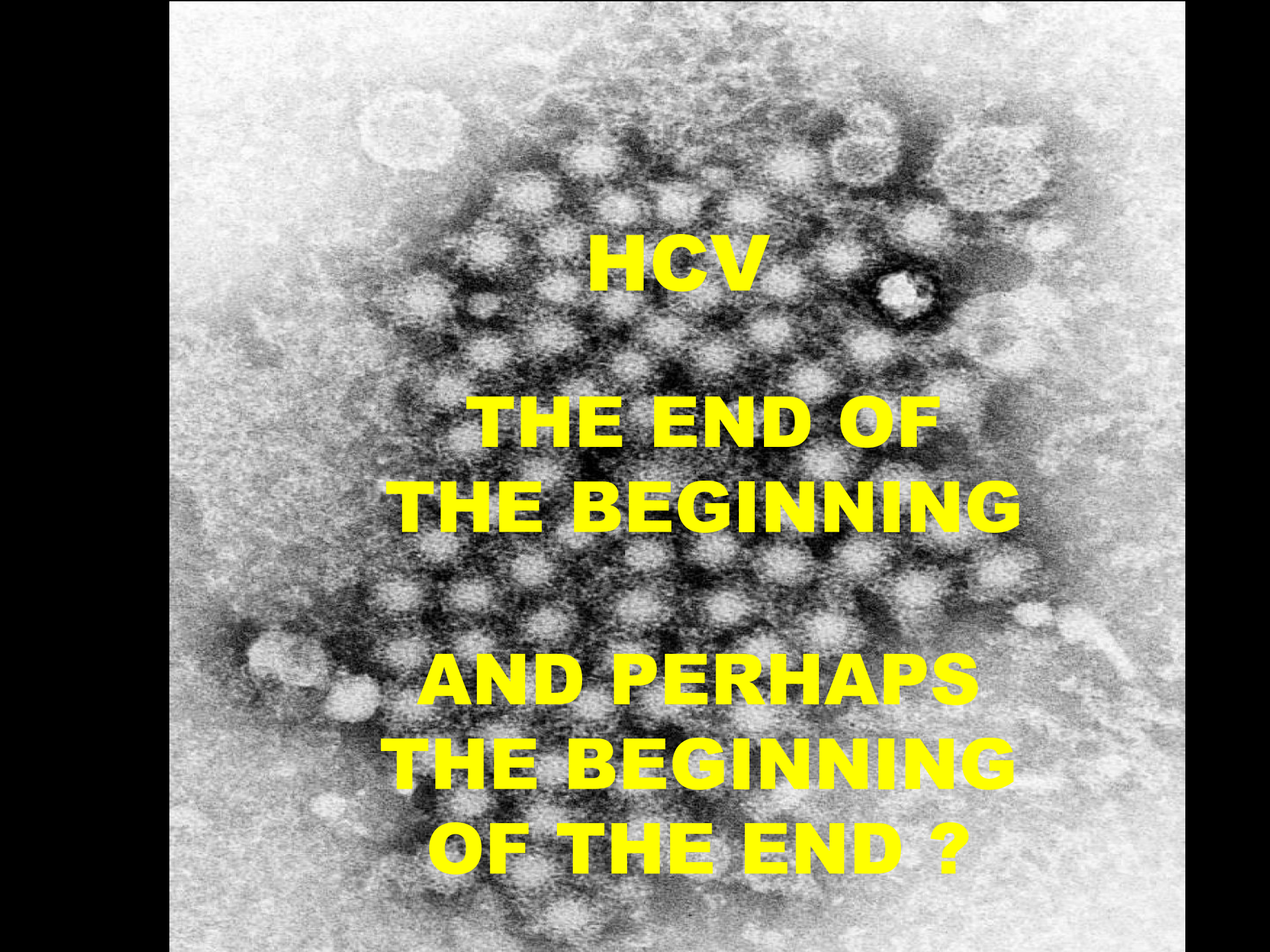


The background of the slide is a grayscale electron micrograph showing numerous spherical Hepatitis C Virus (HCV) particles. These particles have a distinct outer envelope and a darker, textured core. They are scattered across the field of view, with some appearing more clearly than others. The overall texture is grainy and high-magnification.

HCV

**THE END OF
THE BEGINNING**

**AND PERHAPS
THE BEGINNING
OF THE END ?**

TWO INTERTWINED STORIES

- 1) The story of my life (abridged version)**
- 2) The life (and possible death) of the Hepatitis C Virus**



HJA: YOUTH



I AM NOT REALLY BALD

I AM A HAIR DONOR

THE ROCHESTER YEARS





SELECTIVE SERVICE SYSTEM

Approval Not Required.

ORDER TO REPORT FOR INDUCTION

BRING THIS ORDER WITH YOU FOR ADMITTANCE
TO NEW FEDERAL OFFICE BUILDINGTexas Local Board No. 112
Selective Service System
Rm 8A38, 819 Taylor Street
Fort Worth, Texas 76102

(LOCAL BOARD STAMP)

October 27, 1966

(Date of mailing)

SELECTIVE SERVICE NO.

41 112 46 1333

The President of the United States,

To

Harvey Alter
Rochester, NY

15

GREETING:

You are hereby ordered for induction into the Armed Forces of the United States, and to report
at Rm 8A38, 819 Taylor Street
Fort Worth, Texas 76102
(Place of reporting).on NOV 16 1966 at 6:30 A.M.
(Date) (Hour)

for forwarding to an Armed Forces Induction Station.

(Member or clerk of Local Board)

IMPORTANT NOTICE

(Read Each Paragraph Carefully)

IF YOU HAVE HAD PREVIOUS MILITARY SERVICE, OR ARE NOW A MEMBER OF THE NATIONAL GUARD OR A RESERVE COMPONENT OF THE ARMED FORCES, BRING EVIDENCE WITH YOU. IF YOU WEAR GLASSES, BRING THEM. IF MARRIED, BRING PROOF OF YOUR MARRIAGE. IF YOU HAVE ANY PHYSICAL OR MENTAL CONDITION WHICH, IN YOUR OPINION, MAY DISQUALIFY YOU FOR SERVICE IN THE ARMED FORCES, BRING A PHYSICIAN'S CERTIFICATE DESCRIBING THAT CONDITION, IF NOT ALREADY FURNISHED TO YOUR LOCAL BOARD.

Valid documents are required to substantiate dependency claims in order to receive basic allowance for quarters. Be sure to take the following with you when reporting to the induction station. The documents will be returned to you. (a) FOR LAWFUL WIFE OR LEGITIMATE CHILD UNDER 21 YEARS OF AGE—original, certified copy or photostat of a certified copy of marriage certificate, child's birth certificate, or a public or church record of marriage issued over the signature and seal of the custodian of the church or public records; (b) FOR LEGALLY ADOPTED CHILD—certified court order of adoption; (c) FOR CHILD OF DIVORCED SERVICE MEMBER (Child in custody of person other than claimant)—(1) Certified or photostatic copies of receipts from custodian of child evidencing serviceman's contributions for support, and (2) Divorce decree, court support order or separation order; (d) FOR DEPENDENT PARENT—affidavits establishing that dependency.

Bring your Social Security Account Number Card. If you do not have one, apply at nearest Social Security Administration Office. If you have life insurance, bring a record of the insurance company's address and your policy number. Bring enough clean clothes for 3 days. Bring enough money to last 1 month for personal purchases.

This Local Board will furnish transportation, and meals and lodging when necessary, from the place of reporting to the induction station where you will be examined. If found qualified, you will be inducted into the Armed Forces. If found not qualified, return transportation and meals and lodging when necessary, will be furnished to the place of reporting.

You may be found not qualified for induction. Keep this in mind in arranging your affairs, to prevent any undue hardship if you are not inducted. If employed, inform your employer of this possibility. Your employer can then be prepared to continue your employment if you are not inducted. To protect your right to return to your job if you are not inducted, you must report for work as soon as possible after the completion of your induction examination. You may jeopardize your reemployment rights if you do not report for work at the beginning of your next regularly scheduled working period after you have returned to your place of employment.

Willful failure to report at the place and hour of the day named in this Order subjects the violator to fine and imprisonment. Bring this Order with you when you report.

If you are so far from your own local board that reporting in compliance with this Order will be a serious hardship, go immediately to any local board and make written request for transfer of your delivery for induction, taking this Order with you.

**THE FIRST
CRITICAL
TURNING
POINT**

THE SECOND CRITICAL TURNING POINT



REJECTION



There is no
elevator to

success

You have
to take
the stairs

STUDY DESIGN: NIH PROSPECTIVE STUDIES OF TRANSFUSION-ASSOCIATED HEPATITIS

**Donors samples
for retrospective
testing**



**Heart-lung
machine**

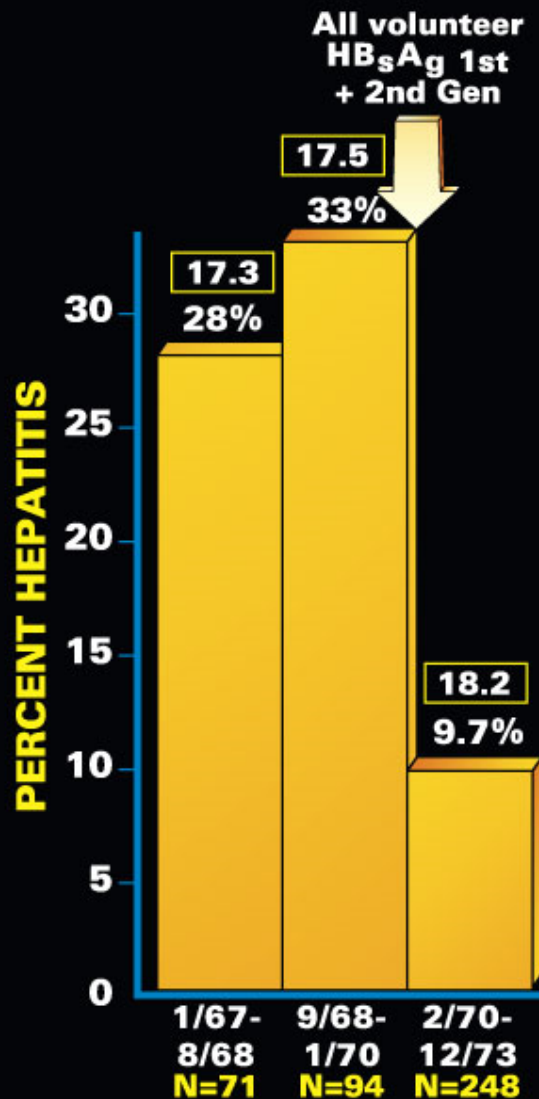


**Recipient
sampling**

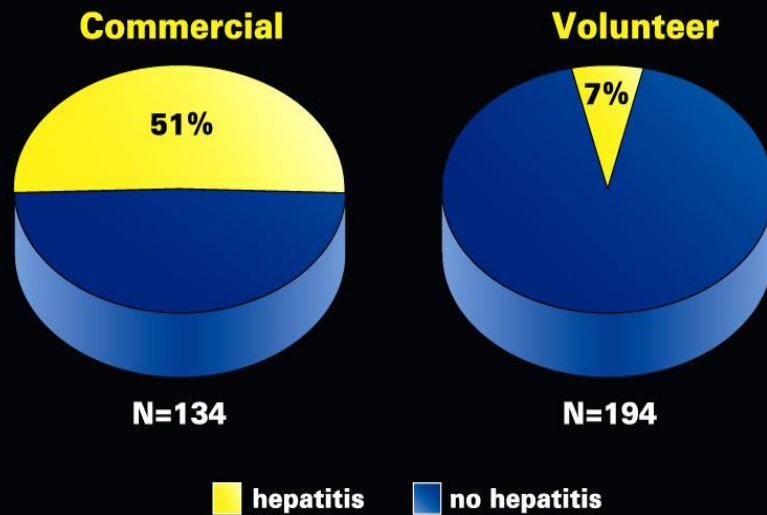


ALT, serology, PCR, storage

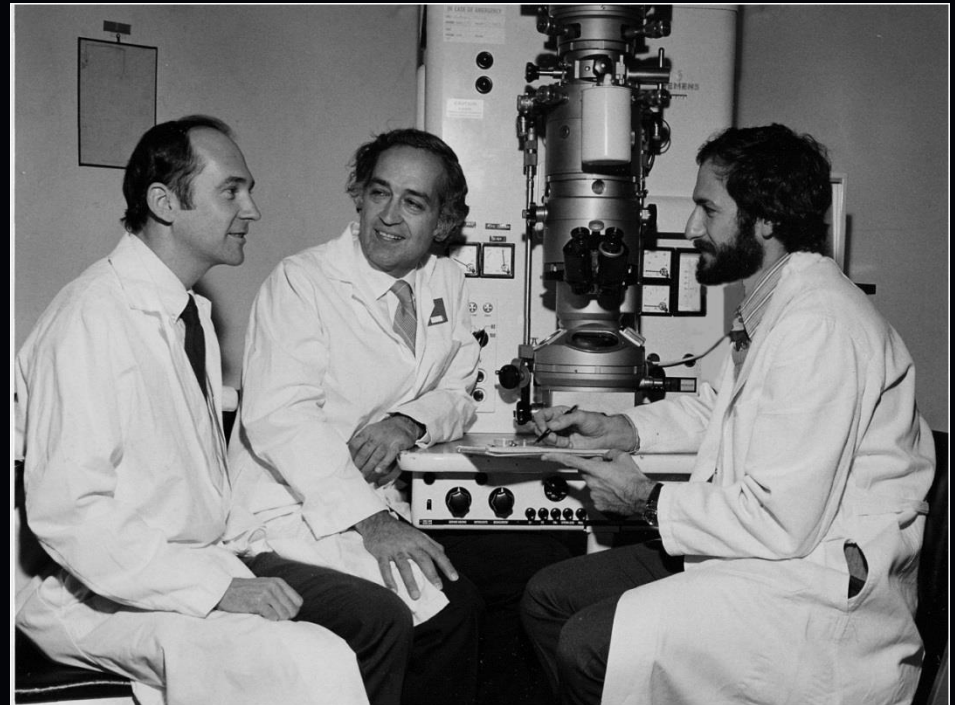
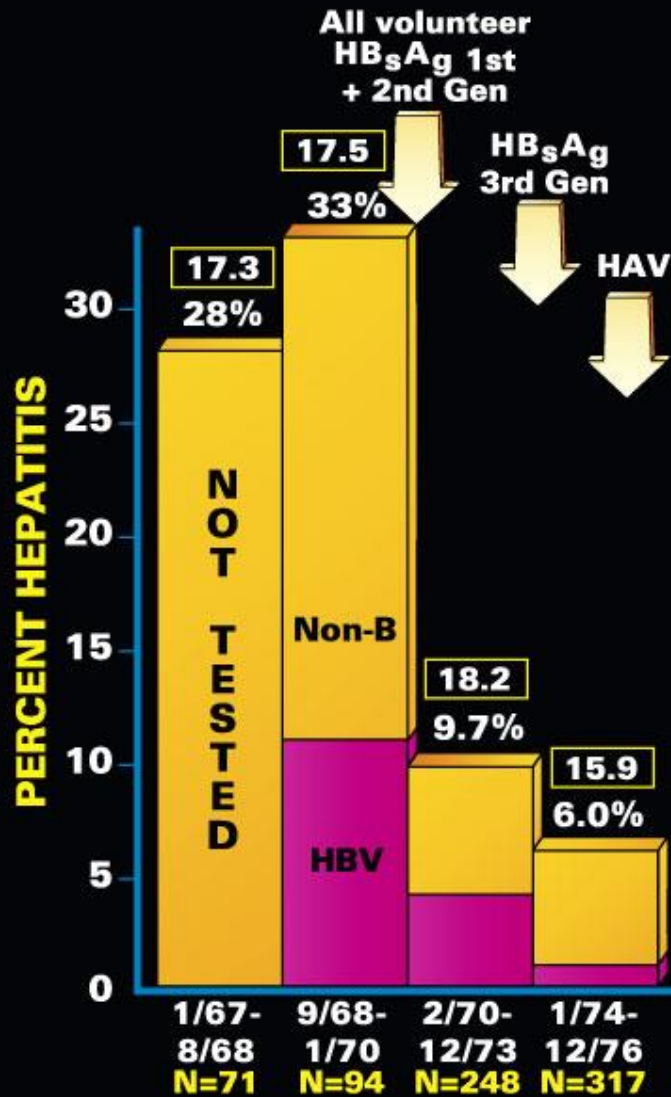
Post-Transfusion Hepatitis at NIH-1



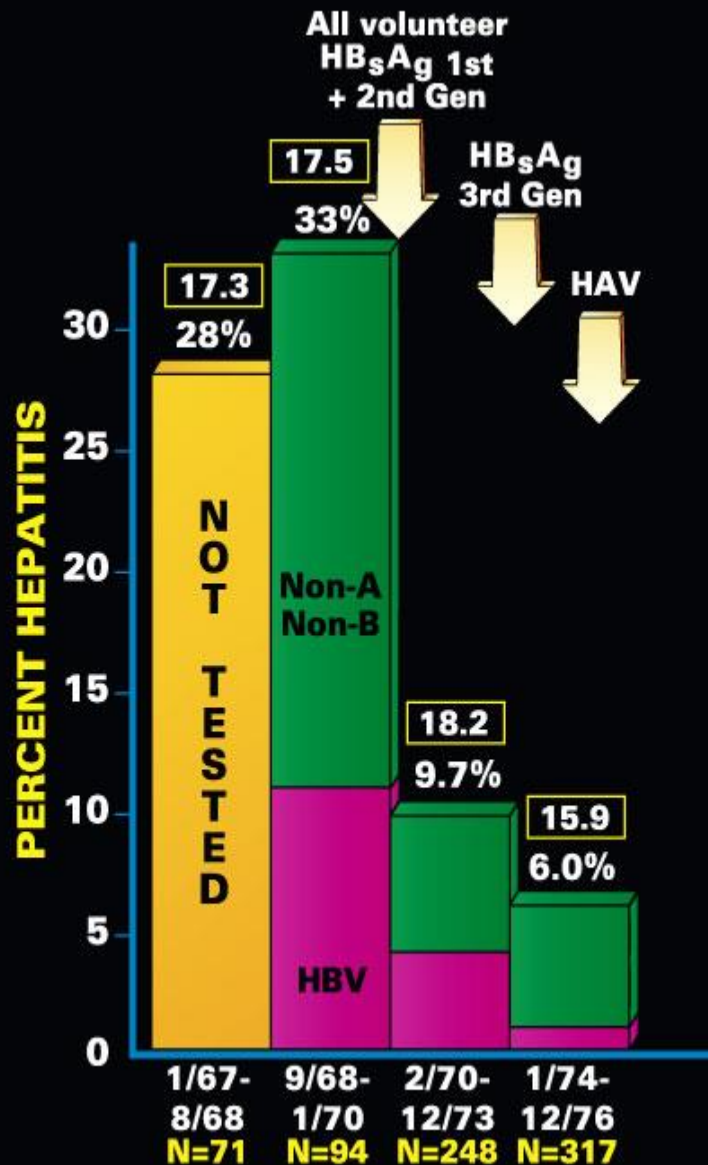
POST-TRANSFUSION HEPATITIS ACCORDING TO DONOR SOURCE



Post-Transfusion Hepatitis at NIH-2



Post-Transfusion Hepatitis at NIH-3

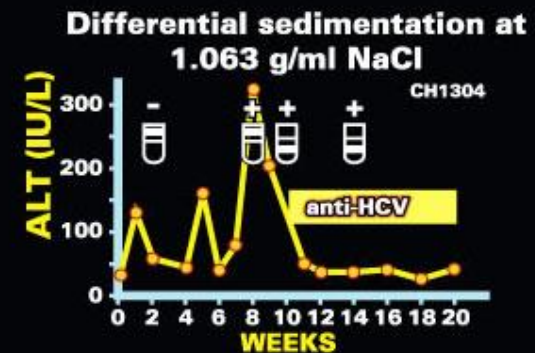
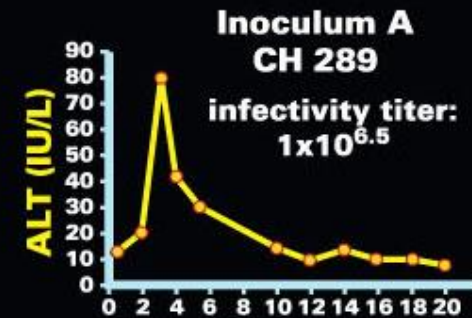
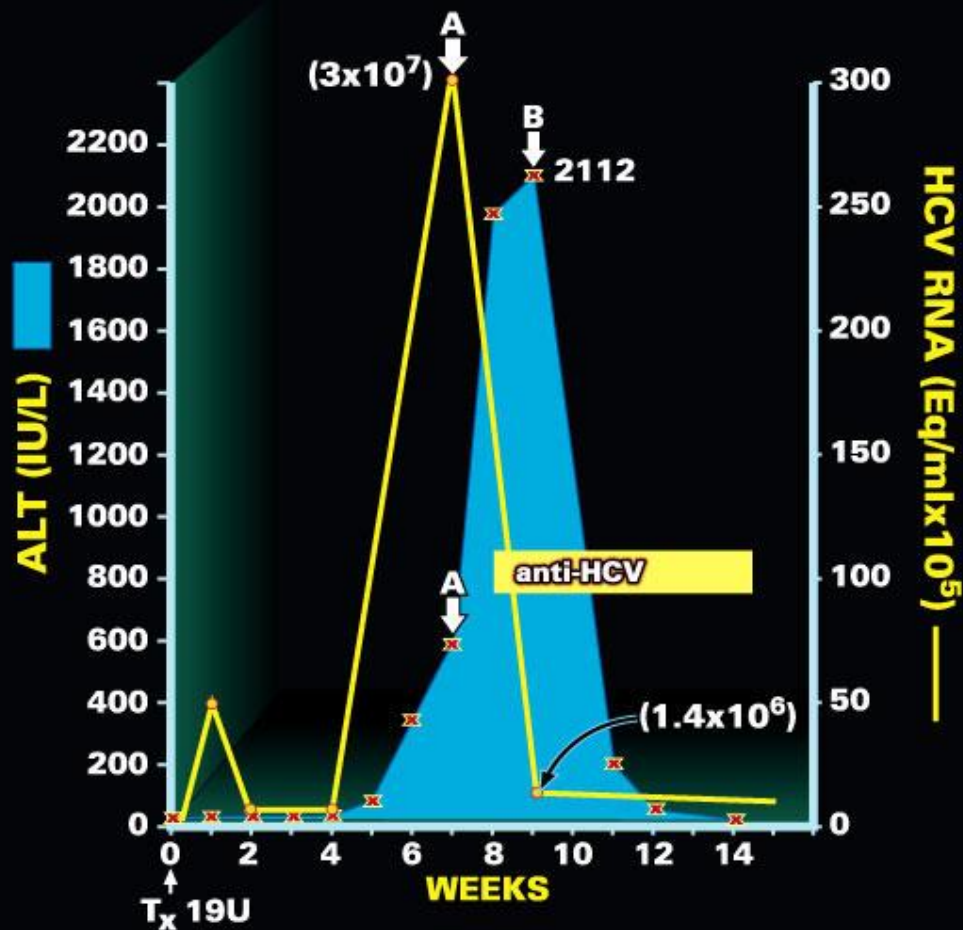


Transmitted From

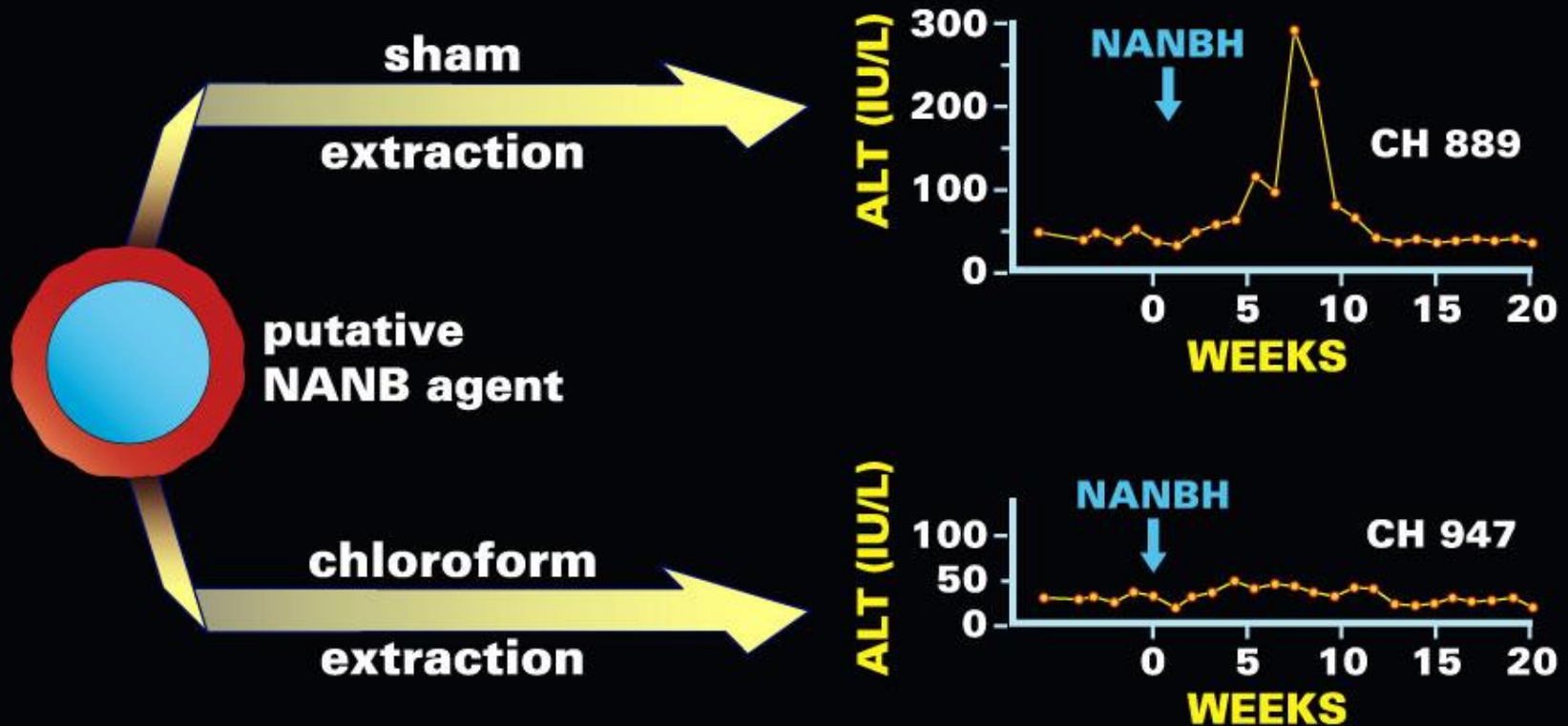
- Patients with acute and chronic NANB hepatitis
- Asymptomatic implicated donors



HEPATITIS C TRANSMISSION VS. VIRAL LOAD AND ANTIBODY RESPONSE IN PATIENT H

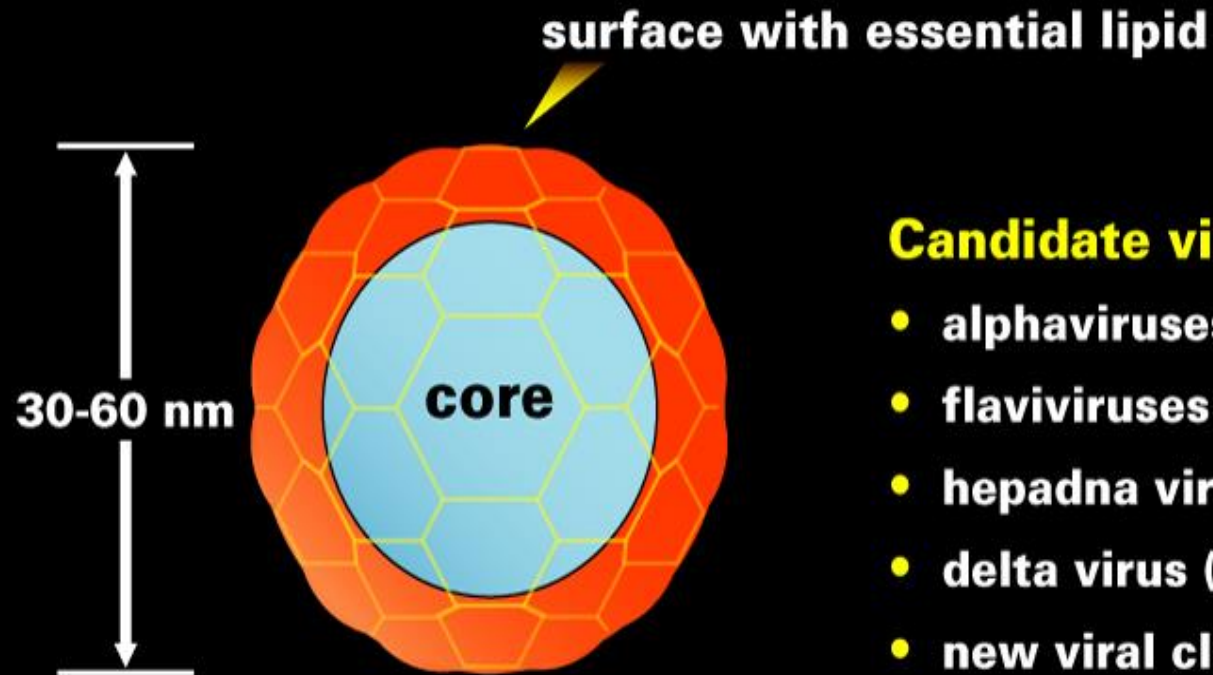


CHLOROFORM EXTRACTION OF H'77 NON-A, NON-B INOCULUM



Feinstone, et al Infection & Immunity 1983; 41: 816

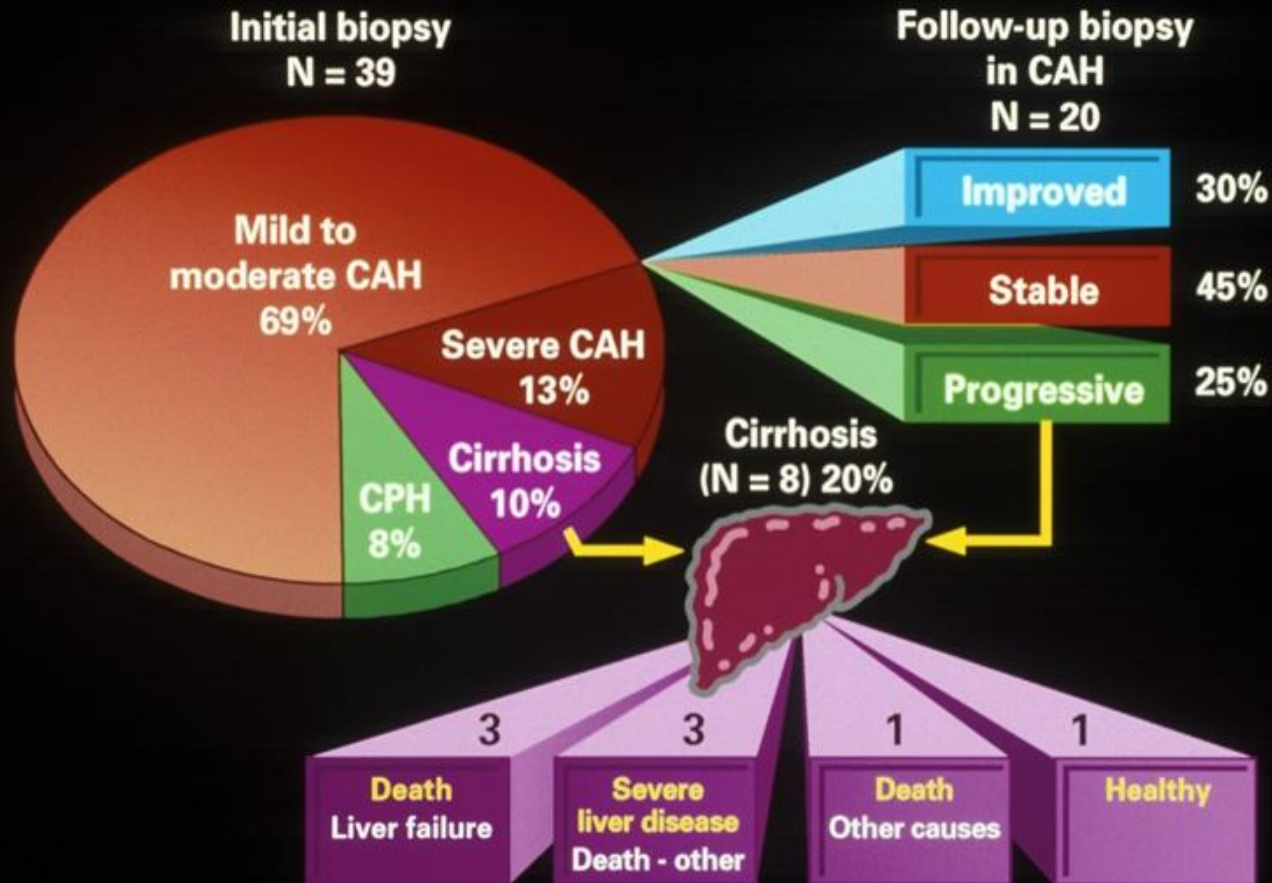
PUTATIVE STRUCTURE OF THE TUBULAR FORMING NON-A, NON-B HEPATITIS AGENT



Candidate viruses

- alphaviruses (RNA)
- flaviviruses (RNA)
- hepadna viruses (DNA)
- delta virus (RNA)
- new viral class

Histologic Diagnosis and Outcome in Transfusion-Associated Hepatitis C

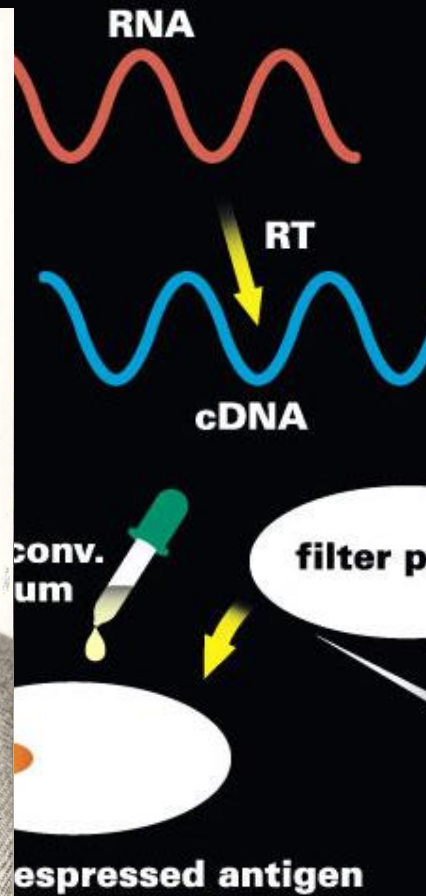
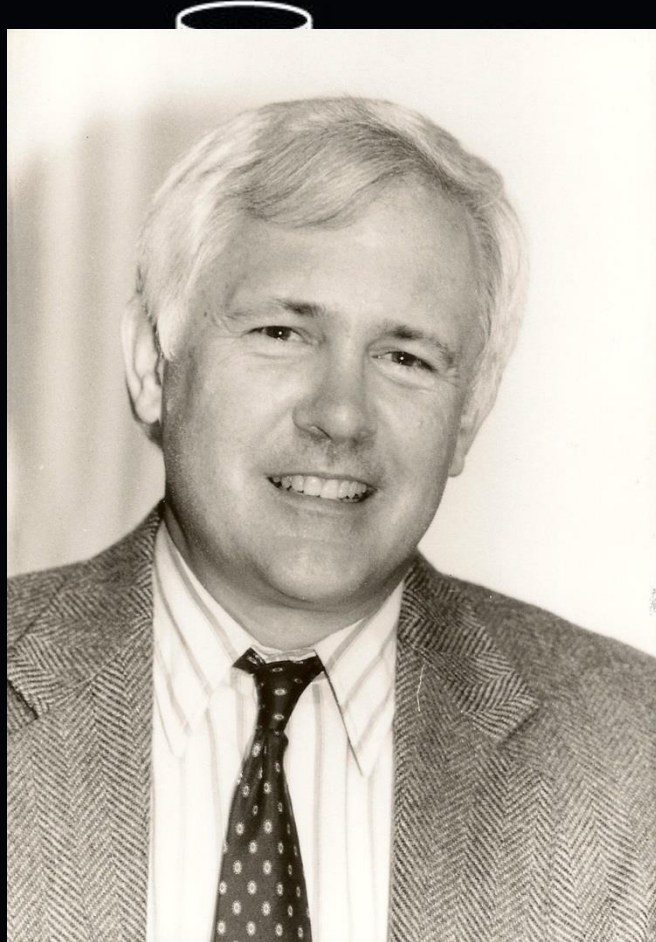


While the clinical severity of NANBH became increasingly evident over the next decade, no serologic, enzymatic, radioimmunologic or early molecular method led to a specific NANB assay or further elucidated the nature of the agent.

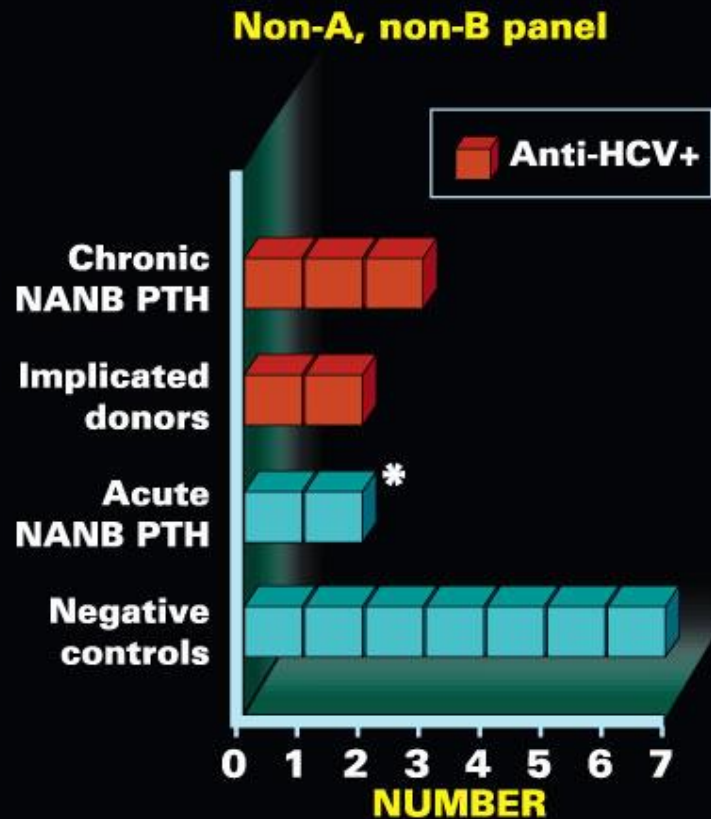
A POEM OF FRUSTRATION

**“I Can’t See The Forest
For The HB Ags”**

CLONING OF NANB AGENT IN GT-11 EXPRESSION VECTOR



VALIDATION OF THE CHIRON DISCOVERY FOR THE DETECTION OF NANB/HCV INFECTION

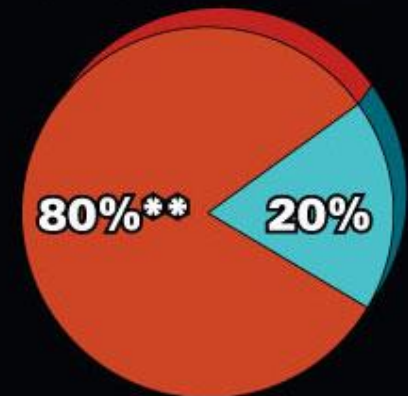


* Subsequent seroconversion

Seroconversion in 15 NANB PTH cases

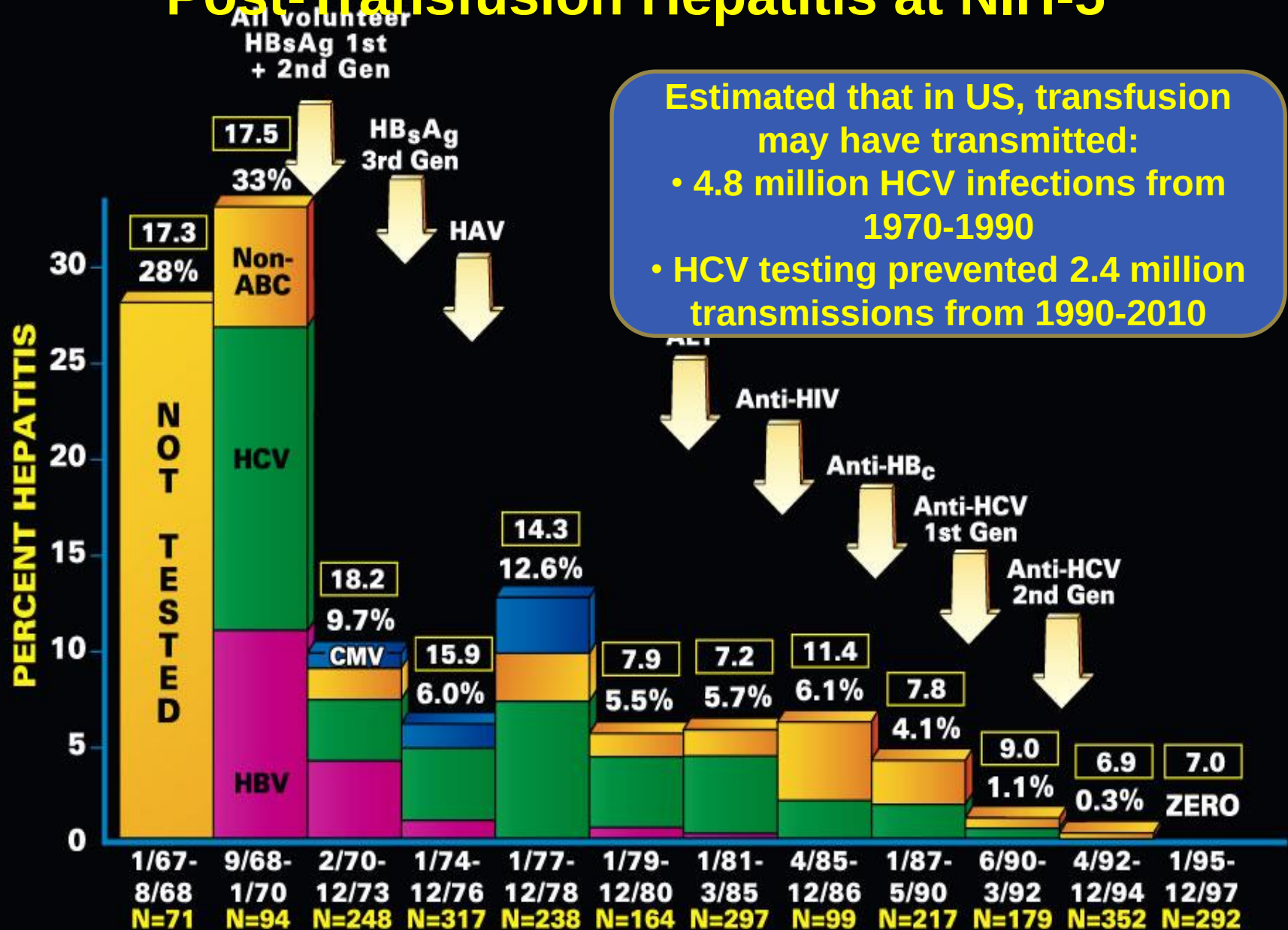


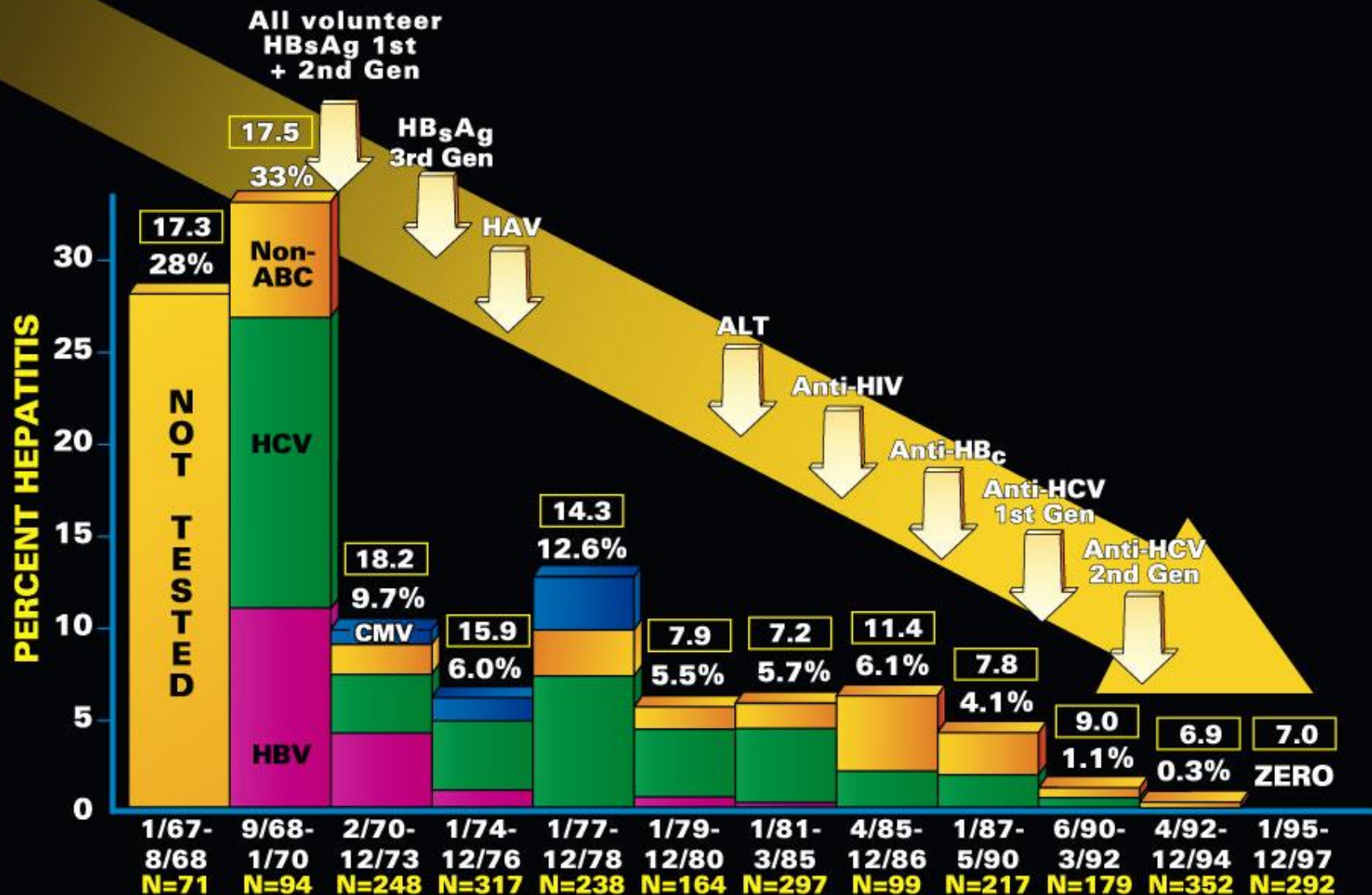
Detection of anti-HCV+ donor in 25 NANB PTH cases



** 88% with 2nd gen. assay

Post-Transfusion Hepatitis at NIH-5





WORK ETHIC OF A GOVERNMENT EMPLOYEE

**I ALWAYS GIVE 100%
AT WORK**

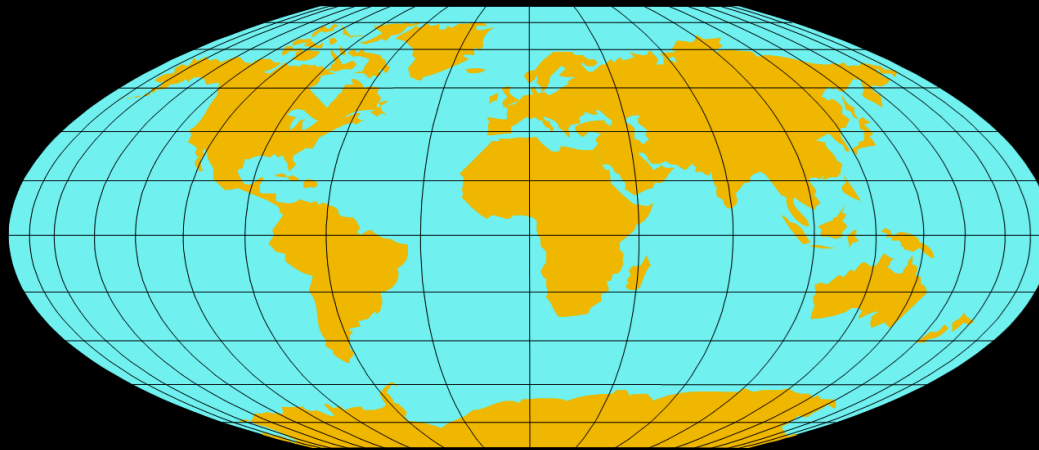
**12% on Monday
23% on Tuesday
37% on Wednesday
23% on Thursday
5% on Friday**

Worldwide Burden of Chronic Viral Hepatitis

World population: 7 billion

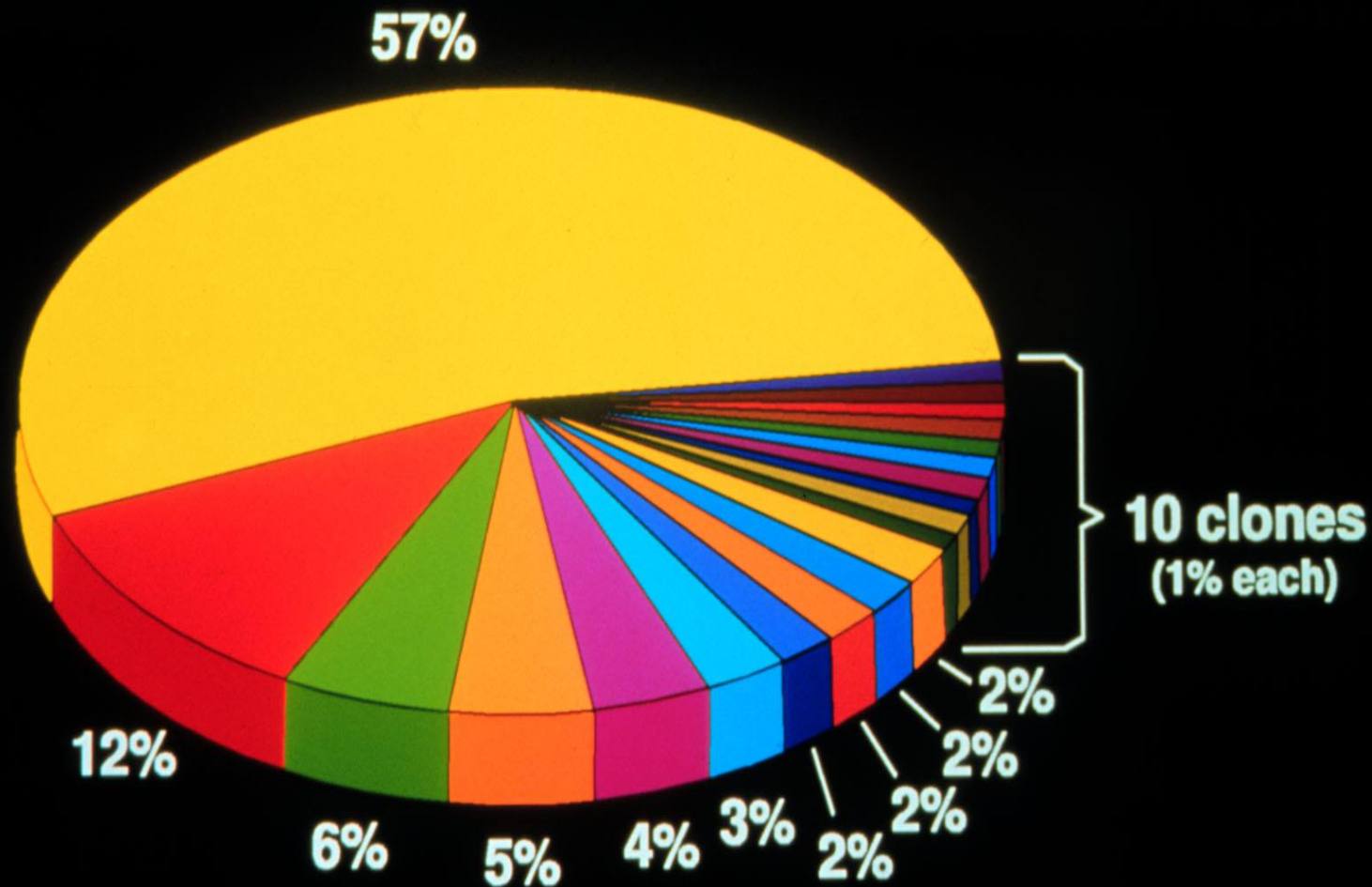
**HBV: 350 million
chronically infected**

**HCV: 70 million
chronically infected**



**5 million
in US**

**75%-85% of HCV
infections become
persistent**

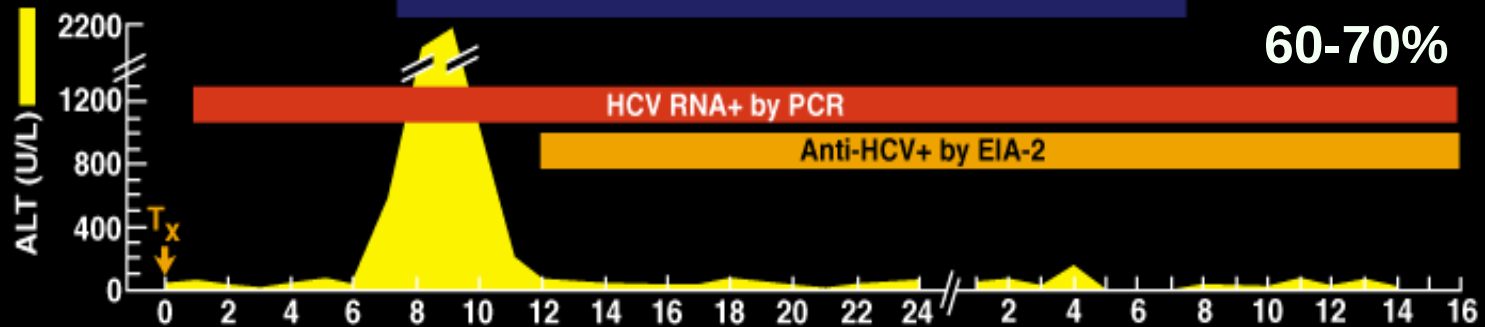


EVOLUTION OF HCV QUASISPECIES IN A PATIENT WITH RAPIDLY PROGRESSIVE CHRONIC HEPATITIS C

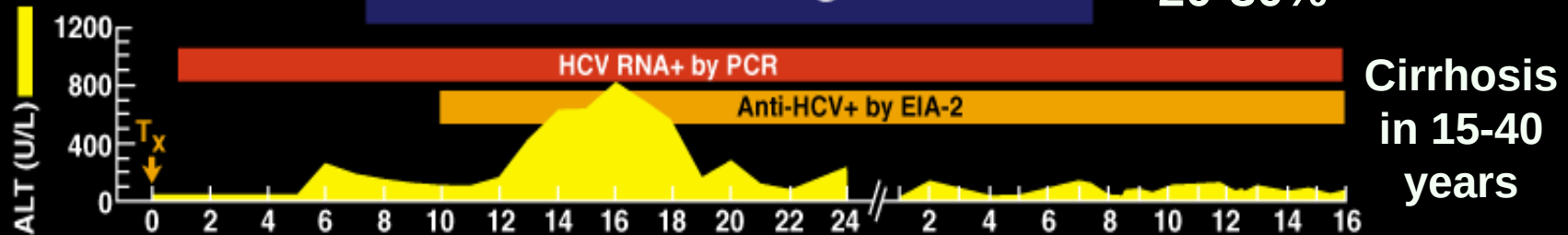


Outcome of Chronic HCV Infection in Transfusion-Associated Hepatitis C

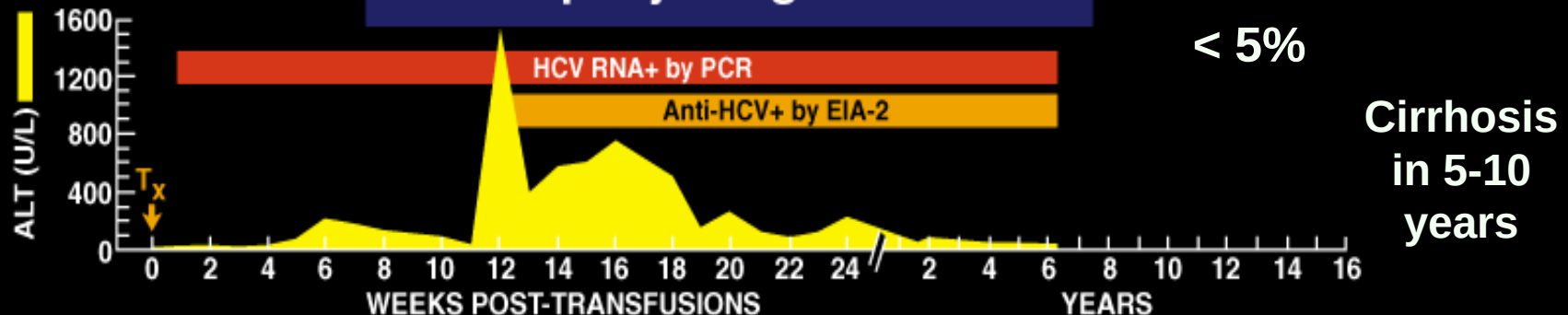
Stable or Slowly Progressive



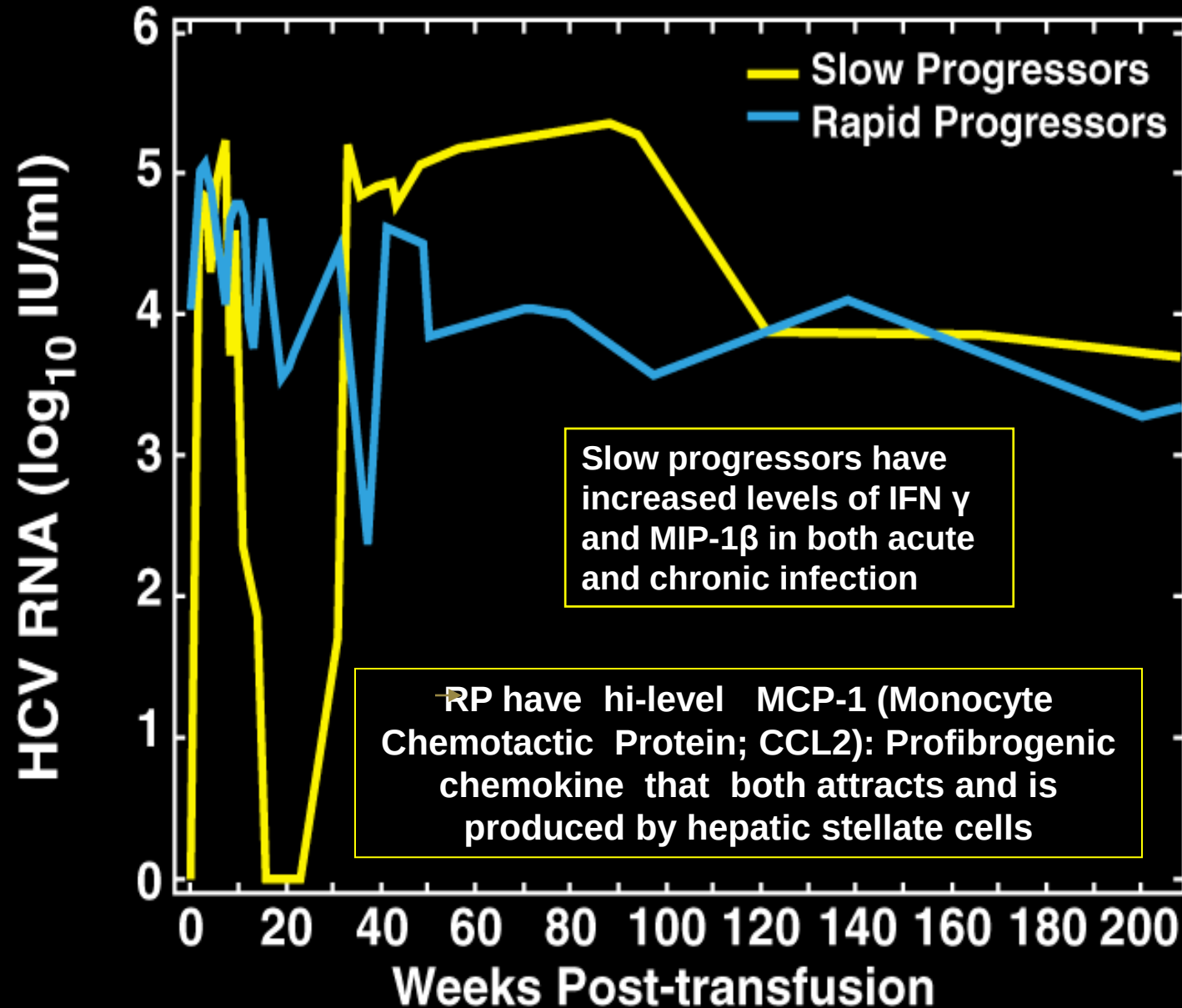
Severe and Progressive



Rapidly Progressive



Slow vs. Rapid HCV Progressors: Viral Load

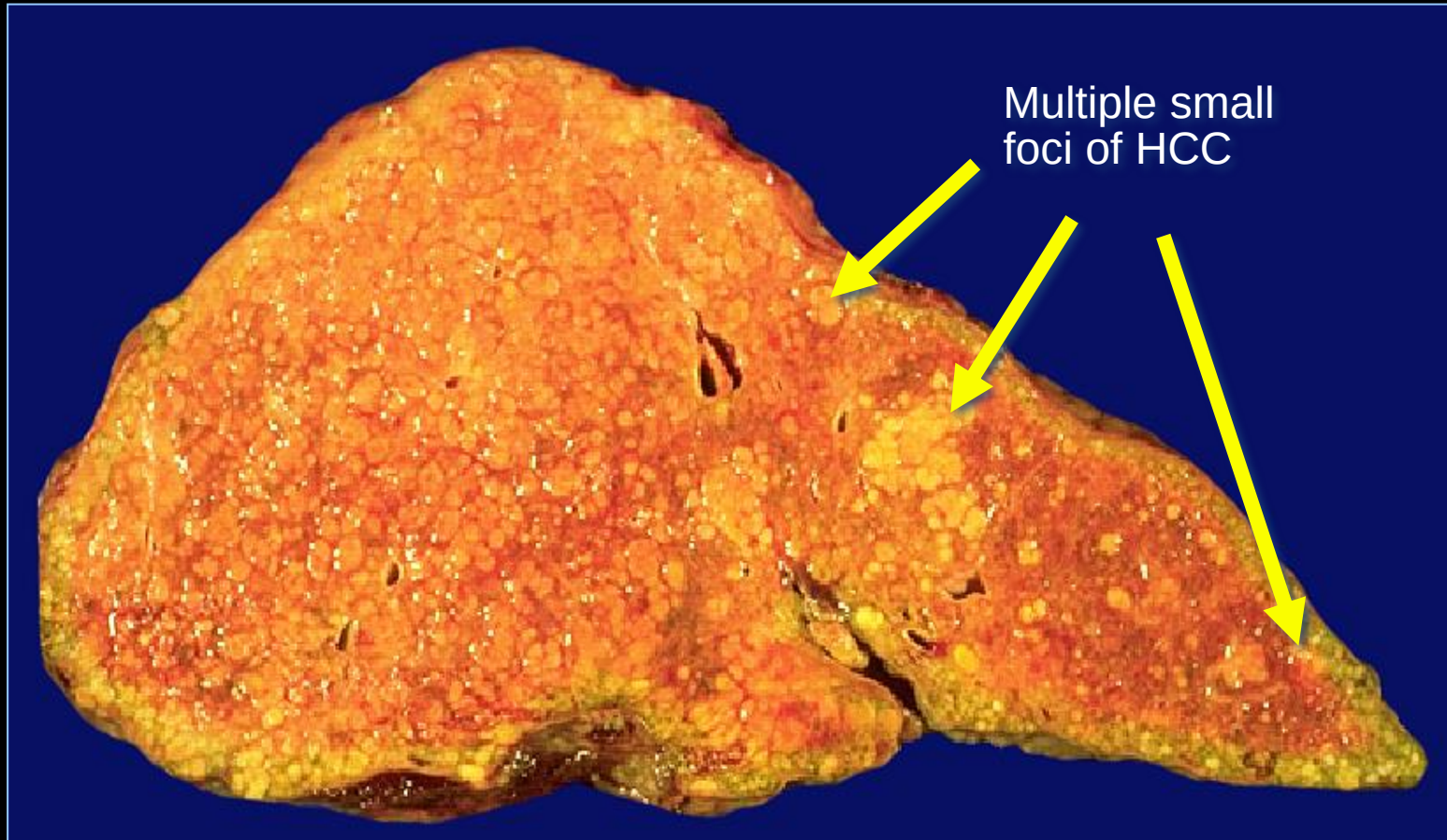


THE MARRIAGE YEARS

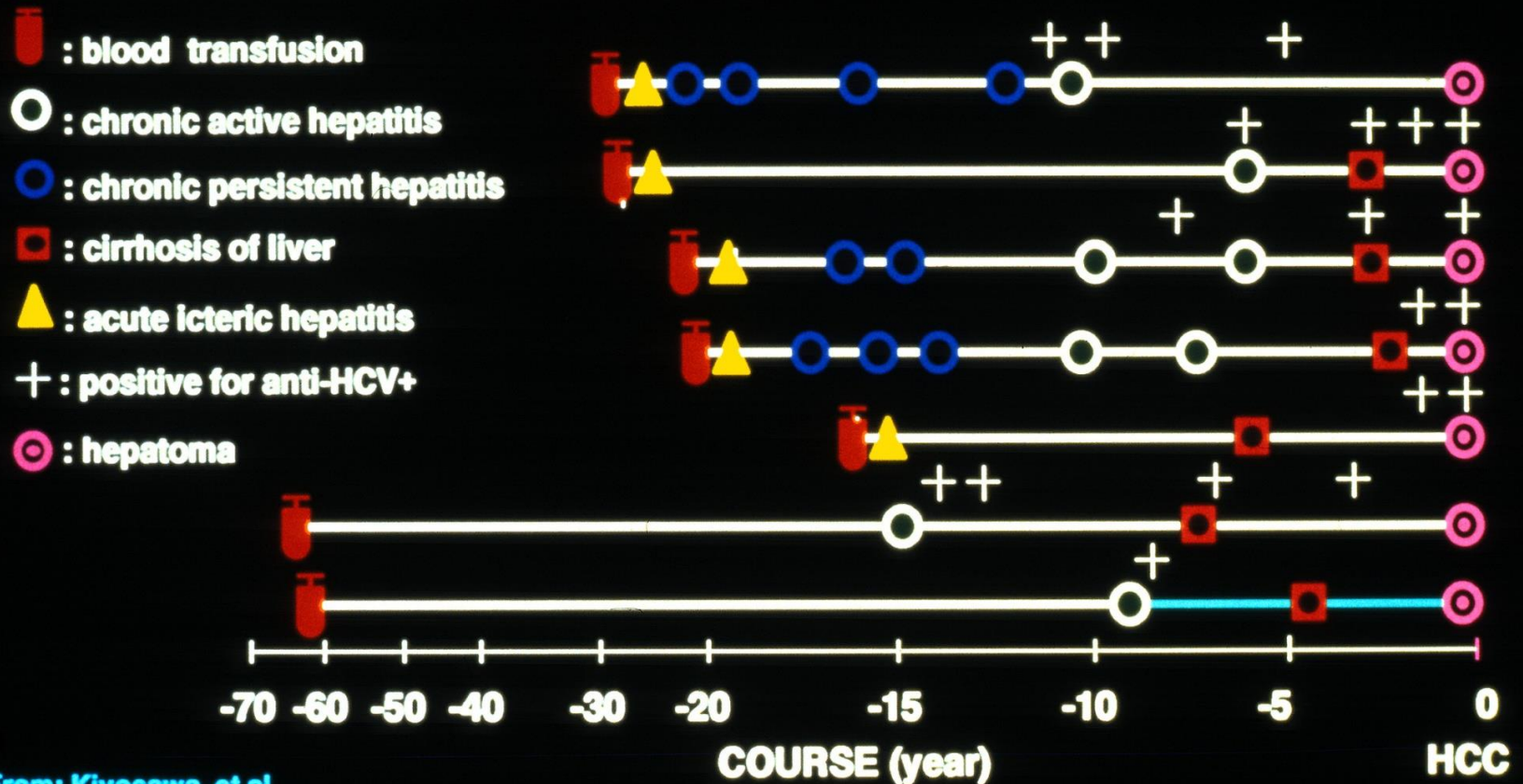
**My wife said,
“you are the answer to my
prayers”**

**“You are not what I prayed
for, but apparently you are
the answer”**

HCV Cirrhosis and HCC

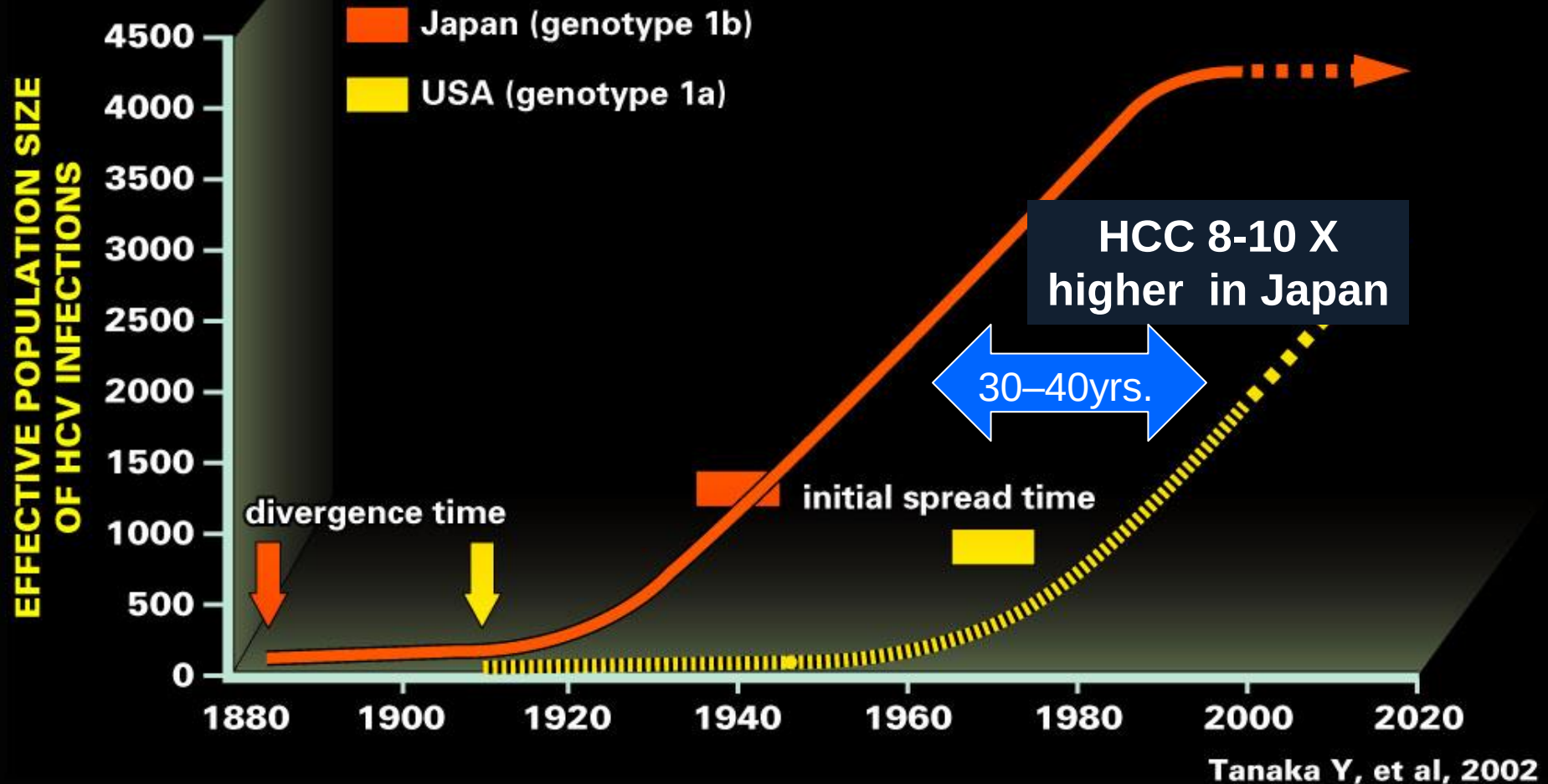


Development of Hepatocellular Carcinoma Following Transfusion

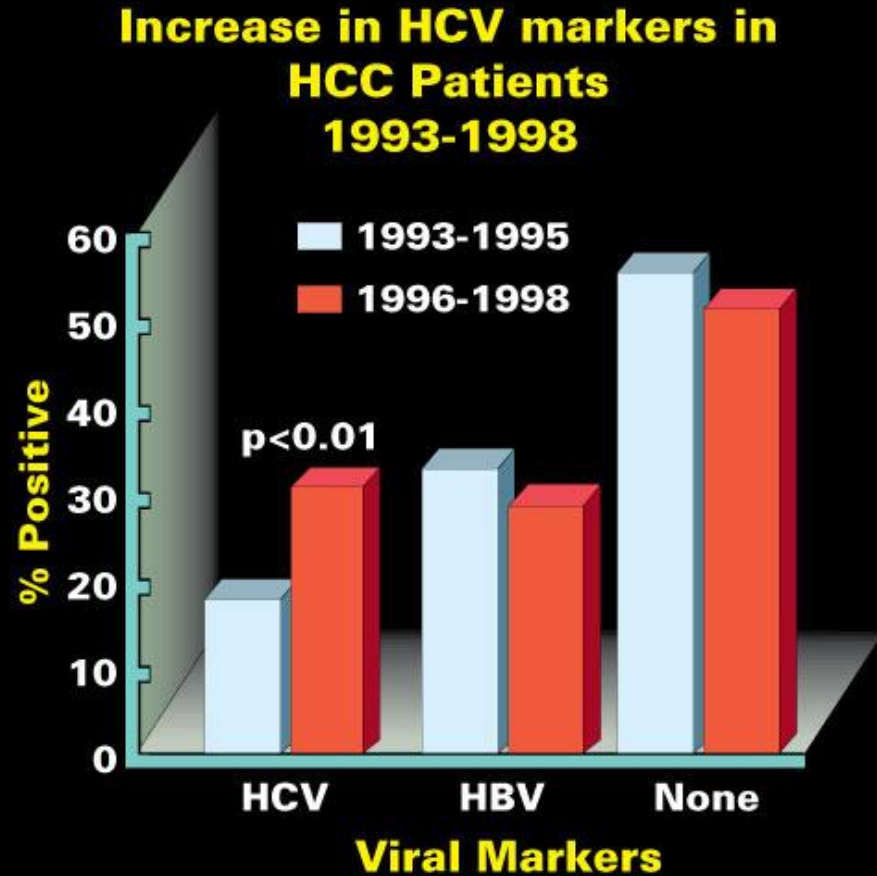
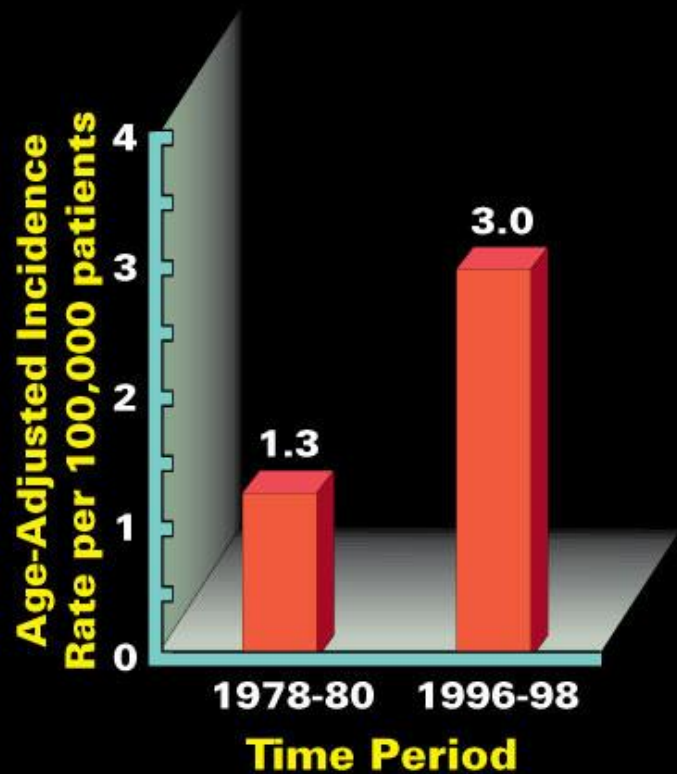


From: Kiyosawa, et al

MOLECULAR CLOCK OF HCV GENOTYPE 1 EVOLUTION IN JAPAN AND THE USA

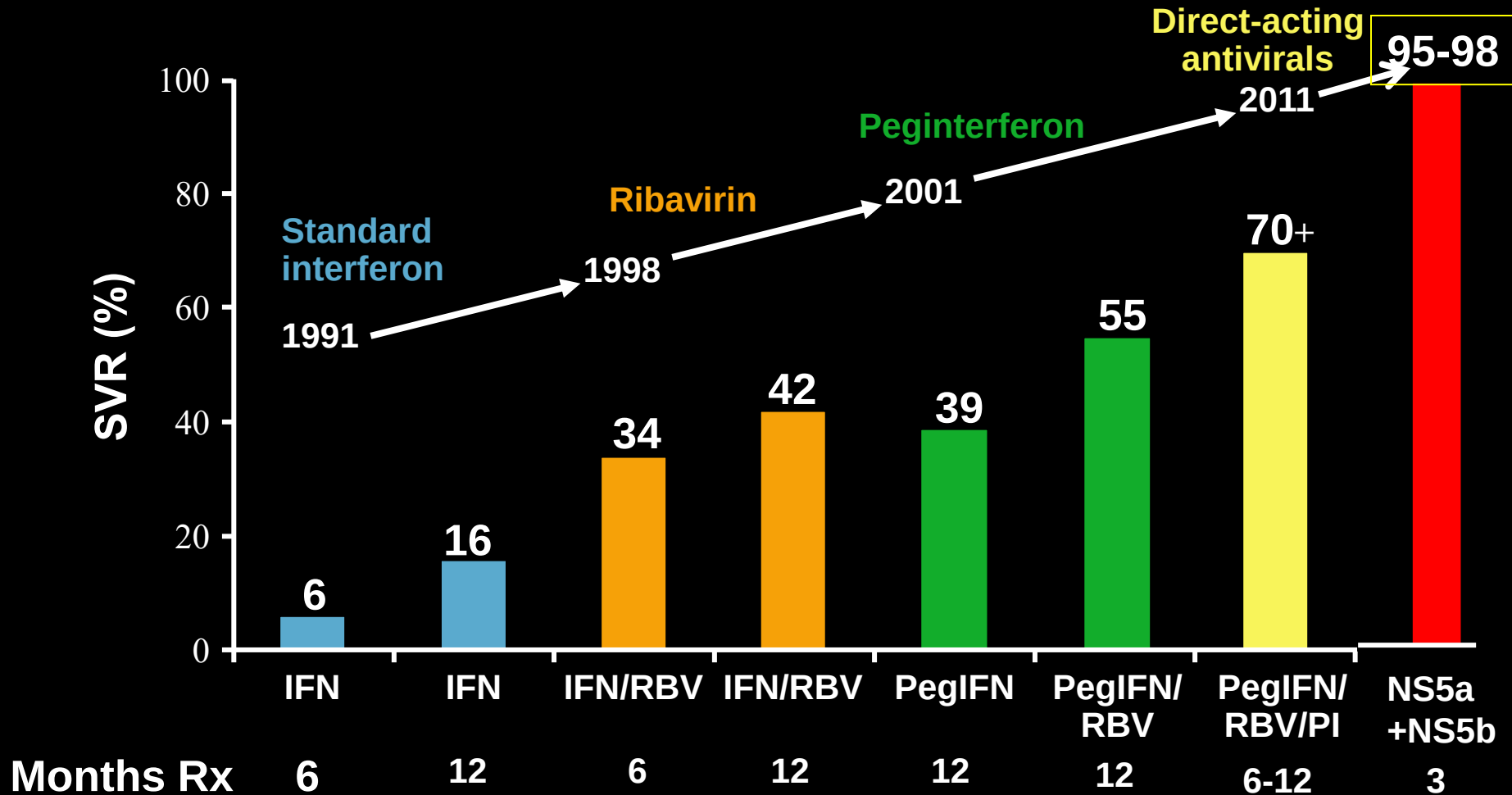


RISING INCIDENCE OF HCC IN THE UNITED STATES



Assuming no changes in standard of care, the total number of patients with advanced liver disease/HCC by 2029 projected to be > 4-fold higher than in 2009

Milestones in Therapy of Gt 1 HCV



THE END OF THE BEGINNING

**COULD THIS BE THE
BEGINNING OF THE END ?**



HCV: THE FUTURE THE GLASS IS HALF-FULL

**With cure rates approaching 100%,
from this time forward, once HCV
infection is identified, no one
should develop cirrhosis or die
from hepatitis C sequelae**

THE GLASS IS HALF-EMPTY HURDLES TO HEPATITS C ERADICATION

Identification of cases:

Estimated that only 20-40% of HCV carriers have been identified

Access to Treatment:

Even among known carriers, only a minority get treated with DAAs, though the proportion treated is increasing

High cost of Drugs:

Cost is the main impediment to treatment preventing the cure of millions. Cure is no longer constrained by science, but is a matter of dollars

VIRAL ELIMINATION: ONE COUNTRY IS WORTH A THOUSAND SPEECHES



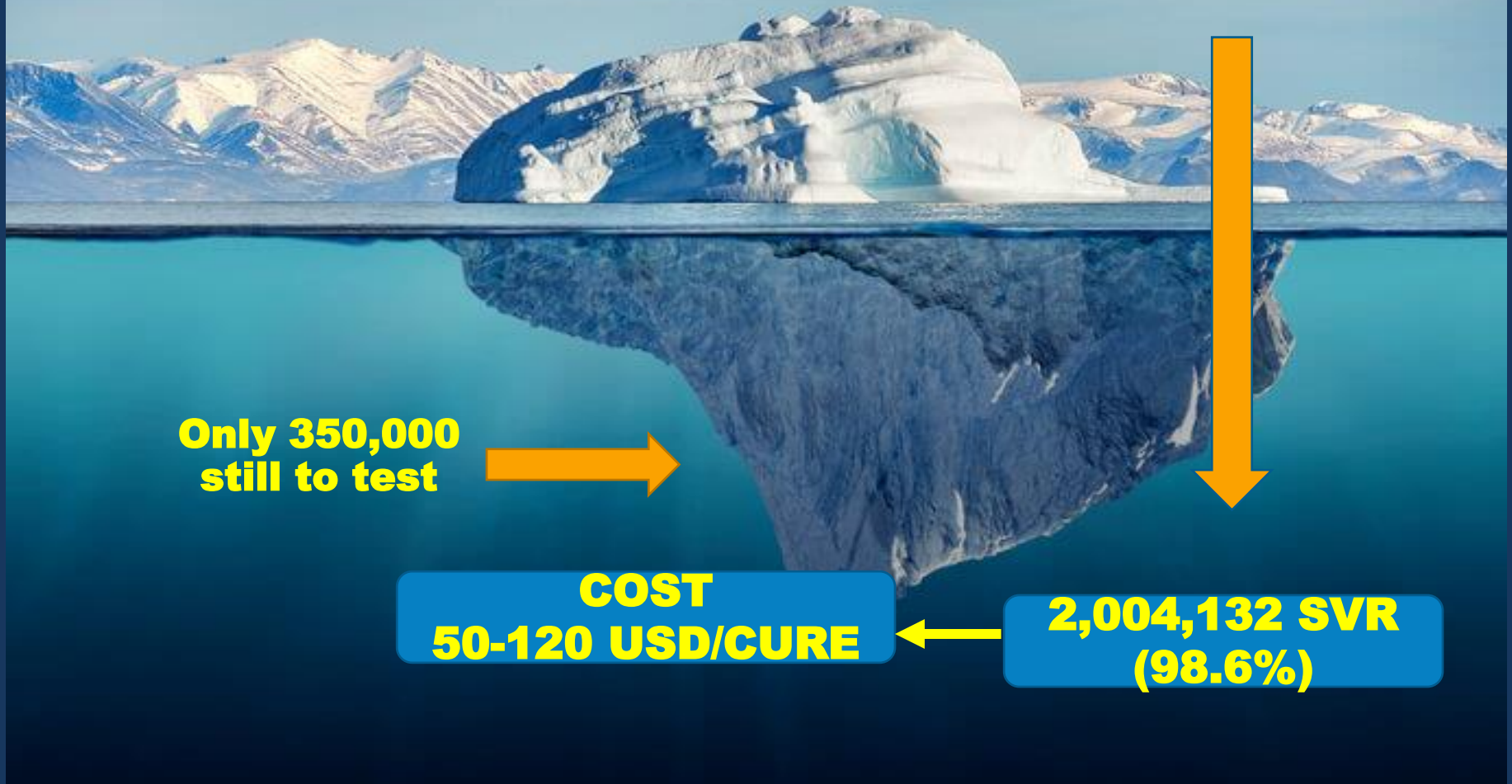
**EGYPT Tested
>60,000,000 Persons
(~4% HCV RNA+)**

**2,032,589 patients
treated (2014-2018)**

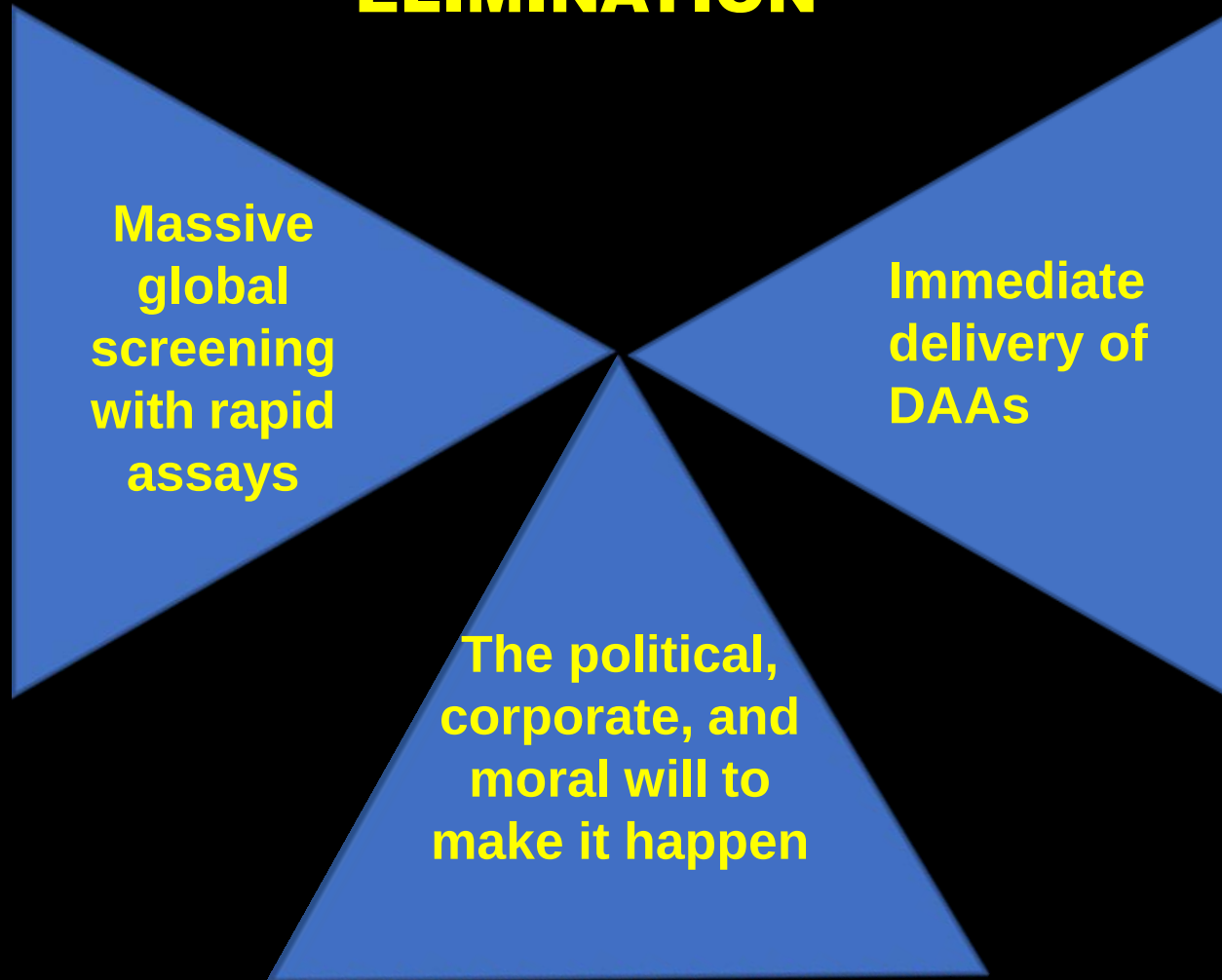
**Only 350,000
still to test**

**COST
50-120 USD/CURE**

**2,004,132 SVR
(98.6%)**



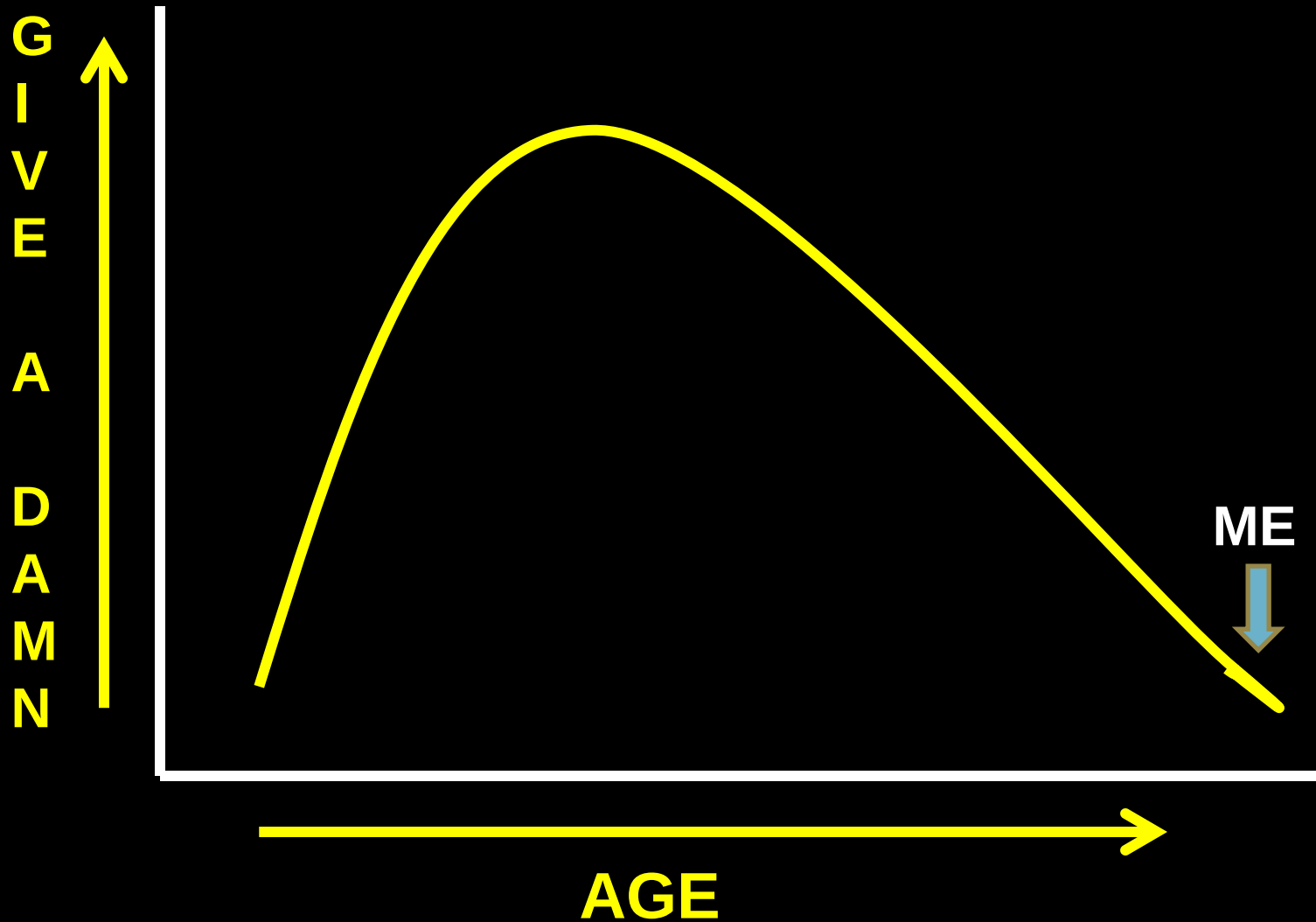
THE TRIANGULATION OF HCV ELIMINATION



The Golden Years



A PHILOSOPHIC PERSEPECTIVE OF LIFE VERSUS AGE



***I NEVER HAD NO
NOBEL DREAMS***

