

Antibody Dynamics in Acute Infection

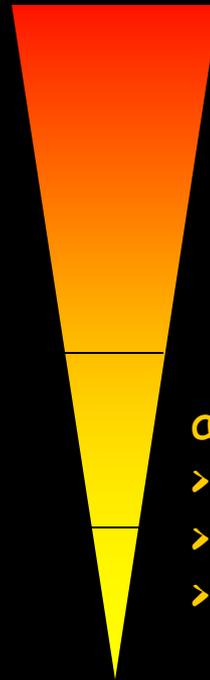


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CDC/2011

Viral Hepatitis Clinic 1997 ~

> 18.000 individuals



acute hepatitis > 2200
> 1000 HAV
> 350 HBV
> 150 HCV

Acute HCV Cohort Rio de Janeiro, Brazil

Time period: 2000 - 2011

N° cases: 105

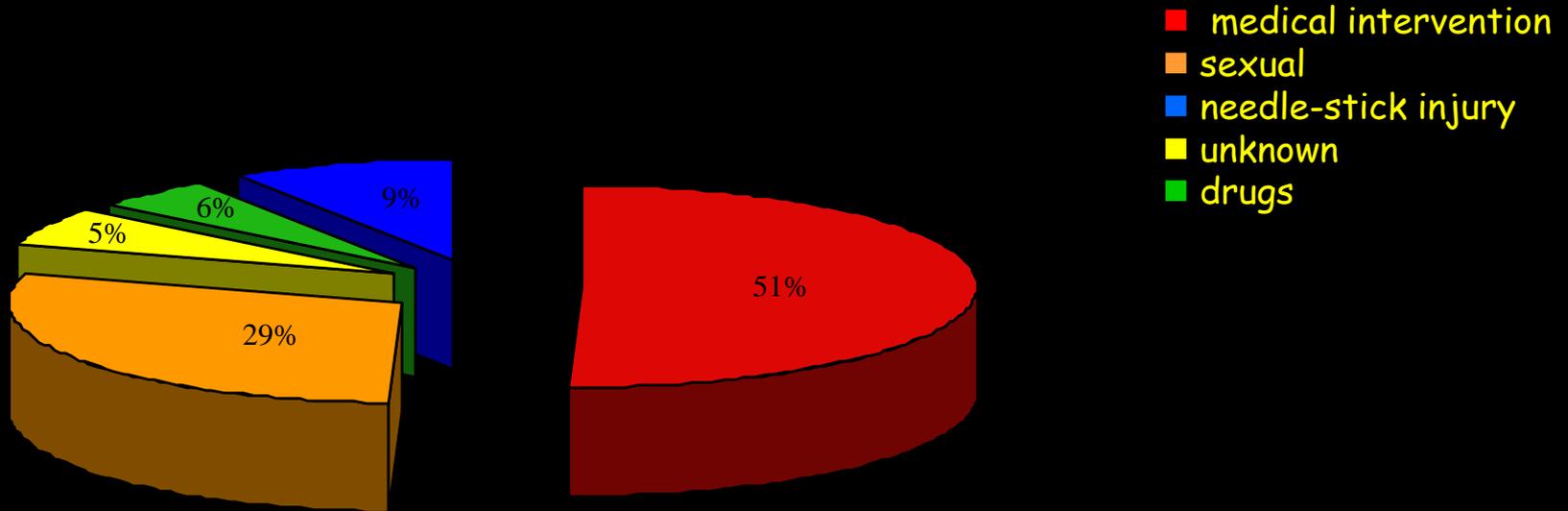
Gender: 45M/60F

Age range: 14 - 73 years

Jaundice: 75%

Diagnosis : 41 cases ⇒ anti-HCV seroconversion
5 cases ⇒ increase of anti-HCV
59 cases ⇒ clinical, laboratory, and
epidemiologic (risk factor)
evidence

Risk Factors & Genotype



Genotype

1	75	(82%)
2	6	(7%)
3	9	(10%)
4	1	(1%)
?	14	

Clinical Outcome

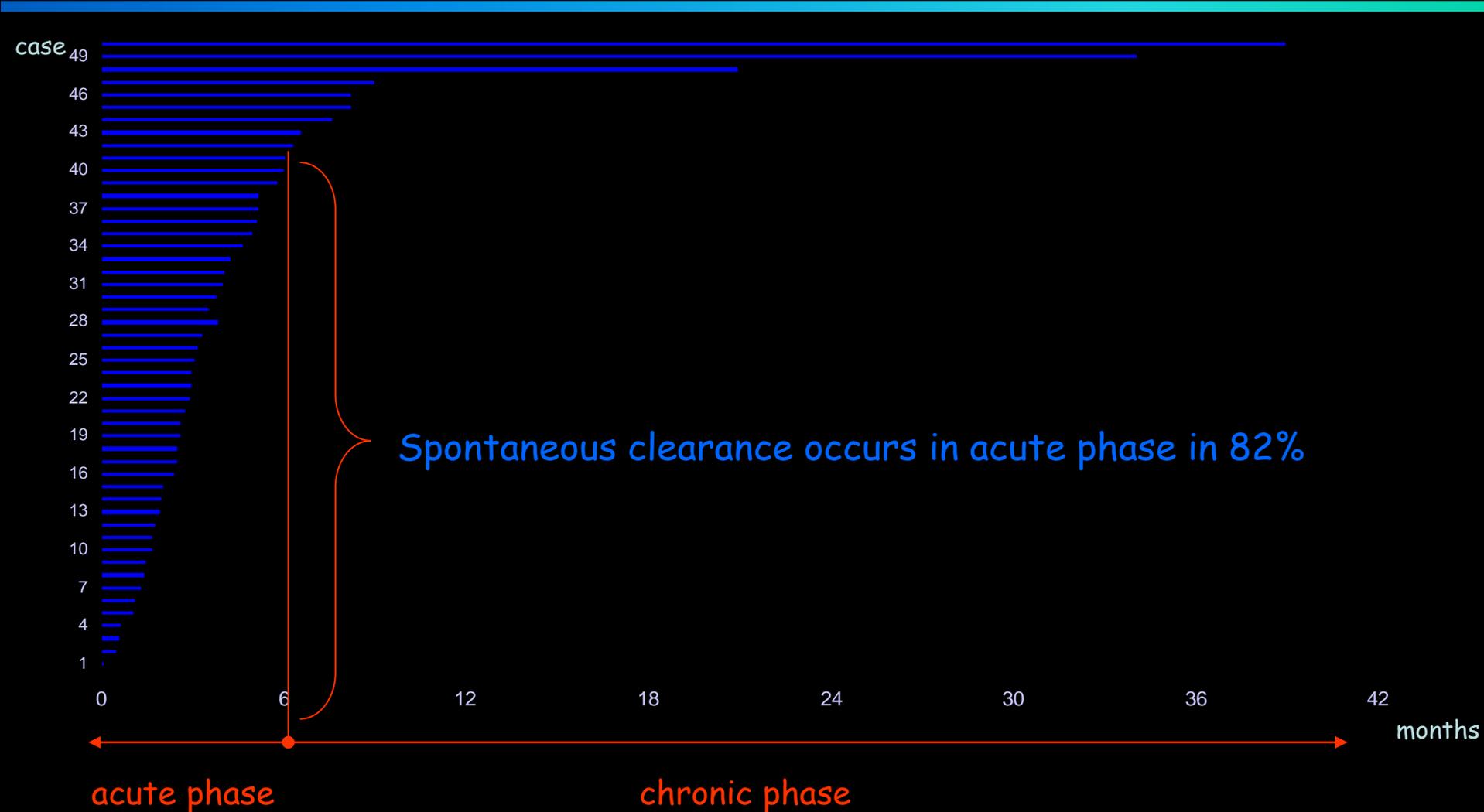
Spontaneous clearance \Rightarrow 50 (52%)

Chronic infection \Rightarrow 46 (48%)

Unknown \Rightarrow 9 (< 6 months follow-up)

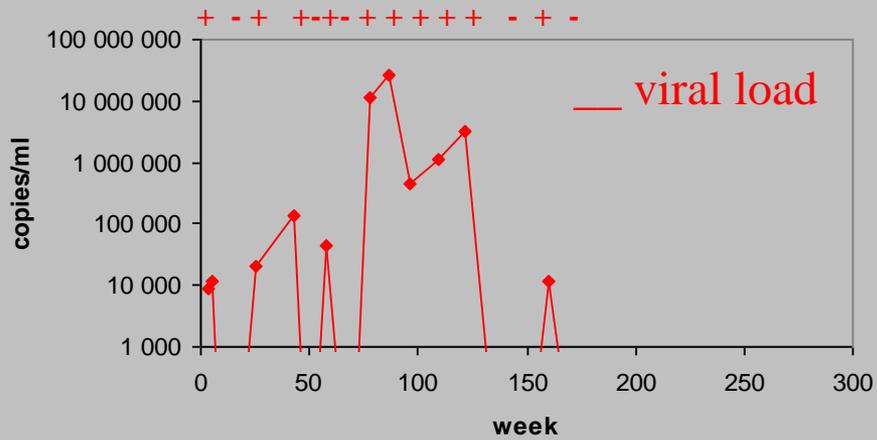
Total 105

Spontaneous Clearance (n=50) Time Point for Undetectable Viremia

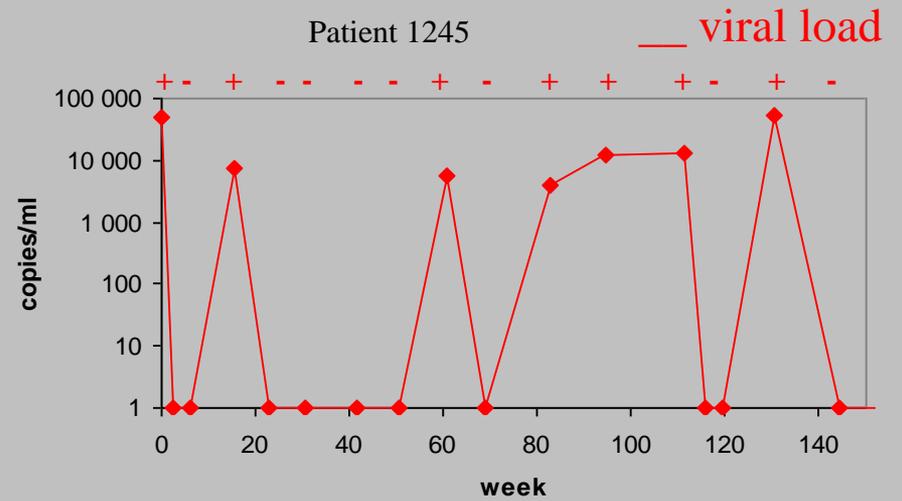


Rationnnale

Patient 111

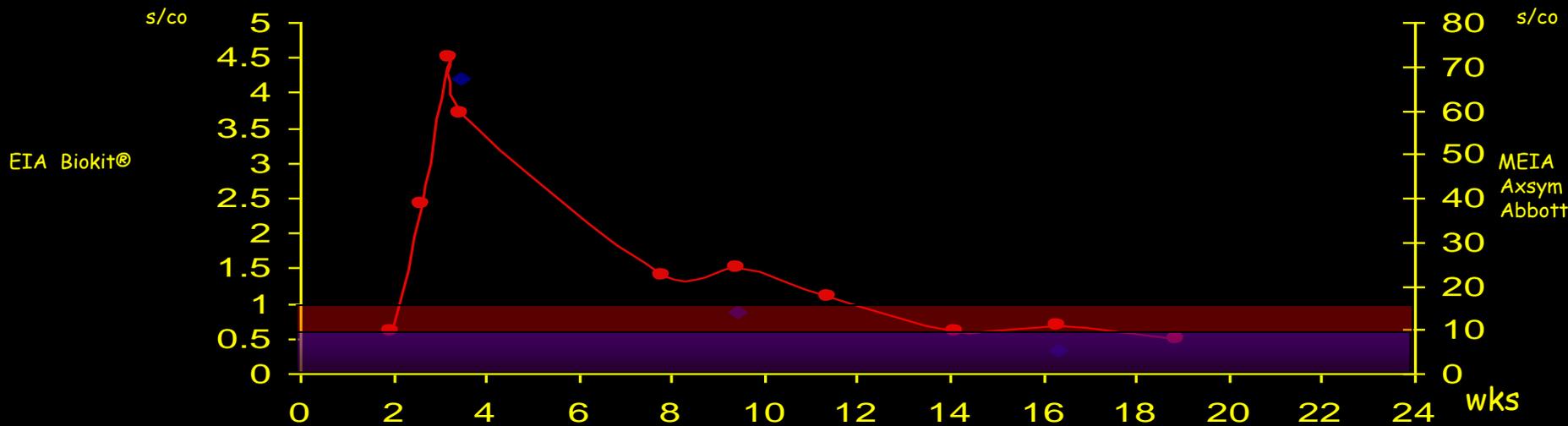


Patient 1245



Seroconversion & seroreversion in acute HCV infection

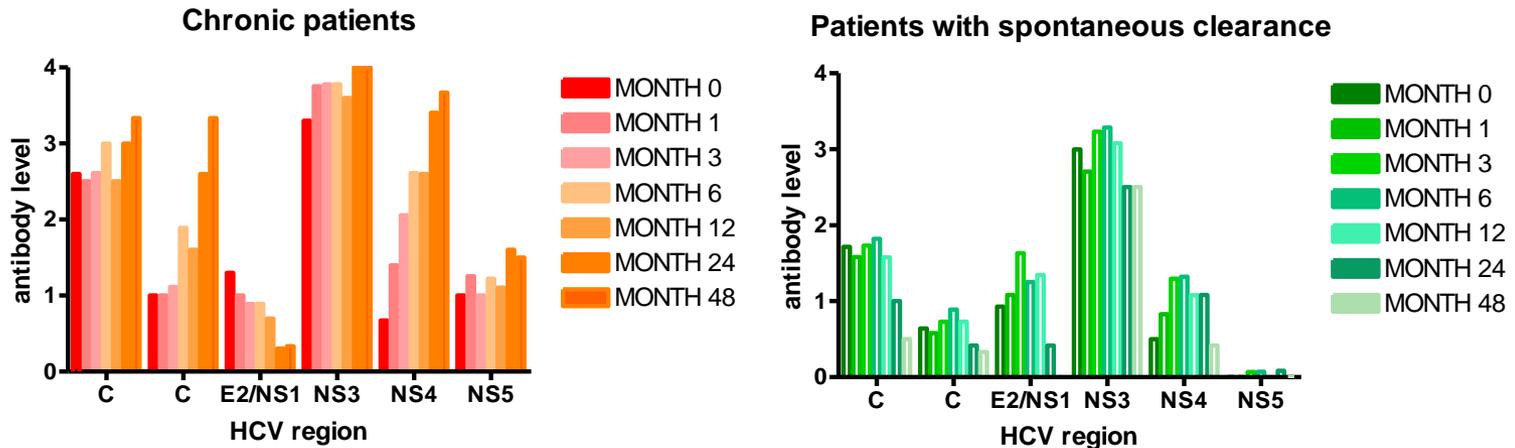
HCV RNA	+	+	-	+	-	-	-	-	-	-
NS3			3+		2+			2+		2+
NS4			2+		2+			1+		1+



MEIA AxSYM/Abbott: $s/co < 10 = 95\%$ HCV RNA negative

Bossi V, Galli C. Quantitative signal of anti-HCV by an automated assay predicts viremia in a population at high prevalence of hepatitis C virus infection. *J Clin Virol.* 2004 May;30(1):45-9.

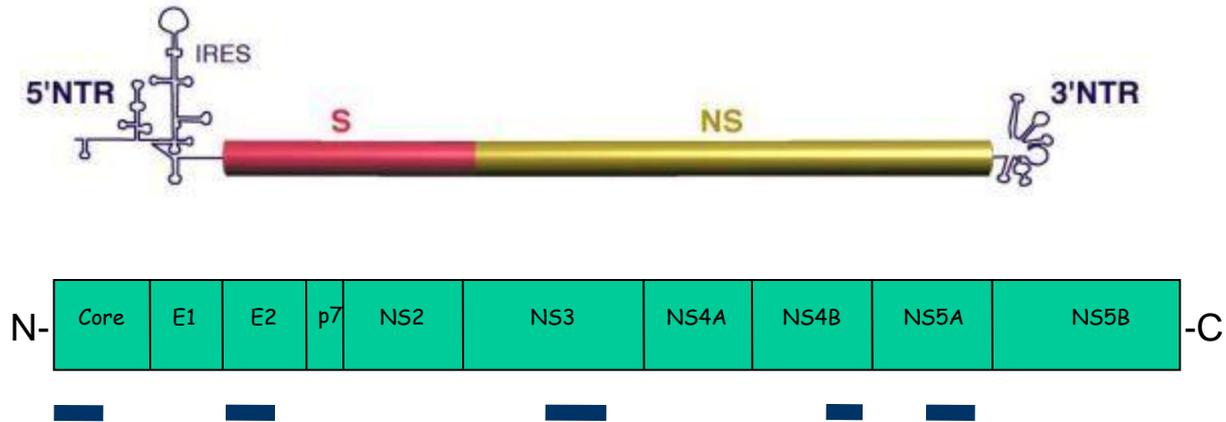
HCV antibody levels by Line Immunoassay *INNO-LIA HCV Ab III*



Outcome	n	C1	C1	E2	NS3	NS4	NS5
Chronic	12	100%	92%	67%	100%	92%	75%
Self-limited	18	83%	61%	50%	100%	67%	17%

Seroconversion/increase: 89% SL, 92% Ch
Seroreversion/decrease: 83% SL, 50% Ch

Profiling IgG secretion along time after HCV infection by ELISA



Core 1-119 - recombinant protein

E2 ecto domain - recombinant protein

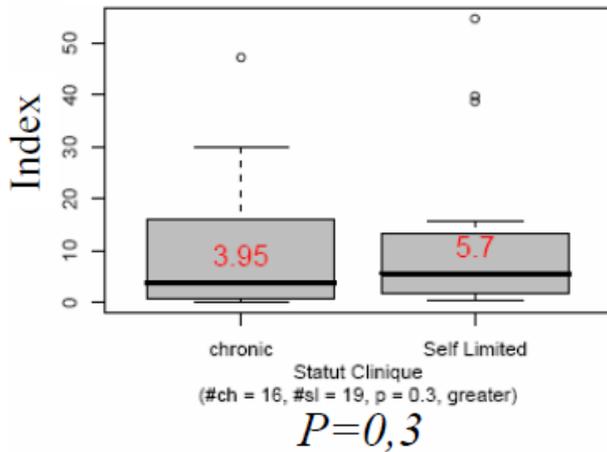
NS3 helicase - recombinant protein

NS4B 1910-1940 - synthetic peptide

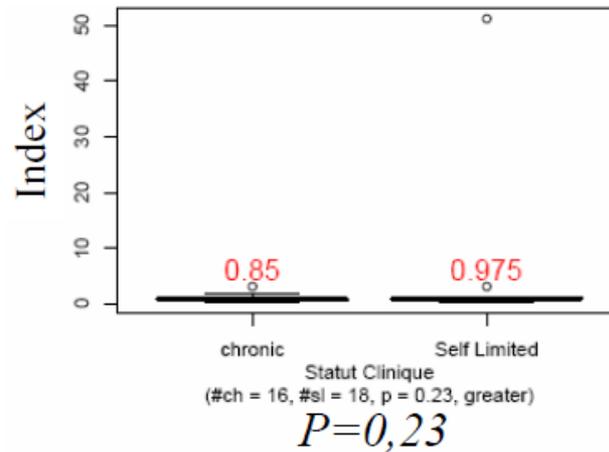
NS5A 2212-2213 - rec protein

Index OD/CO snapshot at week 12

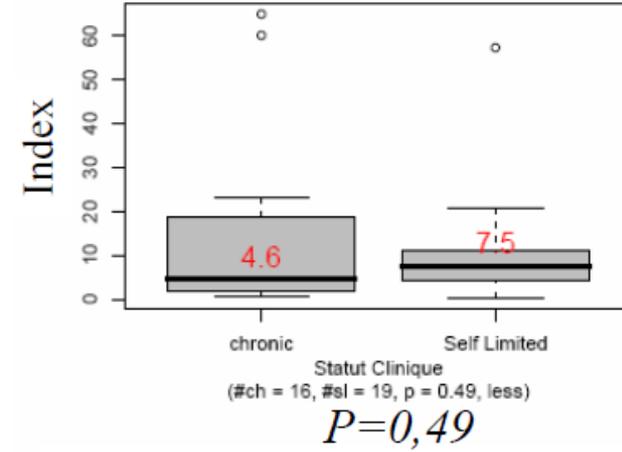
Core



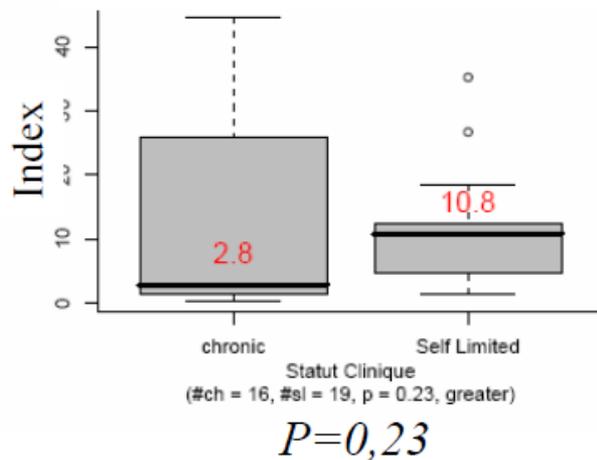
F



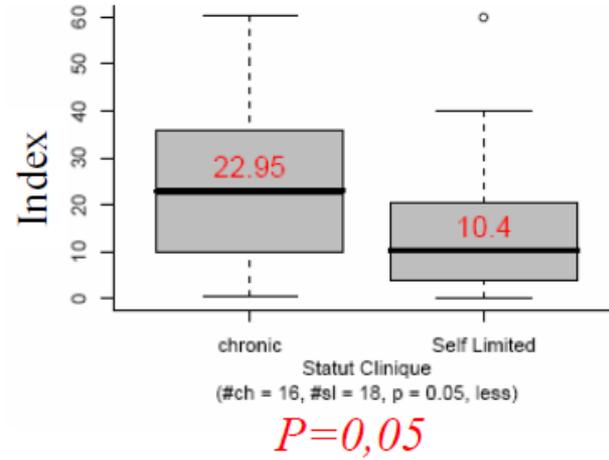
E2



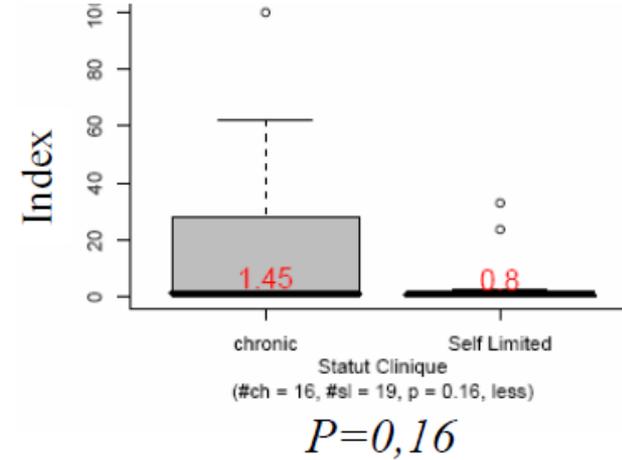
NS3



NS4

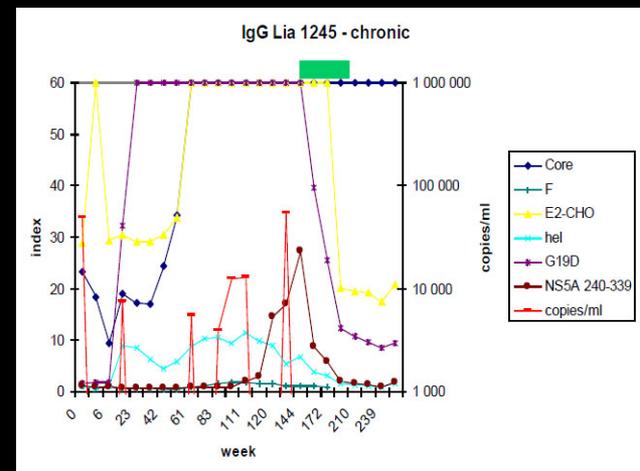
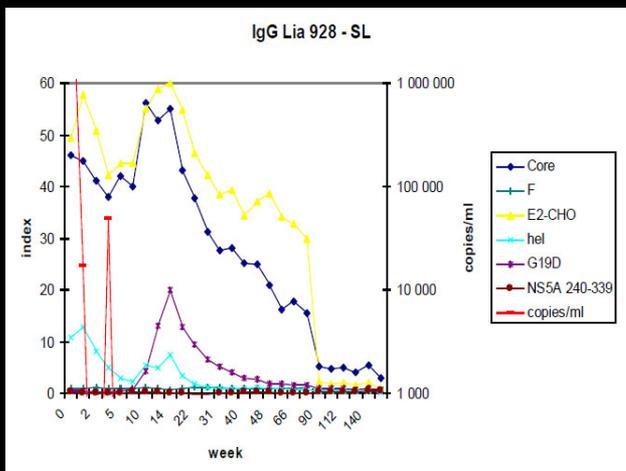
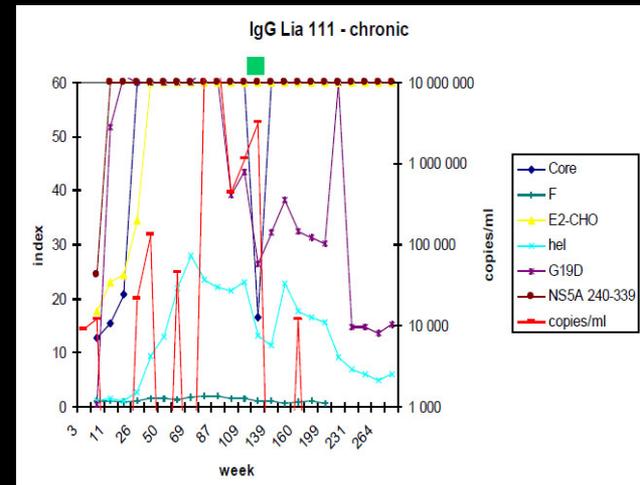
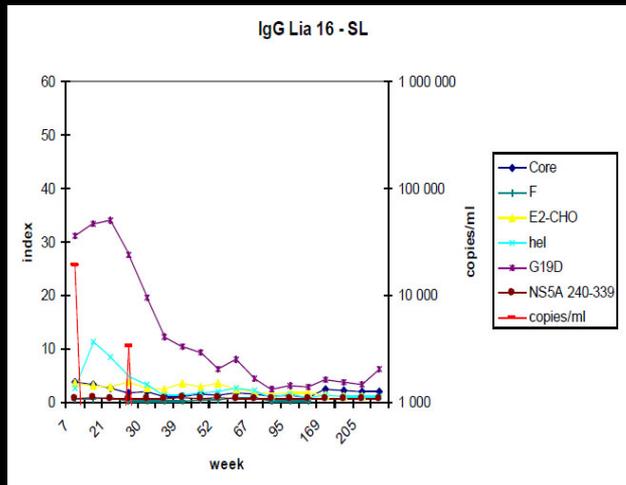


NS5

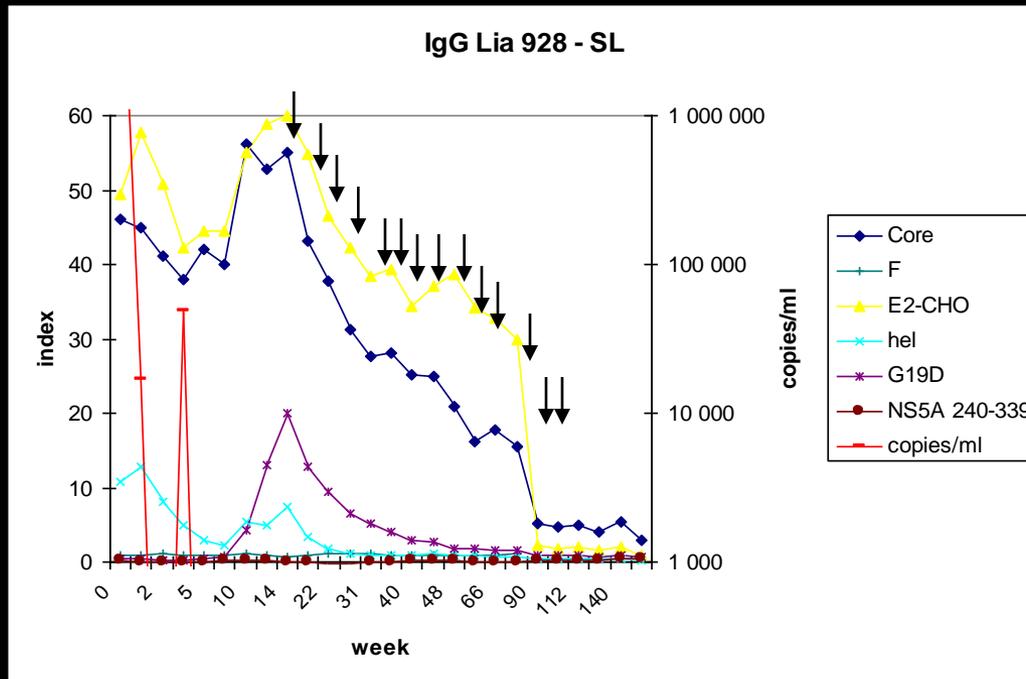


Quick View

IgG secretion and viral load



IgG secretion slope in self-limited patients after week 14

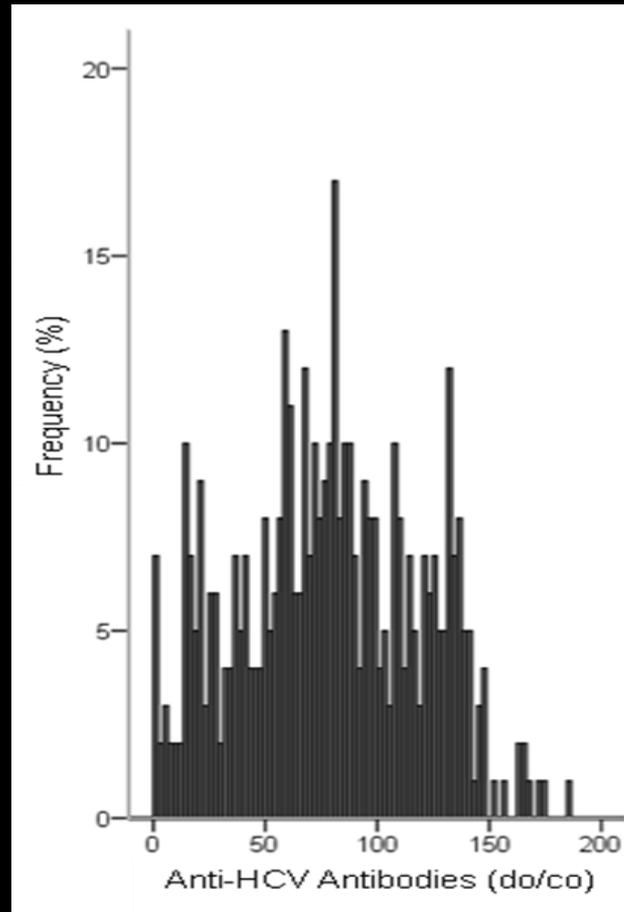


Considering each antigen

number of calculates values
% negative slopes

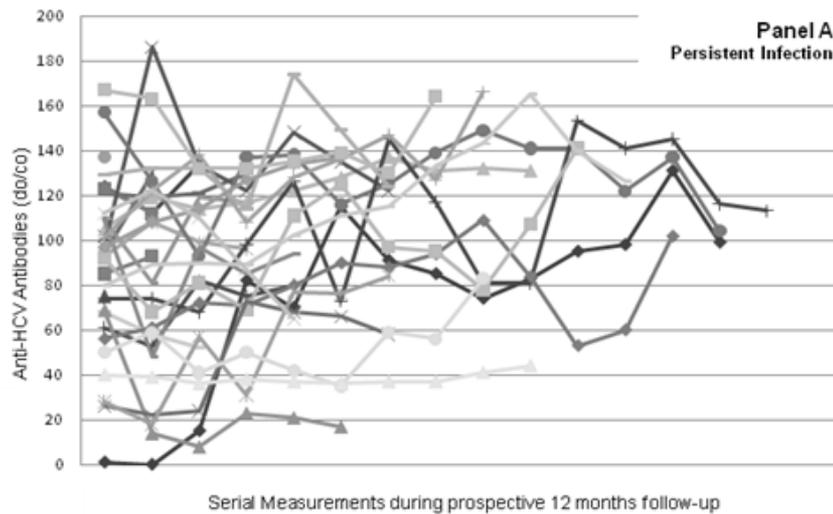
	Core	E2	NS3	NS4	NS5
number of calculates values	269	271	273	265	273
% negative slopes	95%	93%	95%	93%	99%

Distribution of 439 serial anti-HCV antibody measurements (MEIA/Axsym/Abbott) in 65 patients with acute HCV infection during the first 12 months after virus acquisition. (Rio de Janeiro, Brazil, 2001-2009)

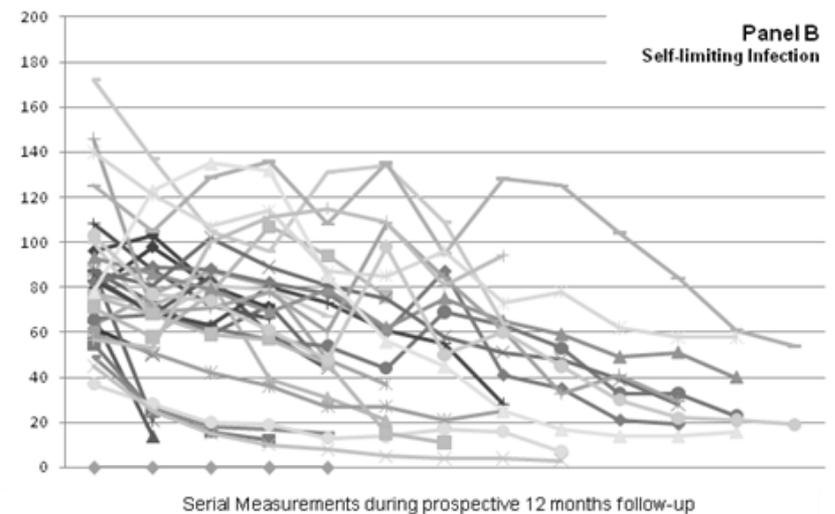


Longitudinal patterns of serial anti-HCV antibody measurements (do/co)

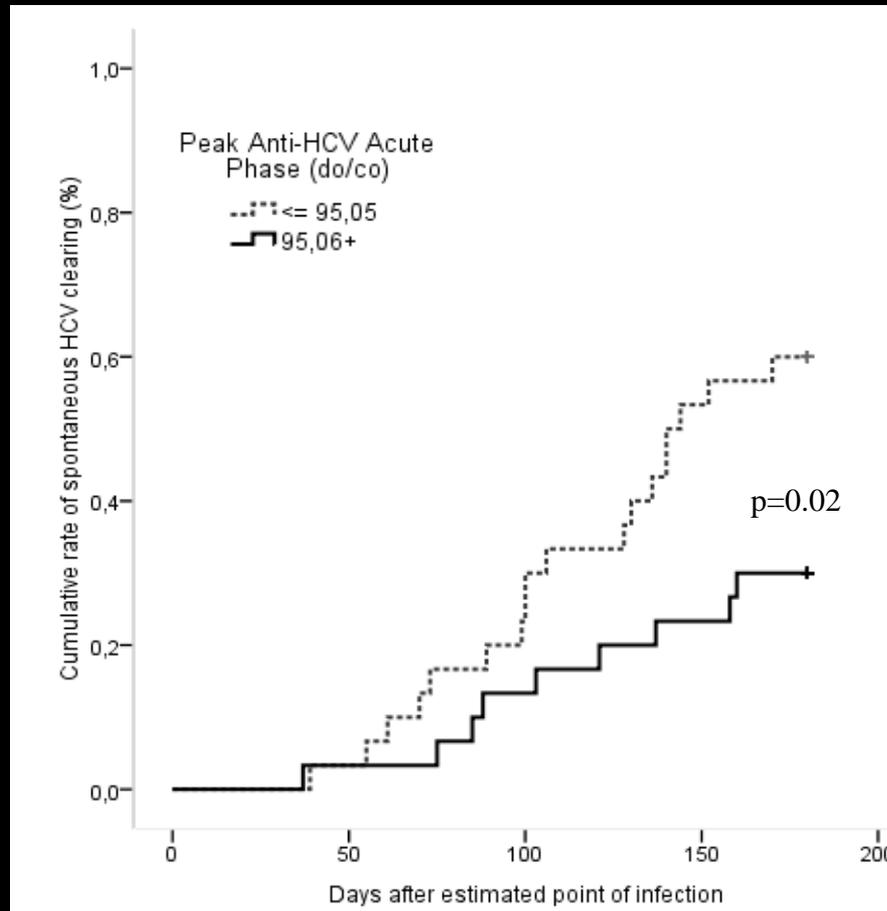
Persistent Infection



Self-Limiting Infection



Spontaneous viral clearance (SVC) was independently related to peak anti-HCV within the first 6 months of follow-up.
(median value of the distribution, 95.05 do/co was used as the cut-off)



Anti-HCV antibodies (s/co) during first 12 months of follow-up in 65 patients with acute HCV infection, stratified according to viral clearing status

Anti-HCV Antibodies (s/co)	Total	SVC ^b (n=34)		Non-SVC (n=31)	p-value SVC vs. Non-SVC	p-value before SVC vs. after SVC
		Before SVC	After SVC			
At Baseline/First Visit	78.7 (60.7-93.8)	n.a. ^c	n.a.	93.9 (67.8-111.9)	0.26	n.a.
Median during follow-up	66.2 (47.8-79.5)	71.0 (55.8-80.0)	55.1 (17.9-71.8)	105.5 (75.4-123.6)	<0.0001	0.04
Serial during follow-up ^d	62.7 (35.2-85.0)	79.4 (66.3-103.0)	56.0 (25.4-79.3)	98.4 (70.4-127.4)	<0.0001	<0.0001

^a Data given as median (interquartile range).

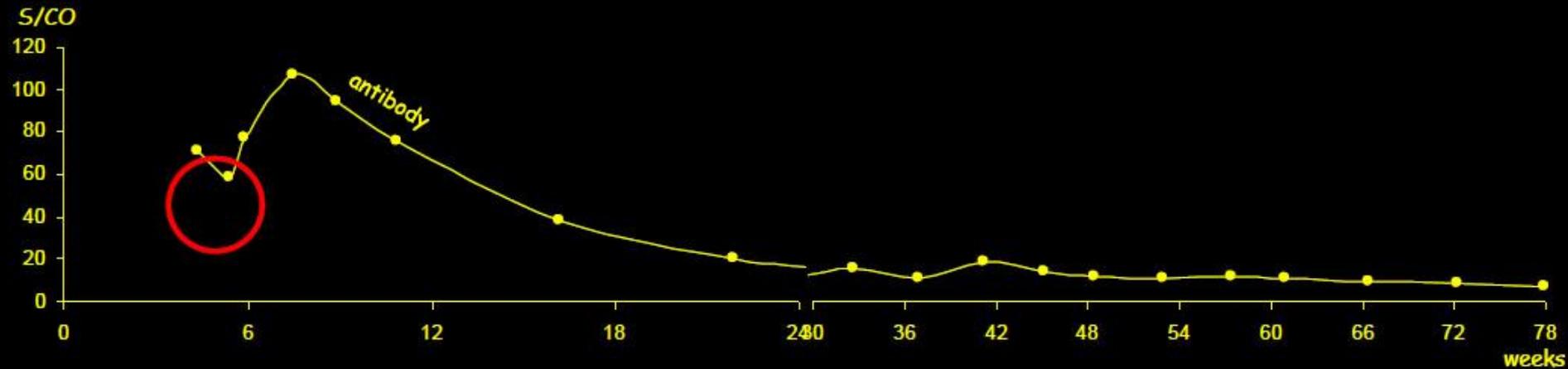
^b Spontaneous Viral Clearance (SVC) was defined as a series of at least 3 negative HCV RNA results within 12 months after the estimated point of infection.

^c n.a. denotes not applicable.

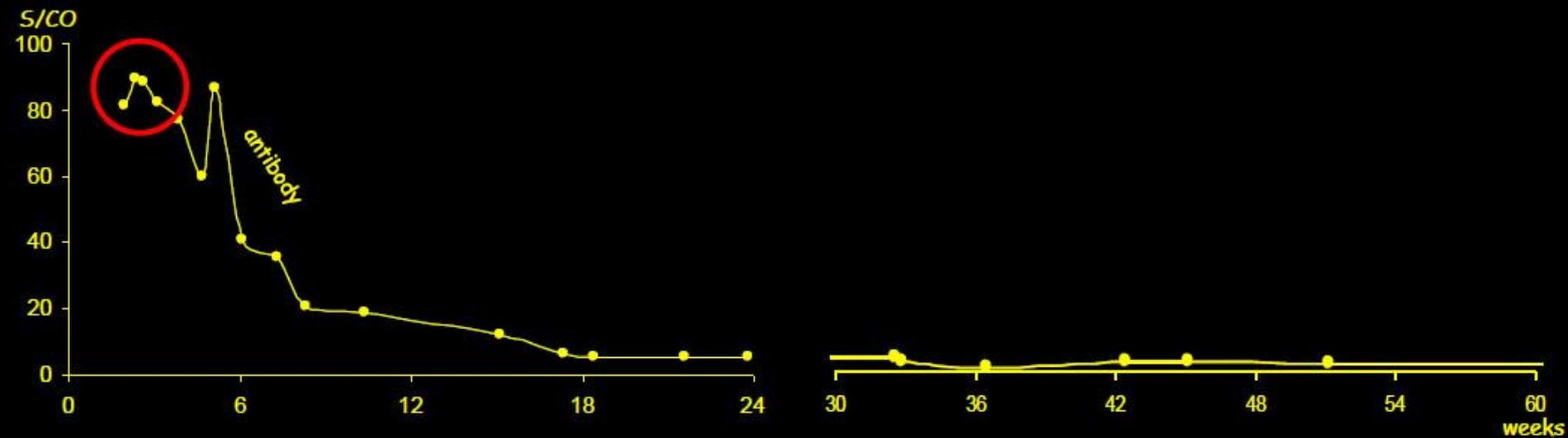
^d All anti-HCV antibody measures per patient during the first 12 months from the estimated date of infection were considered and weighted equally. P-value for group comparison calculated from linear-mixed effects regression.

Start Treatment?

HCV RNA



HCV RNA



Conclusions

Acute Phase of HCV Infection

1. Immediate early treatment is not always necessary, especially among symptomatic patients.
2. Antibody profiles can predict disease outcome.
3. HCV RNA is not the best predictor due to intermittent viremia.
4. Serial follow up recommended during the early phase (ALT, HCV RNA, anti-HCV).
5. In need of diagnostic assays specific for acute HCV infection.

Acknowledgements

BRAZIL

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Patients who accepted to participate in the study

INTERNATIONAL

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Thank you !!!!!

