moderate Increase	Moderate Increase	Moderate Increase
Types of echos	Low-amplitude	High-amplitude	Medium-amplitude	Medium-amplitude	Medium-amplitude
Focal Injuries	no signs observed.	no signs observed.	no signs observed.	no signs observed.	no signs observed.
Portal vein	Normal Appearance	Brillo en pared portal	Normal	Hipertensión portal	Normal
Measurements	12mm.	11 – 13 mm.	12-13 mm.	16 mm.	13 mm.
Spleen	Splenomegaly	Splenomegaly	Normal	Splenomegaly	Normal
Measurements	132 x 66 mm.	157 x 81 mm.	92 x 41mm.	135 x 45 mm.	91 x 45 mm.
Splenic vein	8 mm.	8 mm.		4 mm.	
Ascites	Not present	Not present	Not present	Not present	Not present

Source: Dr. José Cabanillas & Colleagues
Lima – Peru

Favorable evolution was pointed as a **decrease of the increase of echogenicity**, that the liver presented in the first control or a **decrease in hepatic volume**.

Table 13 (Cont.)
Chronic Hepatitis C (HCV)
Three-dimensional ultrasound (control after 28 days)

	White, Susan	Fetterroll, Susan	Doyle, Susan	Hutchines, Geraldine	Stockert, Linda
	Evoluc. Desfavorable	**Favorable Evol.**	**Favorable Evol.**	**Favorable Evol.**	**Favorable Evol.**
Decrease	Increase ascites	Echogenicity	Liver volume	Echogenicity	Echogenicity
Liver	Decreased	Hepatomegaly	Normal	Normal	Hepatomegaly
Right lobe size	108 mm.	186mm.	133 mm.	130 mm.	146-149 mm.
Left lobe size	83 mm.	142mm.	104 mm.	104 mm.	105-124 mm.
Borders	Regular	Regular	Regular	Regular	Regular
Diffuse echogenicity	High Increase	Slight Increase	Slight Increase	Slight Increase	Moderate Increase
Types of echos	high = cirrhosis	Low-amplitude	Low-amplitude	Low-amplitude	Medium and High
Focal Injuries	no signs observed.	no signs observed.	no signs observed.	no signs observed.	no signs observed.
Portal vein	Hypertension Signs	Hypertension Signs	Normal	Normal	Brillo en pared portal
Measurements	13mm.	11 – 14 mm.	11 mm.	10 mm.	15 mm.
Spleen	Splenomegaly	normal	Normal	Normal	Splenomegaly
Measurements	121 x 51 mm.	106 x 62 mm.	87 x 45mm.	97 x 51 mm.	112 x 58 mm.
Splenic vein					
Ascites	present	Not present	Not present	Not present	Not present

Source: Dr. José Cabanillas & Colleagues
Lima – Peru

Favorable evolution was pointed as a **decrease of the increase of echogenicity**, that the liver presented in the first control or a **decrease in hepatic volume**.

As part of the control of tests to measure **liver synthesis capacity**, determination of **CHOLINESTERASE** was performed after 14 and 28 days; while determination of **PREALBUMIN** and **PROTHROMBIN TIME** was only performed after 28 days of treatment.

Since cholinesterase is a product of the synthesis of hepatic metabolism, an increase of its values can be interpreted as an improvement of the function of the hepatocyte.

When analyzing the values found in the determination of **CHOLINESTERASE** between the **initial and the final controls**, we could observe that in **three cases** there was a **high increase** (between 71.1 and 83.1%), in **two cases** there was a **moderate increase** (between 62.1 and 54.9%), in **four cases** there was a **regular increase** (between 34.0 and 40.0%) and in **one case** the increase was **minimum** (15.7%).

See Table 14 and Figure 5

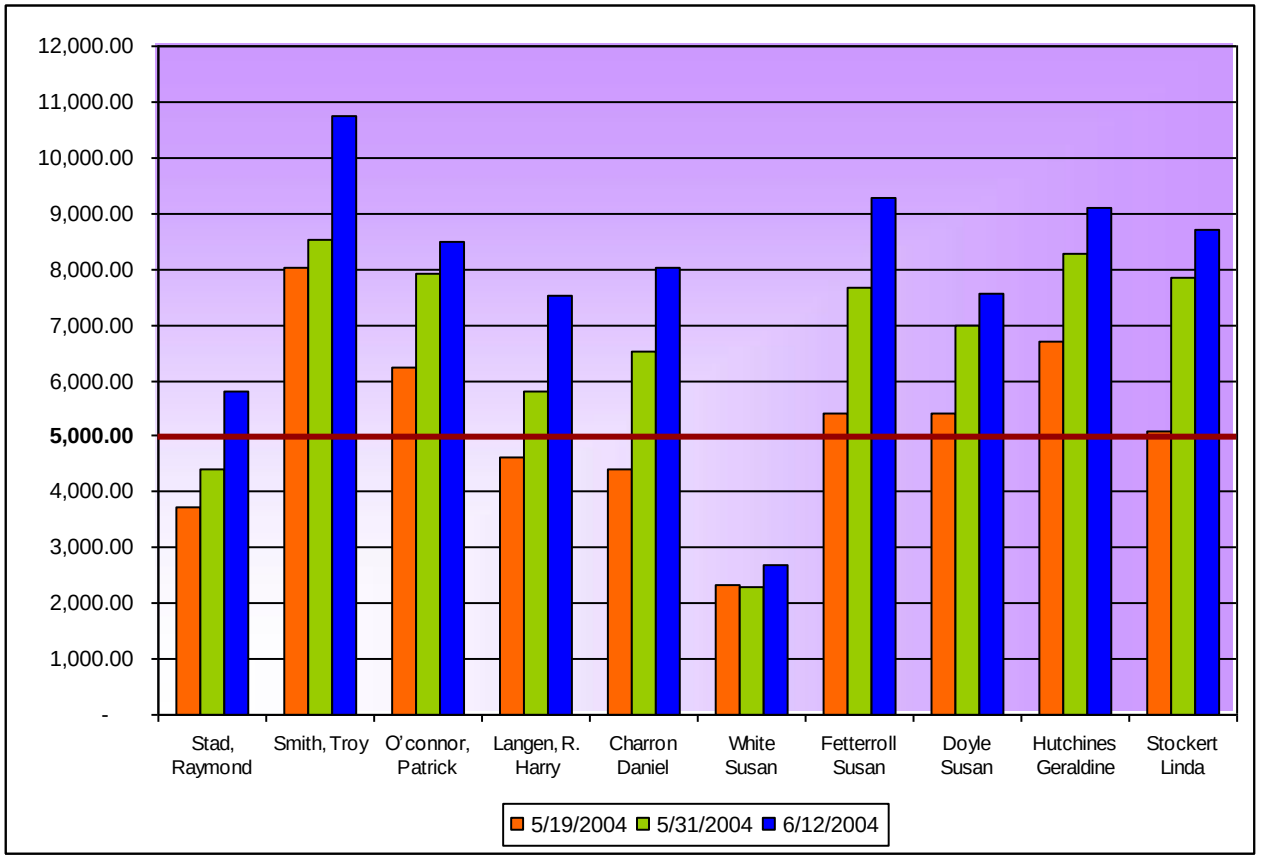
Table 14
Chronic Hepatitis C (HCV)
Evolution of Cholinesterase

	Cholinesterase	Cholinesterase	Cholinesterase	Modification
Date of control	**5/19/04**	**5/31/04**	**6/12/04**	
PATIENTS				
Stad, Raymond	3,742 U/L	4,397 U/L	5,797 U/L	Increase 54.9%
Smith, Troy	8,018 U/L	8,540 U/L	10,749 U/L	Increase 34.0%
O'Connor, Patrick	6,241 U/L	7,905 U/L	8,505 U/L	Increase 36.2%
Langen, R. Harry	4,631 U/L	5,818 U/L	7,507 U/L	Increase 62.1%
Charron, Daniel	4,390 U/L	6,507 U/L	8,039 U/L	Increase 83.1%
White, Susan	GOT (AST) 321 U/L	2,299 U/L	2,687 U/L	Increase 15.7%
Fetterroll, Susan	5,408 U/L	7,673 U/L	9,280 U/L	Increase 71.5%
Doyle, Susan	5,408 U/L	6,973 U/L	7,573 U/L	Increase 40.0%
Hutchines, Geraldine	6,696 U/L	8,284 U/L	9,106 U/L	Increase 35.9%
Stockert, Linda	5,086 U/L	7,828 U/L	8,706 U/L	Increase 71.1%

Source: Dr. José Cabanillas & Colleagues
Lima – Peru

Since **cholinesterase** is a product of the synthesis of hepatic metabolism, an **increase** of its values is interpreted as an improvement of liver function.

Figure 05
Chronic Hepatitis C (HCV)
Evolution of Cholinesterase



Source: Dr. José Cabanillas & Colleagues
Lima – Peru

Since **cholinesterase** is a product of the synthesis of hepatic metabolism, an **increase** of its values is interpreted as an improvement of liver function.

When analyzing the values found in the determination of **PREALBUMIN** between the **initial and the final controls**, we could observe that in **three cases** there was a **significant increase** (between 19.5 and 26.9%), in **four cases** there was a **significant decrease** (between 18.0 and 28.2%) and in **three cases** there were **no significant variations** (between 0.0 and 5.0%).

See Table 15 and Figure 6

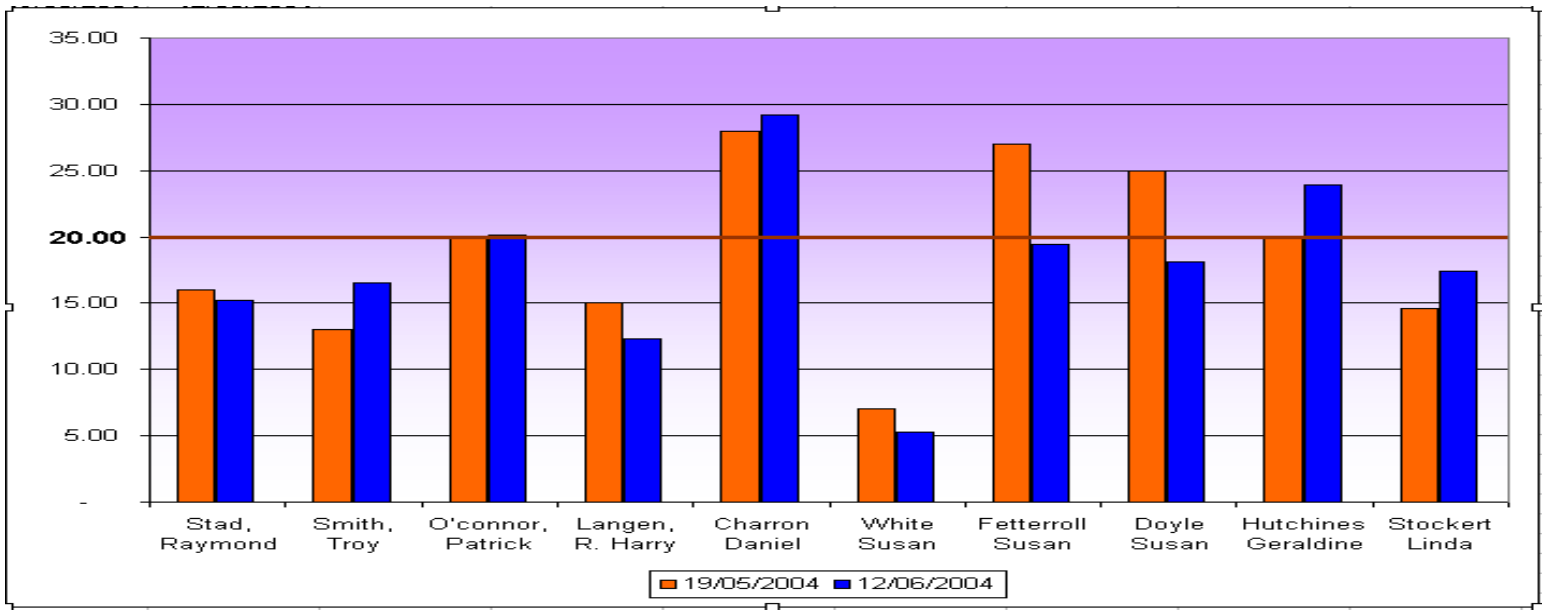
Table 15
Chronic Hepatitis C (HCV)
Evolution of Prealbumin

	Prealbumin	Prealbumin	Modification
Dates of control	**5/19/04**	**6/2/04**	
PATIENTS			
Stad, Raymond	16.0 mgr/dl	15.2 mgr/dl	Decreased 5.0%
Smith, Troy	13.0 mgr/dl	16.5 mgr/dl	Increased 26.9%
O'Connor, Patrick	20.0 mgr/dl	20.1 mgr/dl	No variation 0.0%
Langen, R. Harry	15.0 mgr/dl	12.3 mgr/dl	Decreased 18.0%
Charron, Daniel	28.0 mgr/dl	29.2 mgr/dl	Increased 0.4%
White, Susan	7.0 mgr/dl	5.3 mgr/dl	Decreased 24.7%
Fetterroll, Susan	27.0 mgr/dl	19.4 mgr/dl	Decreased 28.2%
Doyle, Susan	25.0 mgr/dl	18.1 mgr/dl	Decreased 27.6%
Hutchines, Geraldine	20.0 mgr/dl	23.9 mgr/dl	Increased 19.5%
Stockert, Linda	14.6 mgr/dl	17.4 mgr/dl	Increased 24.2%

Source: Dr. José Cabanillas & Colleagues
Lima – Peru

Since **prealbumin** is a product of the synthesis of hepatic metabolism, an **increase** of its values is interpreted as an **improvement of liver function**.

Figure 06
Chronic Hepatitis C (HCV)
Evolution of Prealbumin



Source: Dr. José Cabanillas & Colleagues
Lima - Peru

Since **prealbumin** is a product of the synthesis of hepatic metabolism, an **increase** of its values is interpreted as an **improvement of liver function**.

When analyzing the values found in the determination of **PROTHROMBIN TIME** between the **initial and the final controls**, established through comparison of **PROTHROMBIN CONCENTRATION** percentages, we could observe that in **four cases** there was an increase in a **high percentage** (between 24.8% and 33.3%); in **four cases** there was a **moderate increase** (between 19.2% and 8.8%); in **one case** there was a **decrease** of 9.0%, while in the remaining case there was **no significant variation**, with a decrease of 0.5%. See **Table 16 and Figure 7**

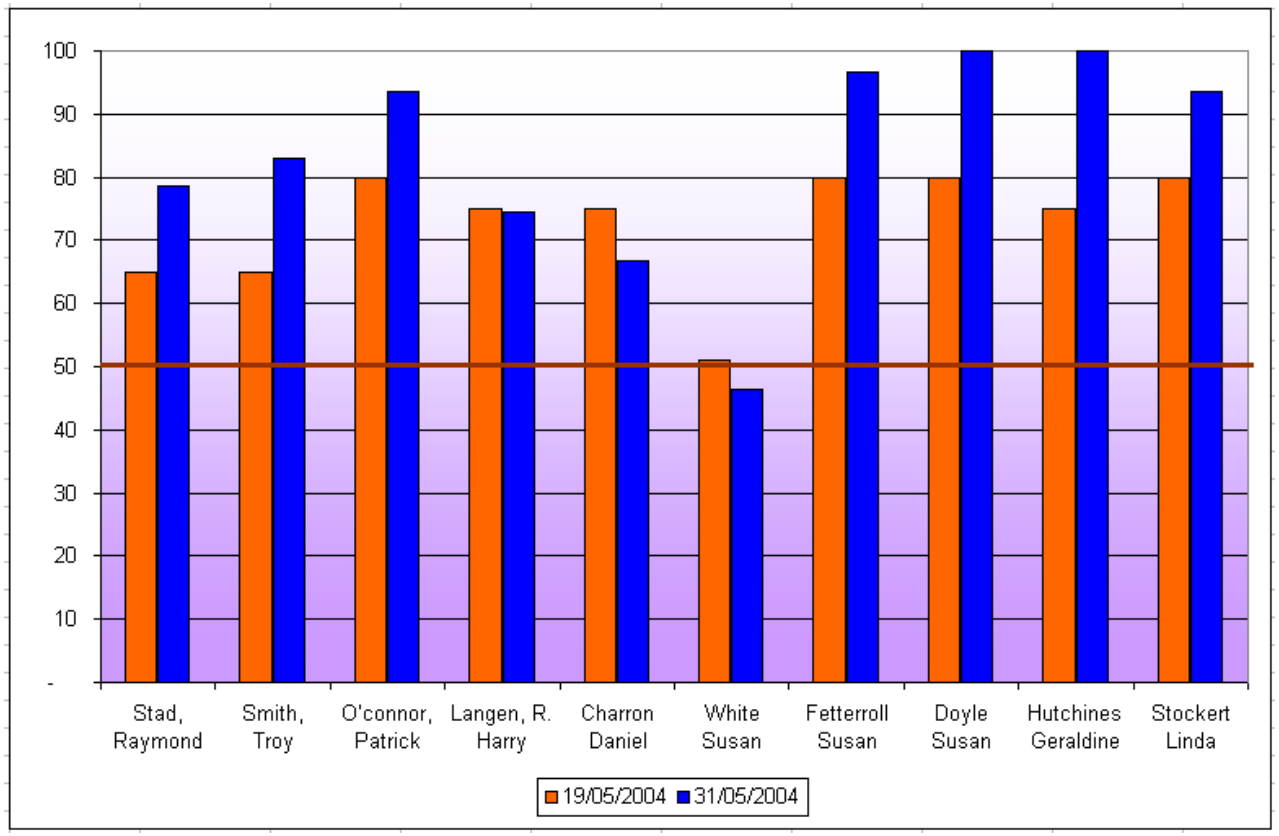
Table 16
Chronic Hepatitis C (HCV)
Evolution of Prothrombin time

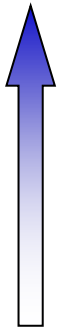
	Prothrombin time	Concentr. of Prothrombin	Prothrombin time	Concentr. of Prothrombin	Modification
Dates of control	**5/19/04**	**5/19/04**	**6/12/04**	**6/12/04**	
PATIENTS					
Stad, Raymond	15.0 seg.	65.0%	13.2 seg.	78.6%	Increased 24.8%
Smith, Troy	15.0 seg.	65.0%	12.8 seg.	83.0%	Increased 27.7%
O'Connor, Patrick	13.0 seg.	80.0%	12.0 seg.	93.6%	Increased 17.0%
Langen, R. Harry	14.0 seg.	75.0%	13.6 seg.	74.6%	Decreased 0.5%
Charron, Daniel	14.0 seg.	75.0%	12.5 seg.	66.7%	Increased 16.0%
White, Susan	18.0 seg.	51.0%	18.4 seg.	46.3%	Decreased 9.0%
Fetterroll, Susan	13.0 seg.	80.0%	11.8 seg.	96.6%	Increased 19.2%
Doyle, Susan	13.0 seg.	80.0%	11.5 seg.	100%	Increased 25.0%
Hutchines, Geraldine	14.0 seg.	75.0%	11.5 seg.	100%	Increased 33.3%
Stockert, Linda	13.0 seg.	80.0%	12.0 seg.	93.6%	Increased 8.8%

Source: Dr. José Cabanillas & Colleagues
Lima – Peru

Since **prothrombin** is a product of the synthesis of hepatic metabolism, an **increase** of its values is interpreted as an **improvement of liver function**.

Figure 07
Chronic Hepatitis C (HCV)
Evolution of Prothombin Concentration





Normal Values

Source: Dr. José Cabanillas & Colleagues
Lima – Peru

Since **prothrombin** is a product of the synthesis of hepatic metabolism, an **increase** of its values is interpreted as an **improvement of liver function**.

As part of the tests conducted to assess **liver structural alterations** caused by fibrosis and hepatocyte degeneration, determination of **BILIRUBIN** and **ALKALINE PHOSPHATASE** was perfomed.

The comparative analysis of bilirubin control between the **beginning and the end** of treatment showed that out of the **four cases** with values above normal, three attained a **decrease** of initial values in 4.6%, 36.9% and 15.4%, while in the remaining case there was an increase of 23.3%. In the other **six cases** values, that were within normal limits, stayed **the same**. See Table 17 and Figure 8

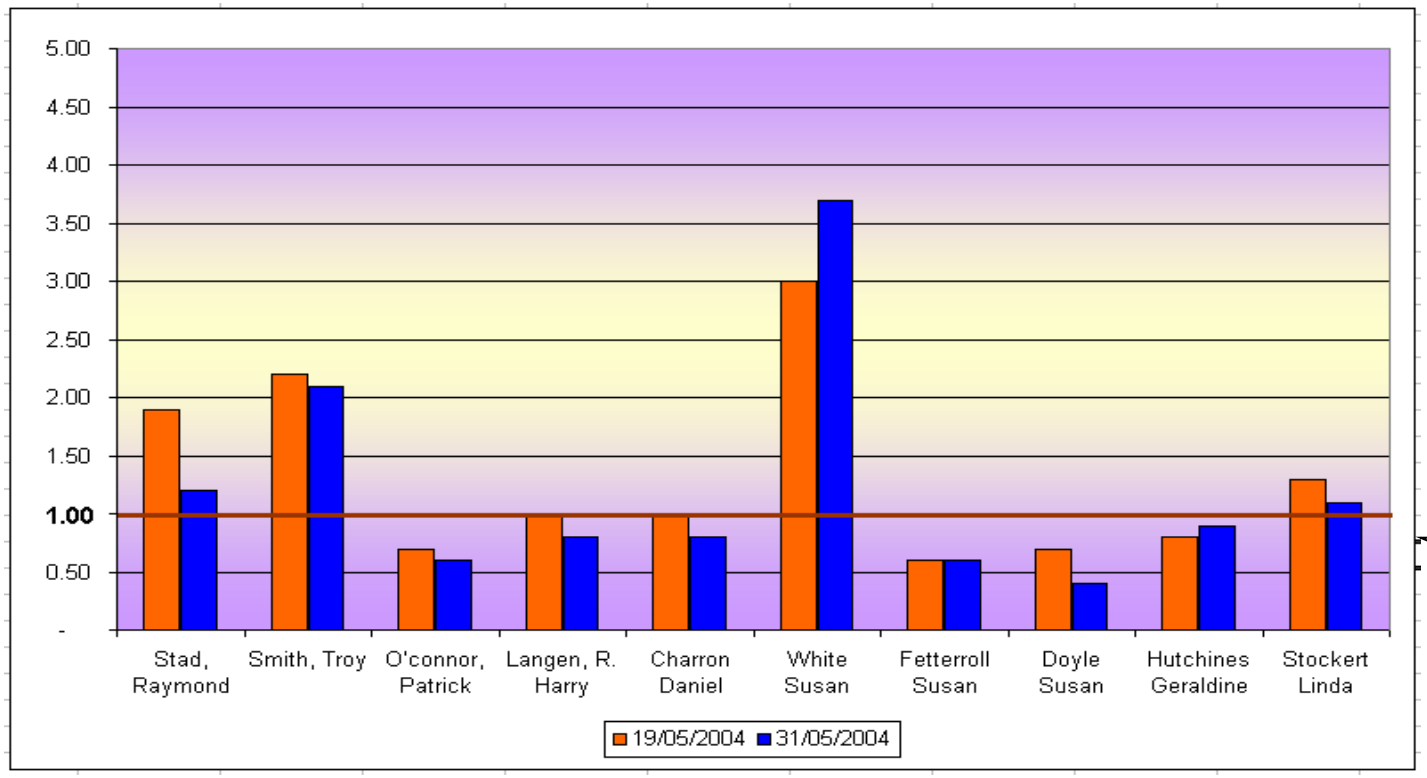
Table 17
Chronic Hepatitis C (HCV)
Evolution of Bilirubin

Bilirubin							
	Total	**Direct**	**Indirect**	**Total**	**Direct**	**Indirect**	**Modifications**
Dates of control	**5/19/04**	**5/19/04**	**5/19/04**	**12/06/2004**	**6/12/04**	**6/12/04**	
PATIENTS							
Stad, Raymond	1.90 mg/dl	0.60 mg/dl	1.30 mg/dl	1.20 mg/dl	0.50 mg/dl	0.70 mg/dl	Decreased 36.9%
Smith, Troy	2.20 mg/dl	0.60 mg/dl	1.60 mg/dl	2.10 mg/dl	0.60 mg/dl	1.50 mg/dl	Decreased 4.6%
O'Connor, Patrick	0.70 mg/dl	0.30 mg/dl	0.40 mg/dl	0.60 mg/dl	0.20 mg/dl	0.40 mg/dl	Normal
Langen, R. Harry	1.00 mg/dl	0.40 mg/dl	0.60 mg/dl	0.80 mg/dl	0.30 mg/dl	0.50 mg/dl	Normal
Charron, Daniel	1.00 mg/dl	0.20 mg/dl	0.80 mg/dl	0.80 mg/dl	0.20 mg/dl	0.60 mg/dl	Normal
White, Susan	3.00 mg/dl	1.20 mg/dl	1.80 mg/dl	3.70 mg/dl	1.40 mg/dl	2.30 mg/dl	Increased 23.3%
Fetterroll, Susan	0.60 mg/dl	0.20 mg/dl	0.40 mg/dl	0.60 mg/dl	0.10 mg/dl	0.50 mg/dl	Normal
Doyle, Susan	0.70 mg/dl	0.20 mg/dl	0.50 mg/dl	0.40 mg/dl	0.10 mg/dl	0.30 mg/dl	Normal
Hutchines, Geraldine	0.80 mg/dl	0.20 mg/dl	0.60 mg/dl	0.90 mg/dl	0.20 mg/dl	0.70 mg/dl	Normal
Stockert, Linda	1.30 mg/dl	0.40 mg/dl	0.90 mg/dl	1.10 mg/dl	0.30 mg/dl	0.80 mg/dl	Decreased 15.4%

Source: Dr. José Cabanillas & Colleagues
Lima – Peru

Since **bilirubin** increases when liver structure is distorted, its **decrease** is interpreted as an **improvement.**

Figure 08
Chronic Hepatitis C (HCV)
Evolution of Bilirubin



Normal Values

Source: Dr. José Cabanillas & Colleagues
Lima – Peru

Since **bilirubin** increases when liver structure is distorted, its **decrease** is interpreted as an **improvement.**

The comparative analysis of **ALKALINE PHOSPHATASE** controls between the **beginning and the end** of treatment showed that in the case that presented high values at the beginning there was an **increase** of 23.9%, while in the **remaining nine cases values were maintained within normal limits**. See **Table 18 and Figure 9.**

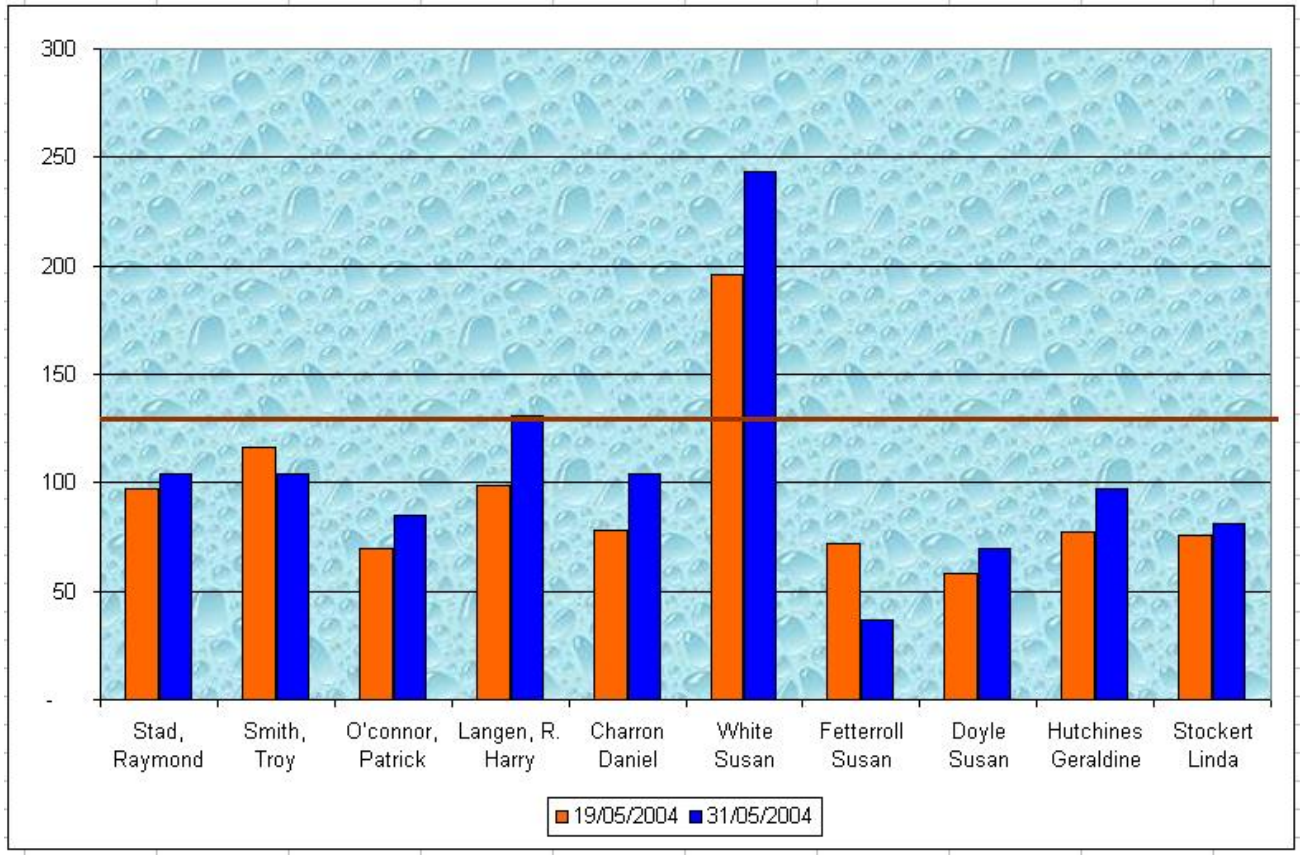
Table 18
Chronic Hepatitis C (HCV)
Evolution of Alkaline Phosphatase

	Alkaline phosphatase	Alkaline phosphatase	Modifications
Dates of control	**5/19/04**	**6/12/04**	
PATIENTS			
Stad, Raymond	97.0 U/L	104.0 U/L	Normal
Smith, Troy	116.0 U/L	104.0 U/L	Normal
O'Connor, Patrick	70.0 U/L	85.0 U/L	Normal
Langen, R. Harry	99.0 U/L	131.0 U/L	Normal
Charron, Daniel	78.0 U/L	104.0 U/L	Normal
White, Susan	196.0 U/L	243.0 U/L	Increased 23.9%
Fetterroll, Susan	72.0 U/L	37.0 U/L	Normal
Doyle, Susan	58.0 U/L	70.0 U/L	Normal
Hutchines, Geraldine	77.0 U/L	92.0 U/L	Normal
Stockert, Linda	76.0 U/L	81.0 U/L	Normal

Source: Dr. José Cabanillas & Colleagues
Lima – Peru

Since **alkaline phosphatase** increases when liver structure is distorted, its **decrease** is interpreted as an **improvement.**

Figure 09
Chronic Hepatitis C (HCV)
Evolution of Alkaline Phosphatase



Normal Values

Source: Dr. José Cabanillas & Colleagues
Lima – Perú

Since **alkaline phosphatase** increases when liver structure is distorted, its **decrease** is interpreted as an **improvement.**

The comparative analysis of **Glutamic Piruvic Transaminase** controls between the **beginning** and the **end** of treatment showed that there was a **decrease** of values in **six cases**, percentages ranged from 6.2 to 84.7 %, in **two cases** there was an **increase** between 16.1 and 57.5 %, while in the remaining **two cases** values remained within **normal numbers**.

A decrease in values of Transaminase is interpreted as a decrease of inflammatory activity on the hepatocyte, specially when it is due to the toxic effect of alcohol.

See Table 19 and Figure 10

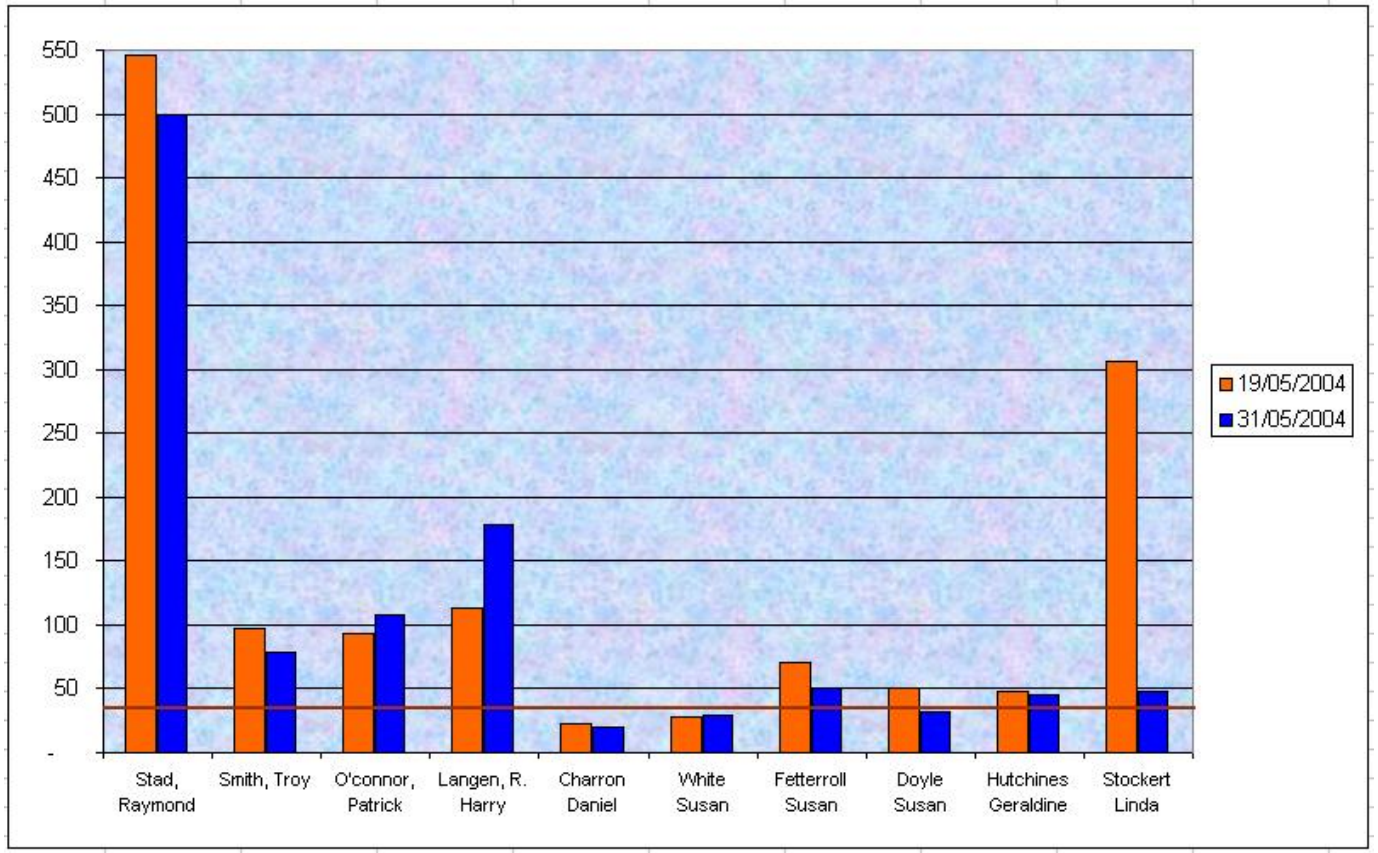
Chronic Hepatitis C (HCV)
Evolution of GPT

	GPT	GPT	Modifications
Dates of control	**5/19/04**	**6/12/04**	
PATIENTS			
Stad, Raymond	546 UI	500 UI	Decreased 8.4%
Smith, Troy	97 UI	79 UI	Decreased 18.6%
O'Connor, Patrick	93 UI	108 UI	Increased 16.1%
Langen, R. Harry	113 UI	178 UI	Increased 57.5%
Charron, Daniel	22 UI	20 UI	Normal
White, Susan	28 UI	29 UI	Normal
Fetterroll, Susan	71 UI	51 UI	Decreased 28.2%
Doyle, Susan	50 UI	32 UI	Decreased 36.0%
Hutchines, Geraldine	48 UI	45 UI	Decreased 6.2%
Stockert, Linda	306 UI	48 UI	Decreased 84.7%

Source: Dr. José Cabanillas & Colleagues
Lima – Peru

A **decrease** of **GPT (ALT)** is interpreted as a **decrease** of **inflammatory activity** on the hepatocyte .

Figure 10
Chronic Hepatitis C (HCV)
Evolution of GPT



Source: Dr. José Cabanillas & Colleagues
Lima – Perú

A **decrease** of **GPT (ALT)** is interpreted as a **decrease** of **inflammatory activity** on the hepatocyte

The comparative analysis of **Glutamic Oxaloacetic Transaminase** controls between the **beginning** and the **end** of treatment showed that in **five cases** values **decreased** between 3.8 and 74.3 %; while in **two cases** values **increased** in 30.2 and 31.2 %; in the other **three cases** values remained within **normal limits**.

A decrease in values of Transaminase is interpreted as a decrease of inflammatory activity on the hepatocyte, specially when it is due to the toxic effect of alcohol.

See Table 20 and Figure 11

Chronic Hepatitis C (HCV)
Evolution of GOT

	GOT	GOT	Modifications
Dates of control	**5/19/04**	**6/12/04**	
PATIENTS			
Stad, Raymond	340 UI	327UI	Decreased 3.8%
Smith, Troy	62 UI	52 UI	Decreased 16.1%
O'Connor, Patrick	65 UI	71 UI	Decreased 9.2%
Langen, R. Harry	96 UI	125 UI	Increased 30.2%
Charron, Daniel	21 UI	19 UI	Normal
White, Susan	48 UI	63 UI	Increased 31.2%
Fetterroll, Susan	55 UI	41UI	Decreased 25.5%
Doyle, Susan	41 UI	31UI	Normal
Hutchines, Geraldine	29 UI	32 UI	Normal
Stockert, Linda	214 UI	55 UI	Decreased 74.3%

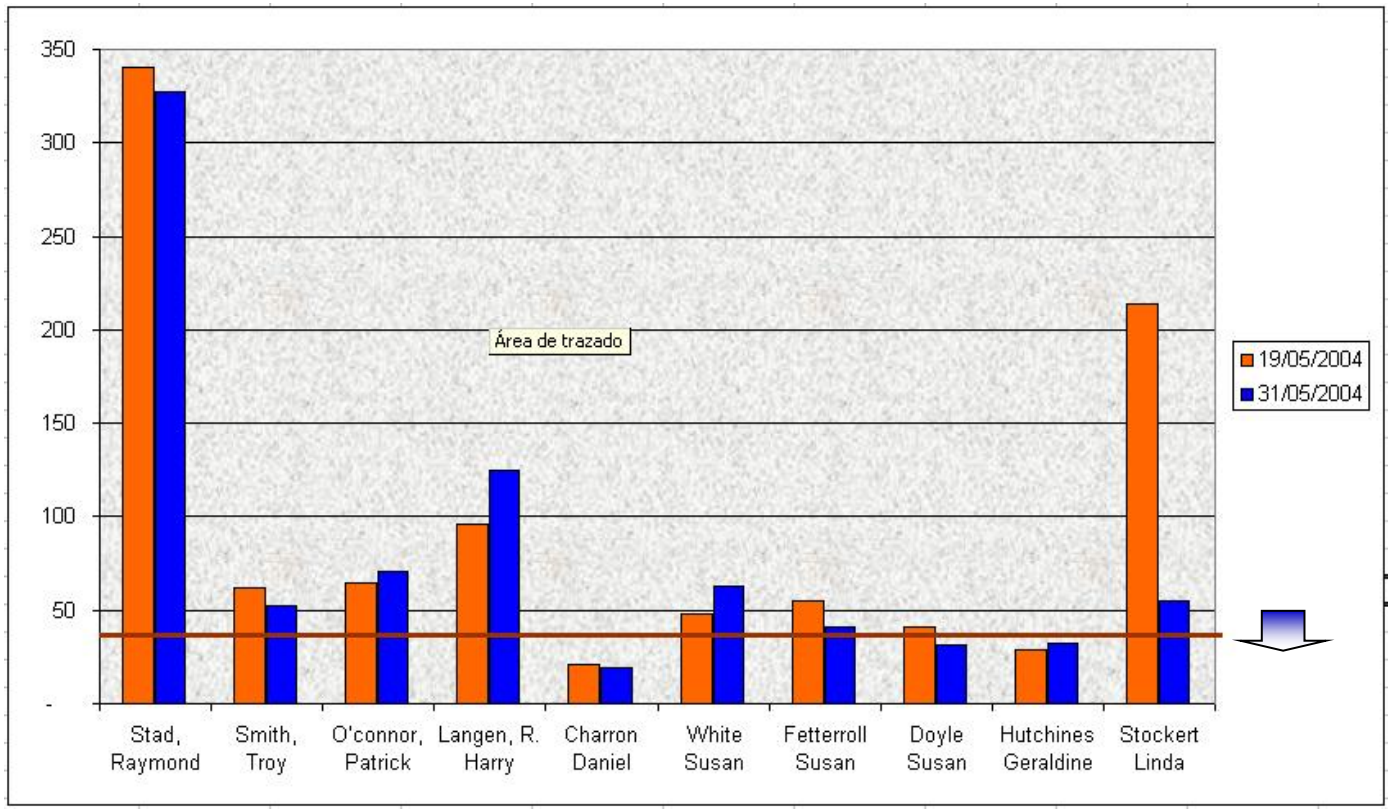
Source: Dr. José Cabanillas & Colleagues
Lima – Peru

A **decrease** of **GOT (AST)** is interpreted as a **decrease** of **inflammatory activity** on the hepatocyte.

Figure 11

Chronic Hepatitis C (HCV)

Evolution of GOT



Normal Values

Source: Dr. José Cabanillas & Colleagues
Lima – Peru

A **decrease** of **GOT (AST)** is interpreted as a **decrease** of **inflammatory activity** on the hepatocyte.

The comparative analysis of determination of **Gamma Glutamyl Transpeptidase** enzyme between the beginning and the end of the assay showed a **decrease** between 11.7 and 48.6% in **three cases**, while there was an increase of 5.7 and 2.1 % in **two of the cases**; in the other **five cases** values remained within **normal limits**.

A decrease in values of Gamma Glutamyl Transpeptidase is interpreted as a decrease of inflammatory activity on the hepatocyte, specially when it is due to the toxic effect of alcohol.

See Table 21 and Figure 12

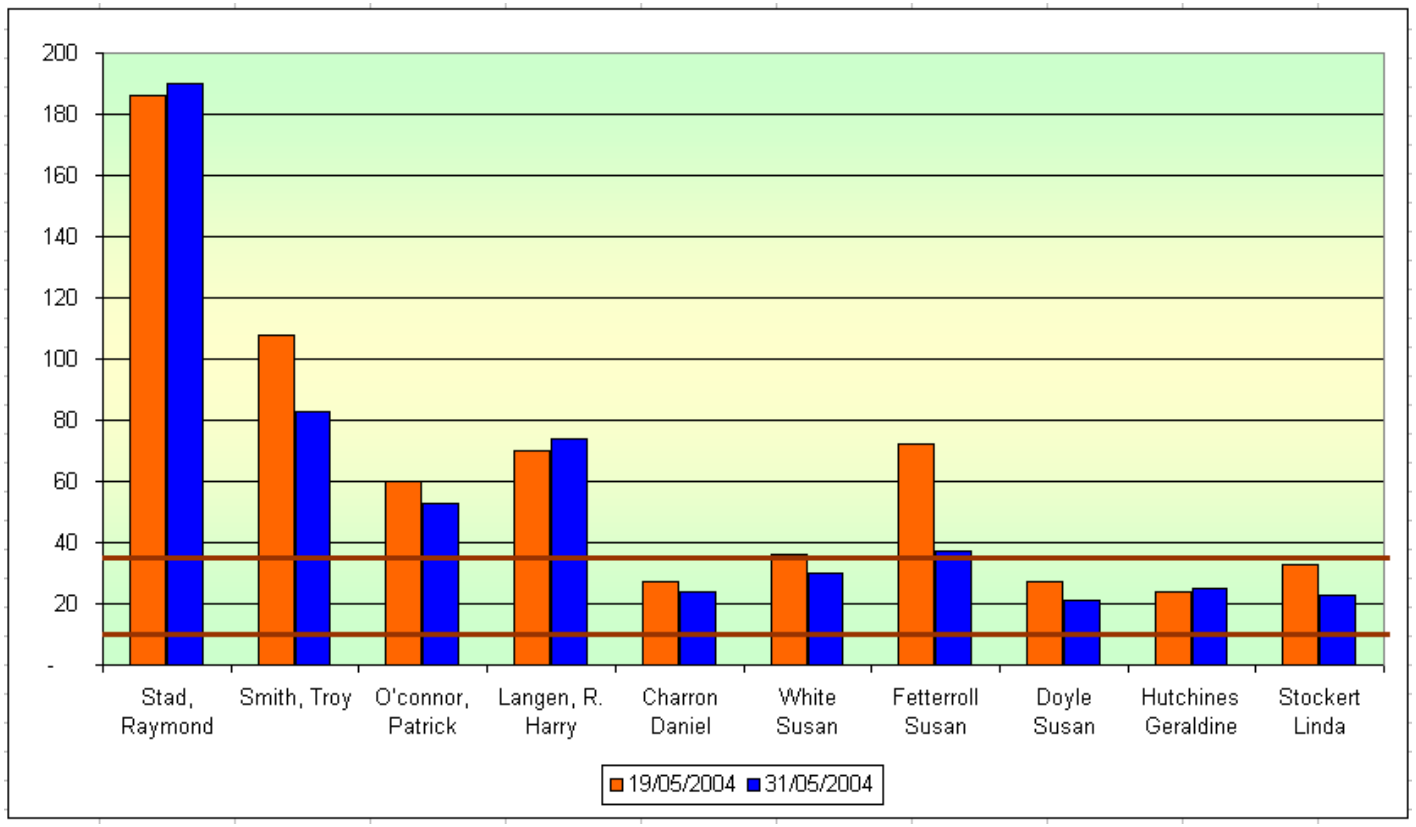
TABLE 21
Chronic Hepatitis C (HCV)
Evolution of GGT

	GGT	GGT	Modifications
Dates of control	**5/19/04**	**6/12/04**	
PATIENTS			
Stad, Raymond	186 U/L	190 U/L	Increased 2.1%
Smith, Troy	108 U/L	83 U/L	Decreased 23.1%
O'Connor, Patrick	60 U/L	53 U/L	Decreased 11.7%
Langen, R. Harry	70 U/L	74 U/L	Increased 5.7%
Charron, Daniel	27 U/L	24 U/L	Normal
White, Susan	36 U/L	30 U/L	Normal
Fetterroll, Susan	72 U/L	37 U/L	Decreased 48.6%
Doyle, Susan	27 U/L	21 U/L	Normal
Hutchines, Geraldine	24 U/L	25 U/L	Normal
Stockert, Linda	33 U/L	23 U/L	Normal

Source: Dr. José Cabanillas & Colleagues
Lima – Peru

A **decrease** of **GGT** is interpreted as a **decrease** of **inflammatory activity**, specially when it is due to the toxic effect of alcohol.

Figure 12
Chronic Hepatitis C (HCV)
Evolution of GGT



Source: Dr. José Cabanillas & Colleagues
Lima – Peru

A **decrease** in values of **GGT** is interpreted as a **decrease** of **inflammatory activity** on the hepatocyte, specially when it is due to the toxic effect of alcohol.

In both tests, the determination of **TRANSFERRIN** showed values within normal limits in **seven** out of the ten patients that took part in the study; out of the **three** patients that had values above normal in the first test, **one** went **down to normal**, whereas in the other **two cases**, they maintained their above normal values.

See Table 22 and Figure 13

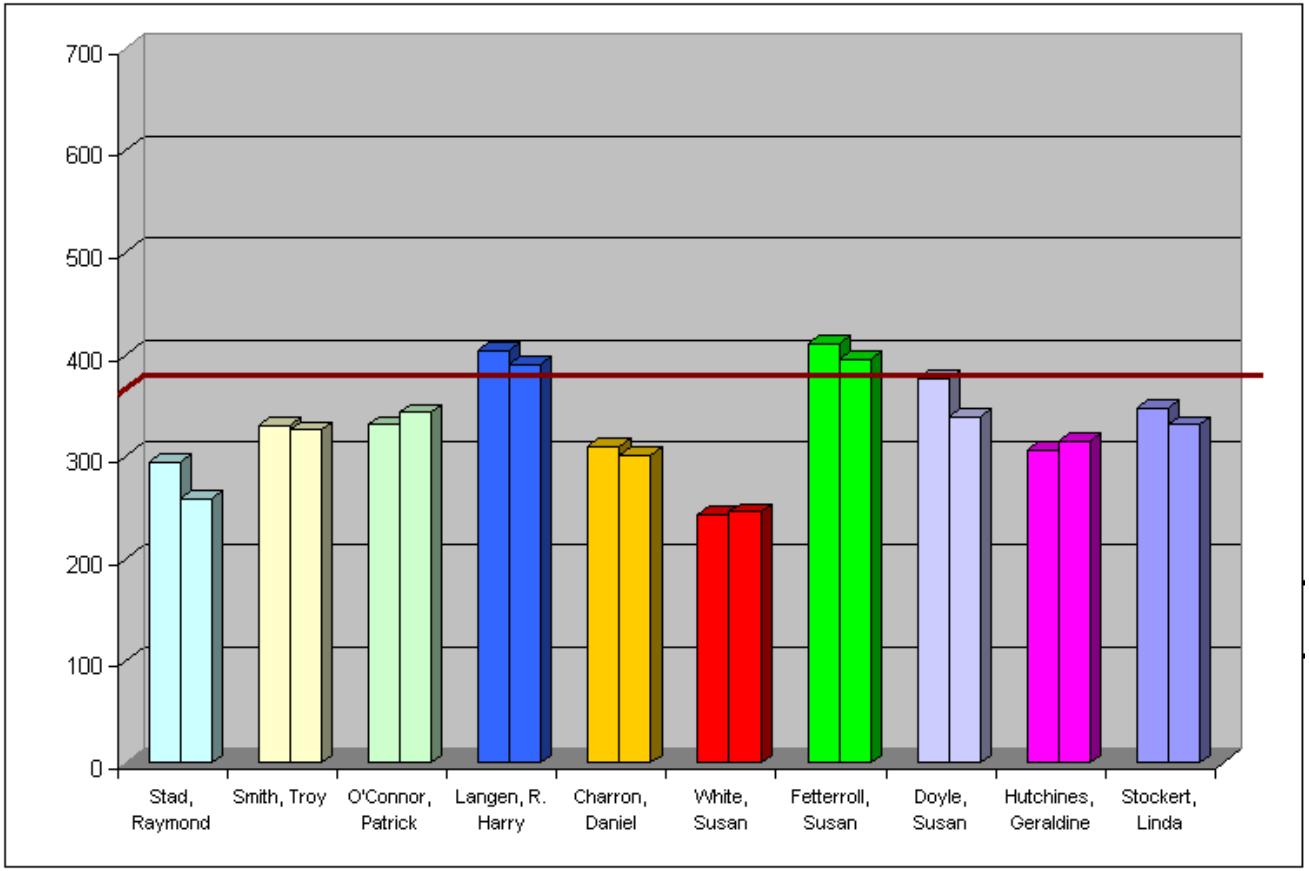
TABLE 22
Chronic Hepatitis C (HCV)
Evolution of Transferrin

	Transferrin		Modifications
Dates of control	**5/19/04**	**6/12/04**	
PATIENTS			
Stad, Raymond	295	259	Normal
Smith, Troy	330	326	Normal
O'Connor, Patrick	331	343	Normal
Langen, R. Harry	404	390	Decreased 3.5%
Charron, Daniel	310	301	Normal
White, Susan	243	246	Normal
Fetterroll, Susan	410	395	Decreased 3.7%
Doyle, Susan	377	339	Decreased 10.1%
Hutchines, Geraldine	306	315	Normal
Stockert, Linda	347	331	Normal

Source: Dr. José Cabanillas & Colleagues
Lima – Peru

An **increase of transferrin** produces accumulation in the liver, which leads to **anatomical damage**.

Figure 13
Chronic Hepatitis C (HCV)
Evolution of Transferrin



Source: Dr. José Cabanillas & Colleagues
Lima – Peru

An **increase of transferrin** produces accumulation in the liver, which leads to **anatomical damage**.

The **initial** determination of **ALPHA FETO-PROTEINS** showed that in **nine** of the cases studied **values were within normal limits**; at the end of the treatment, **eight** maintained **values within normal range**, while **one** of them experienced a **mild increase** going beyond normal limits. The **other** case started with quite high values that even **increased** by the time the **second control** was conducted.

See Table 23 and Figure 14

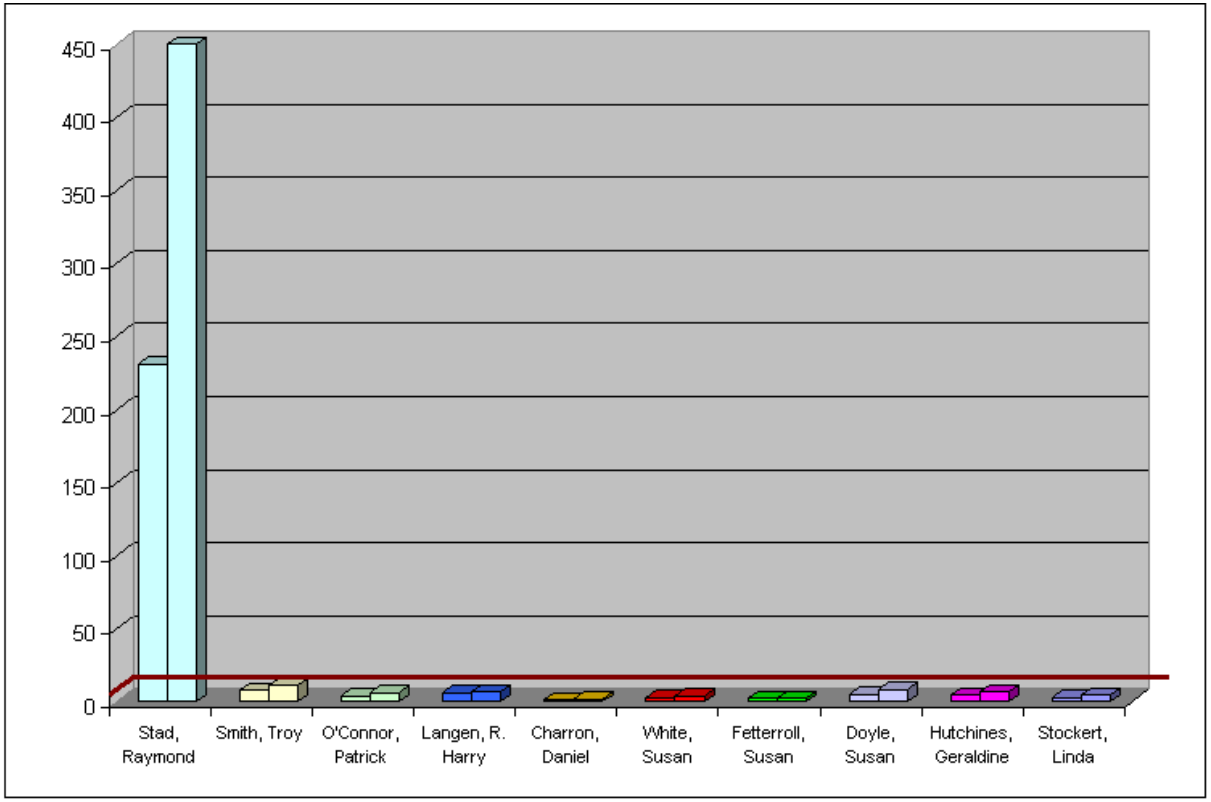
Table 23
Chronic Hepatitis C (HCV)
Evolution of Alpha Feto-Protein

	AFP		Modificaciones
Dates of control	**5/19/04**	**6/12/04**	
PATIENTS			
Stad, Raymond	231.0	454.0	Increased 96.54%
Smith, Troy	7.7	11.0	Increased 42.85%
O'Connor, Patrick	4.3	6.4	Normal
Langen, R. Harry	6.0	6.9	Normal
Charron, Daniel	1.4	1.6	Normal
White, Susan	3.1	3.8	Normal
Fetterroll, Susan	2.5	2.5	Normal
Doyle, Susan	5.4	8.2	Normal
Hutchines, Geraldine	4.4	6.9	Normal
Stockert, Linda	3.0	4.5	Normal

Source: Dr. José Cabanillas & Colleagues
Lima – Peru

AFP is **a tumor marker** used as an indicative of **gastrointestinal cancer.**

Figure 14
Chronic Hepatitis C (HCV)
Evolution of Alpha Feto-Protein



Source: Dr. José Cabanillas & Colleagues
Lima-Peru

AFP is **a tumor marker** used as an indicative of **gastrointestinal cancer.**

Values in the determination of **AMMONIA** were, in the **first control**, **within normal limits** in **nine** of the cases; such values remained **equally normal by the end of the treatment**. The **remaining case** started with **values above normal** that were also maintained.

See Table 24 and Figure 15

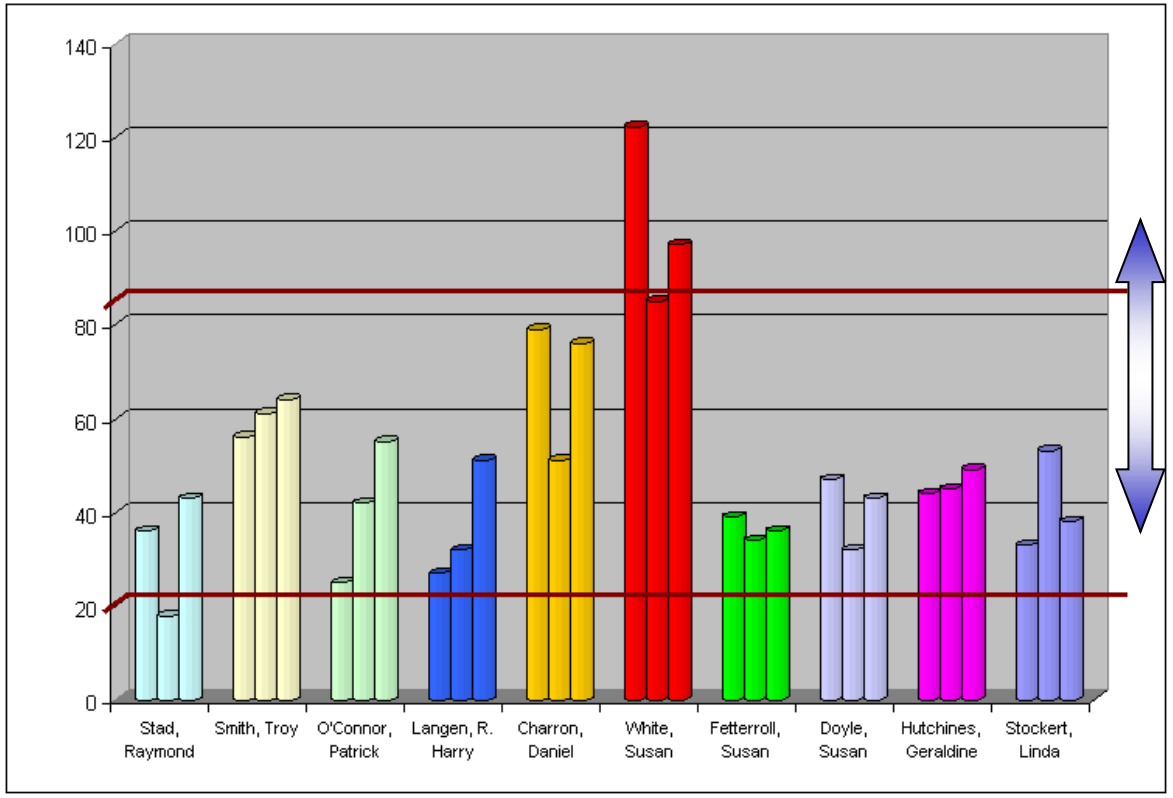
Table 24
Chronic Hepatitis C (HCV)
Evolution of Ammonia

	Ammonia			Modifications
Dates of control	**5/19/04**	**5/31/04**	**6/12/04**	
PATIENTS				
Stad, Raymond	36	18	43	Normal
Smith, Troy	56	61	64	Normal
O'Connor, Patrick	25	42	55	Normal
Langen, R. Harry	27	32	51	Normal
Charron, Daniel	79	51	76	Normal
White, Susan	122	85	97	Decreased 28.49%
Fetterroll, Susan	39	34	36	Normal
Doyle, Susan	47	32	43	Normal
Hutchines, Geraldine	44	45	49	Normal
Stockert, Linda	33	53	38	Normal

Source: Dr. José Cabanillas & Colleagues
Lima – Peru

Ammonia is an internal toxic product. Its **increase** indicates **liver failure**.

Figure 15
Chronic Hepatitis C (HCV)
Evolution of Ammonia



Normal Values

Source: Dr. José Cabanillas & Colleagues
Lima – Peru

Ammonia is an internal toxic product. Its **increase** indicates **liver failure**.

The control of **PLATELET COUNT** at the **beginning** of the assay showed that seven patients had numbers within **normal limits**, which remained equal by the **end** of the treatment. The other **three** cases presented, at the beginning, values **below the minimum established as normal**, 140,000/mm3 , that were also **maintained** at the same range by the end of the treatment.

See Table 25 and Figure 16

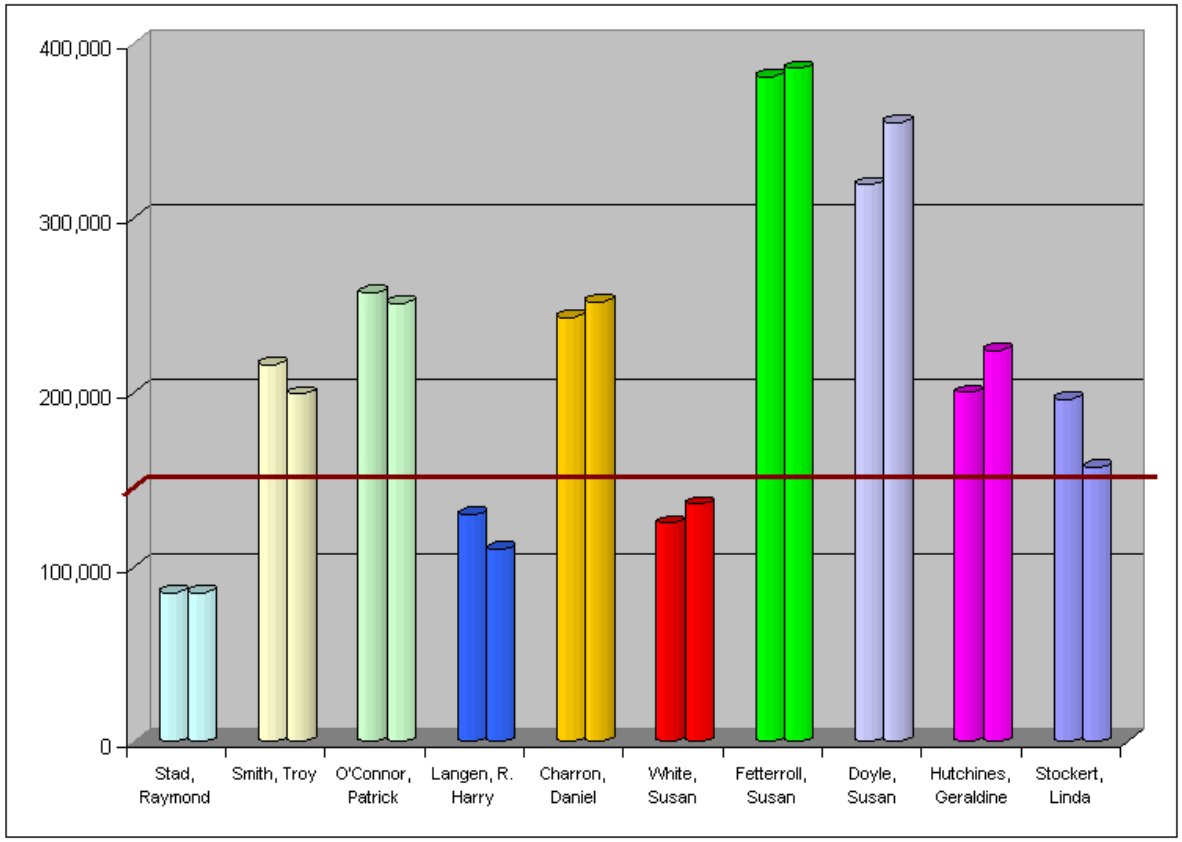
Table 25
Chronic Hepatitis C (HCV)
Evolution of Platelet Count

	Evolution of Platelet Count		Modifications
Dates of control	**5/19/04**	**6/12/04**	
PATIENTS			
Stad, Raymond	85,000	85,200	Values below normal
Smith, Troy	216,000	199,000	Normal
O'Connor, Patrick	257,000	251,000	Normal
Langen, R. Harry	130,000	110,000	Values below normal
Charron, Daniel	243,000	252,000	Normal
White, Susan	125,000	136,000	Values below normal
Fetterroll, Susan	381,000	386,000	Normal
Doyle, Susan	319,000	355,000	Normal
Hutchines, Geraldine	200,000	224,000	Normal
Stockert, Linda	196,000	157,000	Normal

Source: Dr. José Cabanillas & Colleagues
Lima – Peru

A **decrease in platelet count** indicates **enlargement of the spleen**.

Figure 16
Chronic Hepatitis C (HCV)
Evolution of Platelet Count



Normal Values

Source: Dr. José Cabanillas & Colleagues
Lima – Peru

A **decrease in platelet count** indicates **enlargement of the spleen**.

For the **three controls** that we conducted, values in the determination of **TUMOR NECROSIS FACTOR** (TNF-Alpha) **fluctuated** sometimes within the normal range and sometimes above it in an **alternate and irregular** manner. Thus not allowing us to make any comments on it as proof of evolution in the present study.

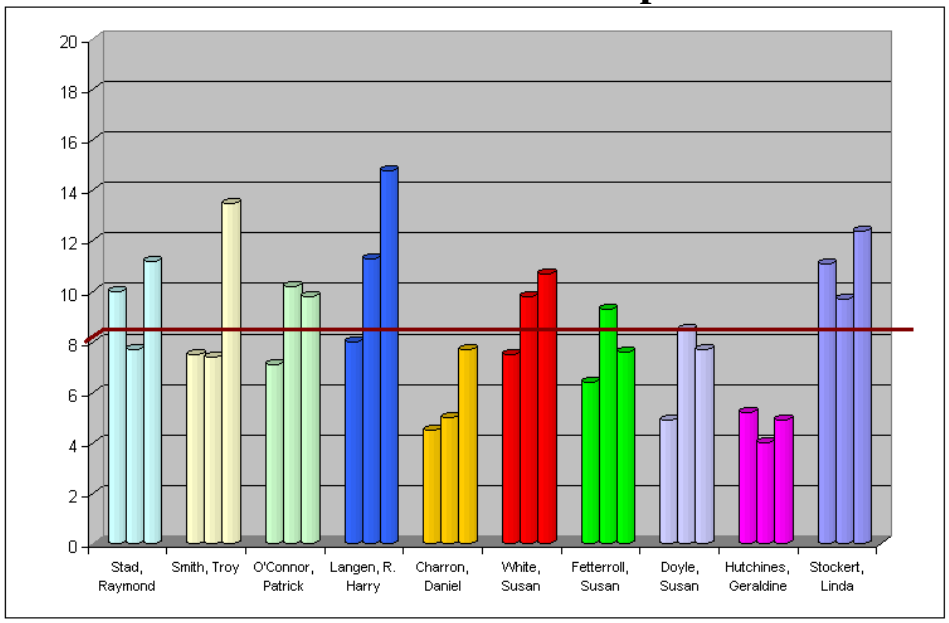
See Table 26 and Figure 17

Table 26
Chronic Hepatitis C (HCV)
Evaluation of TNF-Alpha

	TNF-alpha		
	5/19/04	**5/31/04**	**6/12/04**
PATIENTS			
Stad, Raymond	10.0	7.7	11.2
Smith, Troy	7.5	7.4	13.5
O'Connor, Patrick	7.1	10.2	9.8
Langen, R. Harry	8.0	11.3	14.8
Charron, Daniel	4.5	5.0	7.7
White, Susan	7.5	9.8	10.7
Fetterroll, Susan	6.4	9.3	7.6
Doyle, Susan	4.9	8.5	7.7
Hutchines, Geraldine	5.2	4.0	4.9
Stockert, Linda	11.1	9.7	12.4

Source: Dr. José Cabanillas & Colleagues
Lima – Peru

Figure 17
Chronic Hepatitis C (HCV)
Evaluation of TNF-Alpha



Source: Dr. José Cabanillas & Colleagues
Lima – Peru

Evaluation of Clinical Aspects

Evolution of symptoms and signs

1. General symptoms:

The clinical control at the end of the assay showed a decrease in general symptomatology. **Severe fatigue, lack of concentration and osteoarticular pain** disappeared in some patients and their presence was reduced by 40% in the cases studied; **general discomfort and depression** as well as **muscular pain** were reduced and only present in 30% of patients; whereas **sleep disorders** and the **presence of headache** only reached 20% and 10% respectively.

Moreover, we must mention that in some of the cases in which **general symptoms** persisted, patients experienced varied decreases in the intensity of such symptoms.

2. Gastrointestinal symptoms:

The evolution of **gastrointestinal symptoms** also showed a decrease at the end of the process. **Indigestion and intestinal dysfunction** was present in 30% of cases; **dyspepsia and nausea** reached 20 and 10% of patients whereas **abdominal pain** was no longer present in any of the cases 0%.

We must also mention that those patients in which gastrointestinal discomfort did not disappear, experienced a decrease in intensity; except for one patient that reported an increase of nausea.

3. Signs:

During the treatment, the sign of **pain upon palpation of right hypochondrium** was reduced to 20%; whereas other signs such as **jaundice and palpable liver** remained present in 20% of cases; **palpable spleen** was reduced to 10% whereas other signs such as **ascites, ecchymosis and edema in lower extremities** remained present in one patient, that is, 10% of cases; no patient presented **collateral circulation**.

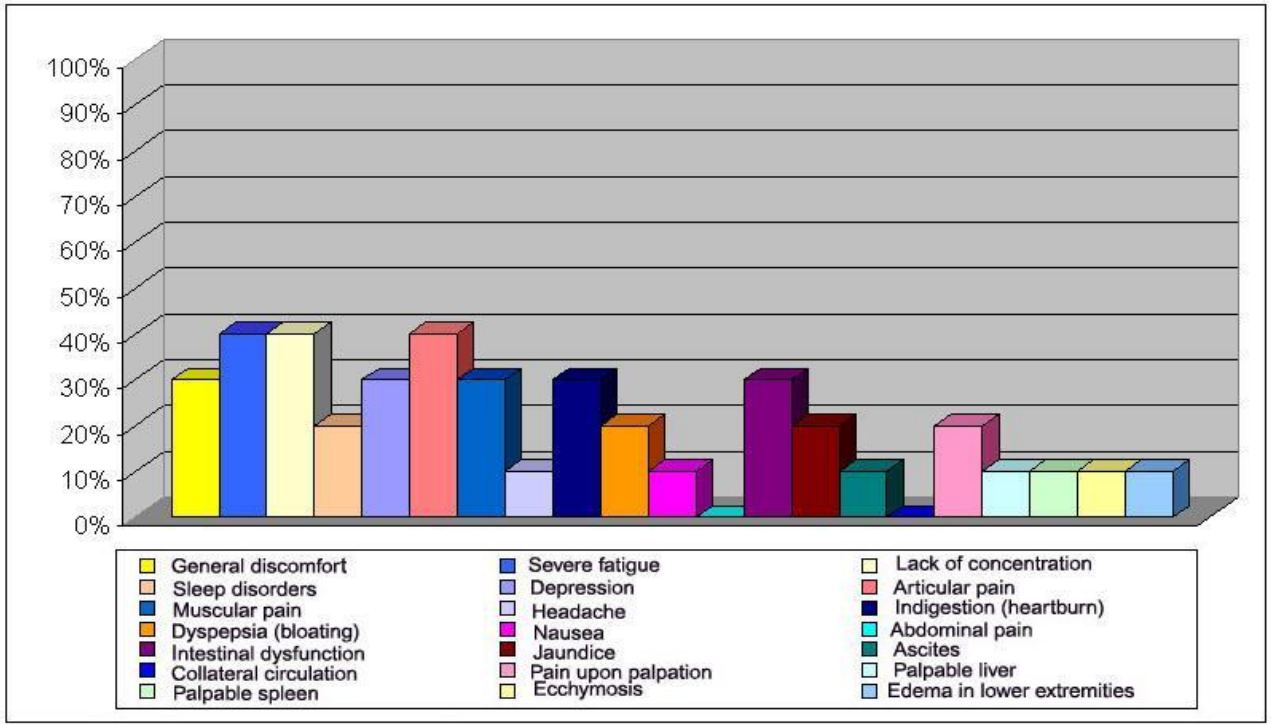
See Table 27 and Figure 18

Table 27
Chronic Hepatitis C (HCV)
Evolution of Symptoms and Signs

Symptoms	Stad, R.	Troy, S.	O'Connor	Langen, H.	Charron	White	Fetterroll	Doyle	Hutchines	Stockert	
I) General											
1.- General discomfort	-	-	-	-	-	+	-	+ decre.	-	+ decre.	30%
2.- Severe fatigue	-	-	-	-	-	+decre.	-	+	+ decre.	+ decre.	40%
3.- Lack of concentration	-	+ decre.	-	-	-	+	-	+	+ decre.	+ decre.	40%
4.- Sleep disorders	-	-	-	-	-	+	-	+ decre.	-	-	20%
5.- Depression	-	-	+ decre.	-	-	+	-	+	-	-	30%
6.- Articular pain	-	-	-	+ decre.	-	+	-	+ decre.	+decre.	+decre.	40%
7.- Muscular pain	-	-	-	+ decre.	-	+	-	-	-	+decre.	30%
8.- Headache	-	-	-	-	-	-	-	-	-	+ decre.	10%
II) Gastrointestinal											
1.- Indigestion (heartburn)	-	+ decre.	-	+ decre.	-	+	-	-	-	-	30%
2.- Dyspepsia (bloating)	-	-	-	-	-	+	-	-	-	+ decre.	20%
3.- Nausea	-	-	-	-	-	+incre.	-	-	-	-	10%
4.- Abdominal pain	-	-	-	-	-	-	-	-	-	-	0%
5.- Instestinal dysfunction	-	-	-	+ decre.	-	+	-	-	+ decre.	-	30%
Signs											
1.- Jaundice	+	-	-	-	-	+	-	-	-	-	20%
2.- Ascites	-	-	-	-	-	+incre.	-	-	-	-	10%
3.- Collateral circulation	-	-	-	-	-	-	-	-	-	-	0%
4.- Pain upon palpation	-	-	-	+ decre.	-	+	-	-	-	-	20%
5.- Palpable liver	-	-	-	+	-	-	-	-	-	-	10%
6.- Palpable spleen	-	-	-	+	-	-	-	-	-	-	10%
7.- Ecchymosis	-	-	-	-	-	+	-	-	-	-	10%
8.- Edema in lower extremities	-	-	-	-	-	+incre.	-	-	-	-	10%

Source: Dr. José Cabanillas & Colleagues
Lima – Peru

Figure 18
Chronic Hepatitis C (HCV)
Evolution of Symptoms and Signs
After Treatment



Source: Dr. José Cabanillas & Colleagues
Lima - Peru

Comparative study of symptoms and signs before and after treatment

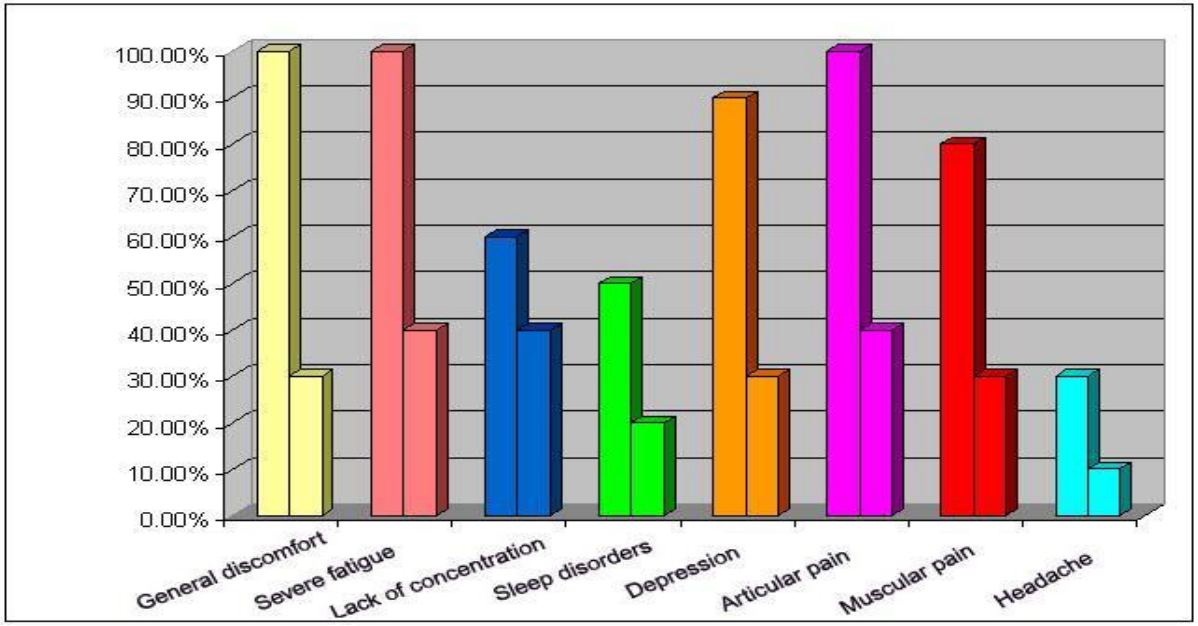
The following graphs allow us to observe, in a comparative study, the frequency of presence of symptoms and signs in the cases studied before and after treatment:

1. General symptoms: **Figure 19**

2. Gastrointestinal symptoms: **Figure 20**

3. Clinical signology: **Figure 21**

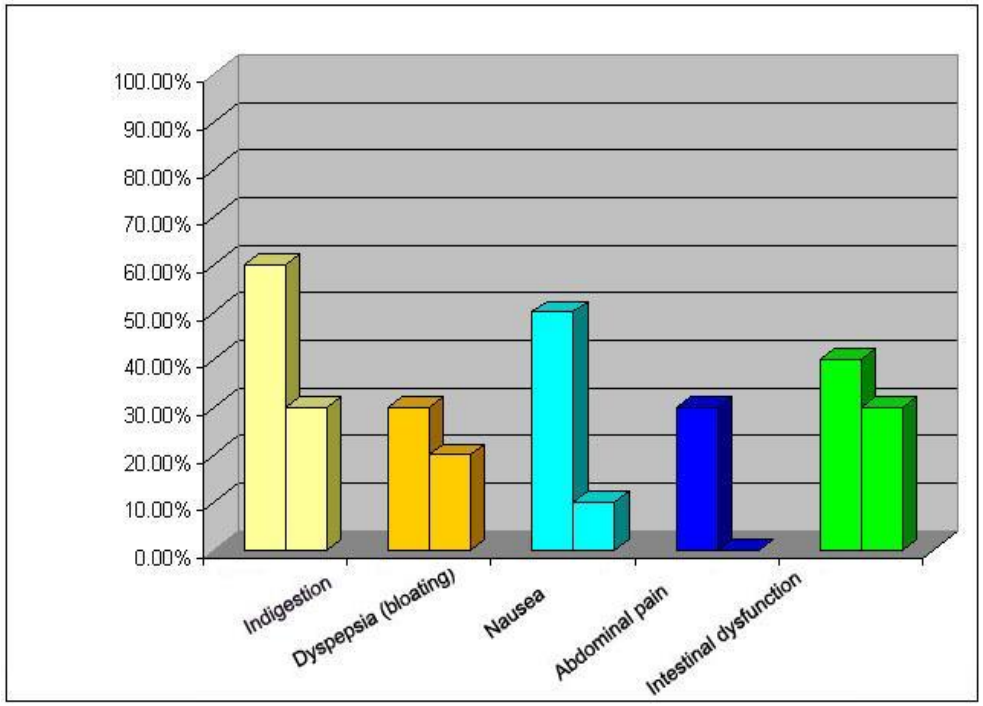
Figure 19
Chronic Hepatitis C (HCV)
Comparative study of symptoms and signs before and after treatment



Source: Dr. José Cabanillas & Colleagues
Lima – Peru

Such **decrease** in the intensity of **symptoms** indicates **patient improvement** after the first 28 days of treatment.

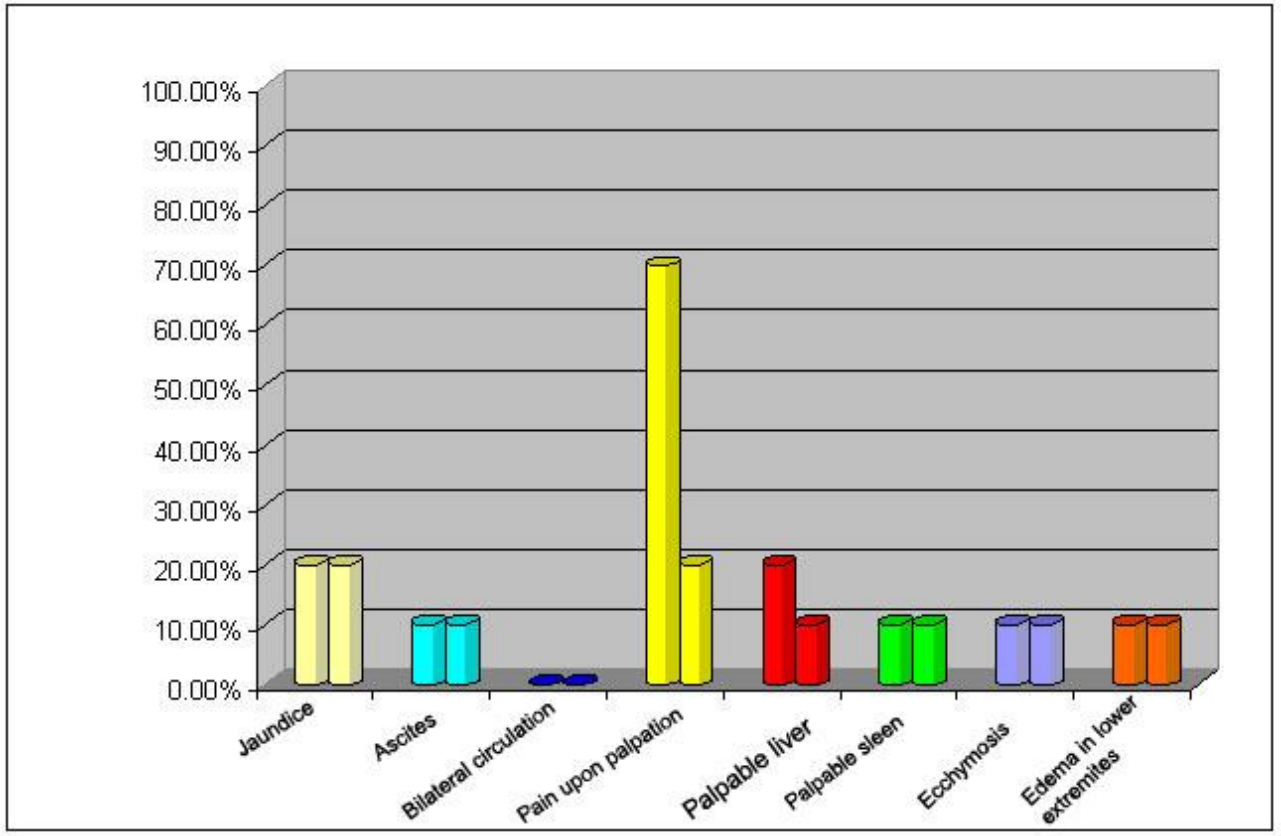
Figure 20
Chronic Hepatitis C (HCV)
Comparative study of symptoms and signs before and after treatment



Source: Dr. José Cabanillas & Colleagues
Lima – Peru

Such **decrease** in the intensity of **symptoms** indicates **patient improvement** after the first 28 days of treatment.

Figure 21
Chronic Hepatitis C (HCV)
Comparative study of symptoms and signs before and after treatment



Source: Dr. José Cabanillas & Colleagues
Lima – Peru

Such **decrease** in the intensity of **symptoms** indicates **patient improvement** after the first 28 days of treatment.

Final Comments

At the beginning of this study, all of the patients manifested the general symptomology associated with chronic Hepatitis C, as well as varying degrees of severity of digestive problems except one control patient (Susan White) only had cirrhosis. Although study participants ranged from three to thirty years in managing their disease, in each case, these symptoms created limitations in their work, as well as in their family and social relationships. In addition, the patients reported varying degrees of depression and anxiety related to their futures.

Clinical symptoms:
Study subjects showed a dramatic improvement in the majority of their symptoms. These included improvement in fatigue, right upper quadrant (liver area) pain and tenderness, dyspepsia, nausea-vomiting, indigestion, headaches, muscle and joint/bone pains.

Prothrombine activity and serum cholinesterase:
There was a significant increase in Prothrombine activity and serum cholinesterase which suggests possible increased protein synthesis by the liver, or at very least, a decrease in their degradation. This improvement in these specific vital liver functions demonstrates one of the most promising indications that A4+L is initiating the liver's recovery.

Health-Related Quality of Life:
The efficacy of A4+ to improve the quality of life was tested by administering the 'SF - 36 Quality of Life Survey' and by Day 14, a markedly improved quality of life was reported by 90% of the study subjects. By Day 28, the patients' well-being and capacity to function were restored to normal levels in 90% of the subjects observed. The score improvements observed in this study by Day 28 were, on average, greater than two standard deviations for nearly all health-related quality of life scales. This degree of improvement has rarely been observed in the thousands of treatment studies of other chronic diseases involving the SF-36 Health Survey.25. The SF - 36 Health Survey is the most commonly used, accepted and generally standardized scale for measurement of patient ‘Quality of Life’.

Depression:
The severity of depression at the start of the study ranged from borderline in 10% of the subjects, mild to moderate depression in 80%, and severe depression in 10%. By the end of the observation period statistically significant improvement in depression was noted and 90% of the subjects reported being free of depression. By the 28th day, the majority of the patients showed marked progress in their degree of relief from depression as well as their changed attitude toward their own futures. Each patient expressed their desire to return to work, and to their family and social relationships. Most important to their mental health was their positive attitude to recuperating their capacity to be 'normal '.

In summary, by day 28 of the study period, the patients had already improved in every aspect of Hepatitis C symptomology. This was demonstrated by the bio -chemical liver testing (in relation to hepatic synthesis) and liver inflammation (shown in ultrasound testing). These tests, in combination with the marked improvement demonstrated by the results on

'Quality of Life SF-36' scale, and the Beck Depression Inventory, provide evidence, of marked decrease of liver inflammation, near elimination of Hepatitis C symptoms, and an overall sense of hope for leading a healthy, 'normal' life. With such highly positive significant physical and mental indicators of marked improvement, in such a high percentage of the patients, continued research of A4+L is clearly warranted.

The results obtained in the ultrasound and different biochemical tests that indicate an improvement in the functional and/or anatomic state of the liver must be evaluated in the new control stages.

There was no case in which the patients reported unpleasant side effects from the therapy performed on them; however, hematological and renal function control tests must be performed periodically.

This work constitutes a very optimistic alternative treatment for patients with chronic Hepatitis C.

The Authors

Bibliography

1. WHO. Hepatitis C: global prevalence. Wkly Epidemiol Rec 1997; 72: 341-4

2. Heintger, T; Wands J R.: Hepatitis C virus: epidemiology and transmission Hepatology 1997; 26; 521-6

3. Yano M; Kumada H, Kage M; The long term pathological evolution of chronic hepatitis C. Hepatology 1996; 23: 1334-40

4. Tremolada F, Casarin C, Alberti: Long tern follow-up of no-A non-B (type C) post-transfusion hepatitis. J Hepatol 1992; 16:273-81

5. Working Group on the evaluation of carcinogenic risk to humans, International agency for research on cancer. Word Health Organization. Monographs on the evaluation of carcinogenic risk to humans 1994; 59: 165-221

6. Rao KV, Anderson RC: Long tern results and complications in renal transplant recipients. Observation en the second decade. Transplantation 1998; 45: 45-52

7. Grotz WH, Peters TH, Schalayer HJ, et al.: Immunosuppressive therapy and hepatitis C virus infection: the clinical course of liver desease. J Mol Med 1996; 74: 407-12

8. Desmet VJ, Gerber M, Hoofnagle JH, Manns Sheuer PJ. : Classification of chronic hepatitis: diagnosis, grading and staging. Hepatology 1994; 19: 1513-20

9. Knodell RG, Ishak KG, Black WC, Chen TS, Craig R, Kaplowitz N, et al. Formulation and application of a numerical scoring system for assessing histological activity in asymptomatic chronic active hepatitis. Hepatology 1981; 1: 431-5

10. Hoofnagle JH, Mullen KD, Jones DB, et al.: Treatment of chronic non-A, non-B hepatitis with recombinant human alpha interferon. A preliminary report. N Engl J Med 1986; 315: 1575-8

11. Lin R, Roach E, Zimmerman M, Strasser S, Farrel GC. : Interferon alpha 2b for chronic hepatitis C: effects of dose increment and duration of treatment and response rate. Results of the first multicentre. Australian trial. J Hepatol 1995; 23: 487-96

12. Lino S, Hino K, Kuroki T, Suzuki H, Yamamoto S.: Treatment of chronic hepatitis C with study high-dose interferon alpha 2b. A multicentre study. Dig Dis Sci 1993; 38: 612-8

13. Hakosako Y, Shirahama T, Katou M, Nakagawa K, Oba K, Mitamura K.: A controlled study to determine the optimal dose regimen of interferon alpha 2b in chronic hepatitis C. Am J Gastroenterol 1995; 90: 1246-9

14. Mc Hutchison JG, Poynard T.: Combination therapy with interferon plus Ribavirin for the initial treatment of chronic hepatitis C. Semin Liver Dis 1999; 19 (suppl 1) : 57-65

15. Davil GL.: Combination therapy with interferon alpha and Ribavirin as treatment of interferon relapse in chronic hepatitis C. Semin Liver Dis 1999; 19 (suppl 1): 49-55

16. Arus Soler E; Rivera L; Fernández A y otros: Tratamiento de la hepatitis crónica C con interferón alfa 2 recombinante. Controlled Clinical Test Rev. Med. Cuba 2000; 39(1): 12-20

17. Gabo KA, Herlong HF, Torbenson MS, et al.: Role of liver biopsy in magament of chronic hepatitis C: A systematic review. Hepatology 2002; 36: 161-72

18. Albanis E, Friedman SL.: Non-invasive markers of hepatic fibrosis. Clin Pers Gastroenterol 2002; 5: 182-87

19. Poynard T, Imbert-Bismut F, Retziu V et al.: An overvien of biochemicol markeds (fibro-test-actitest) diagnostic volucin chronic liver desease: A non-invasive

alternative to liver biopsy. Boston Mass; American Association for the Study of Liver Deseases (AASLD) Nov. 2003. Abstract 03.