“Visions lead to sainthood or the psychiatric clinic, plans lead to action”

The future is not a destination like Greenland, waiting for our arrival; it is something like the Channel Tunnel that we have to imagine, plan and build

The future is here; it is just not evenly distributed

William Gibson

Muir Gray has familial hypercholesterolaemia

Every six months he receives an email reminder from the lab to have a blood test

He receives 2 SMS reminders if no blood sample is received within 2 weeks

If no specimen is received his GP receives a copy email

If there is a result it is sent to the GP and to his Healthspace where it is stored in sequence

Appropriate advice and support is automatically generated

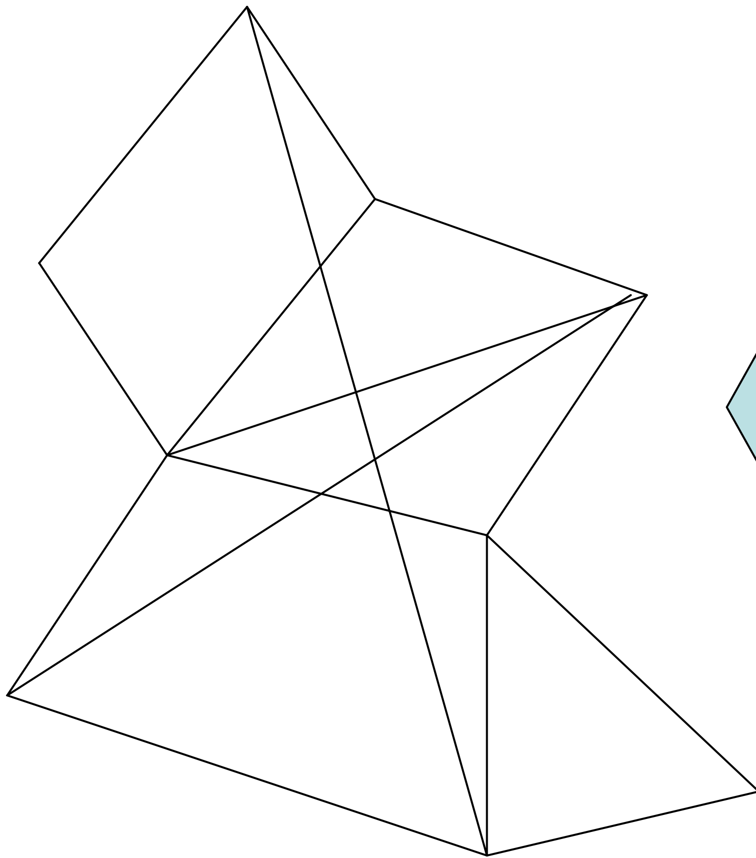
Muir Gray has familial hypercholesterolaemia
he fails to collect his repeat prescription
he gets a text message, remebers, gets an email and the repeat is delivered by the Post Office

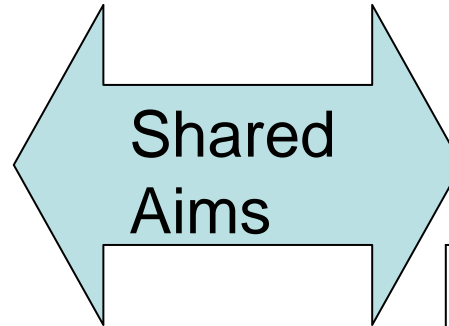
# HEALTHCARE 2012

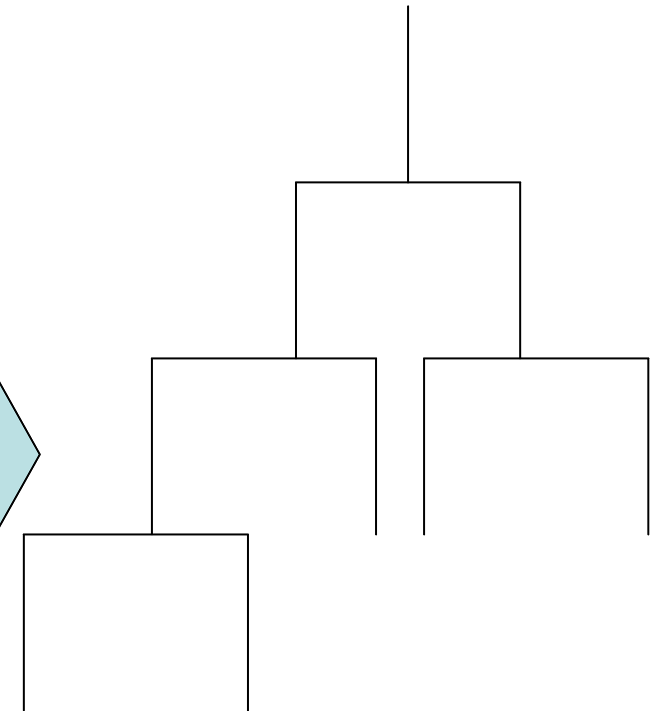
# SERVICES 2012

All serious health problems are managed by more than one bureaucracy and always will be.

They are managed by clinical networks which cross many bureaucracies.





Hypertext organisation
(Nonaka & Takeuchi OUP 1995 ;
The Knowledge Creating Company

Bureaucratic Organisation

# The National IBD Service

# A National IBD Service would have

A National set of objectives, criteria and standards
A nationally agreed templates of a care pathways expressed using the Map of Medicine
A National Dataset
A single specification for all information system providers
A National knowledge base updated annually
A National community of practice, including patients
A single web site
www.nhs.uk/ibd

X local services, where X is >1 and <150

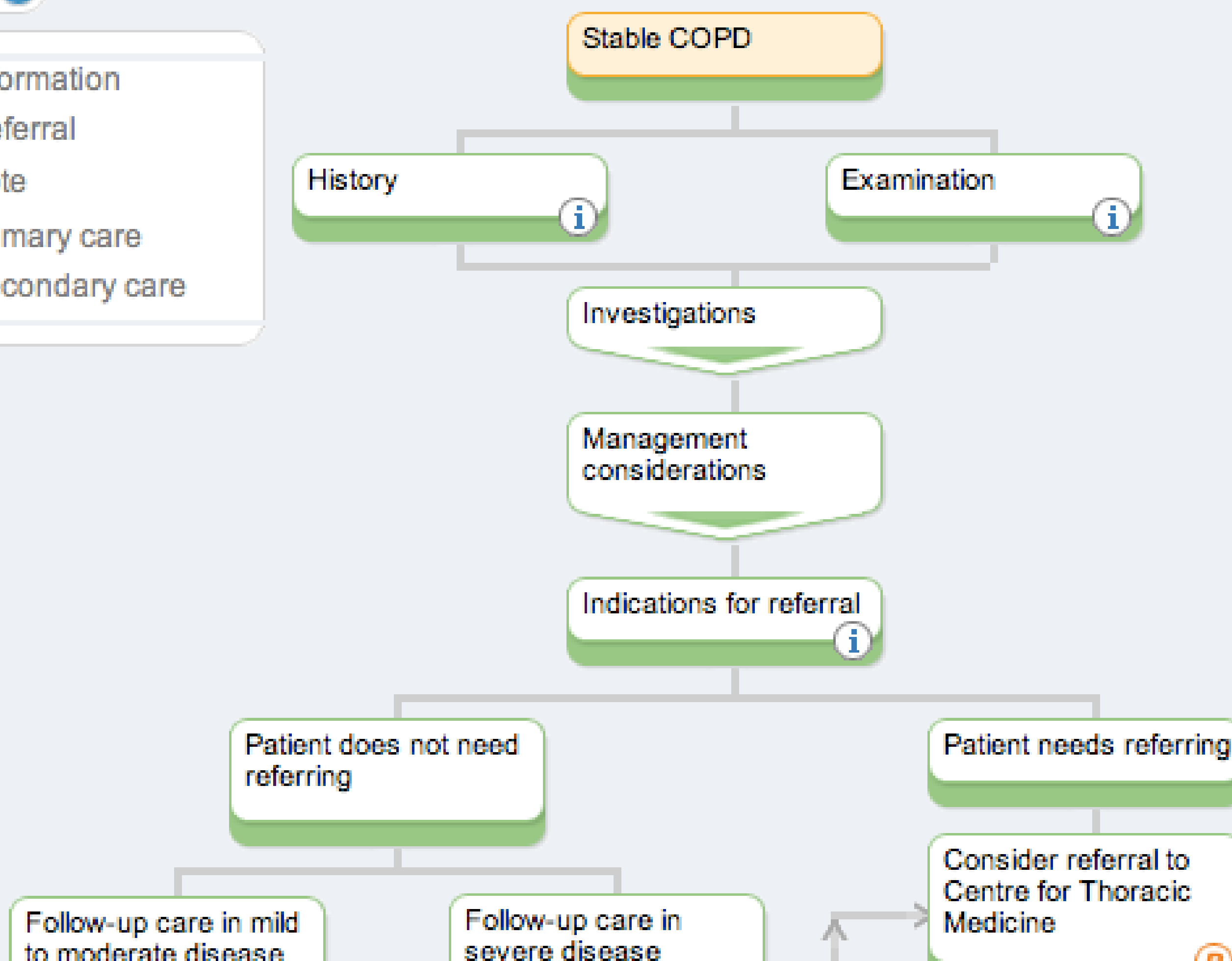
map of medicine®

# Stable COPD

Medicine / Thoracic Medicine / COPD

Key

- Information
- Referral
- Note
- Primary care
- Secondary care



# KNOWLEDGE DELIVERY 2012

Guidance in long esoteric documents can be embedded in lab request and report forms

“The false positive rate [for Hepatitis C] is especially important in low prevalence settings where the number of false positives may exceed the number of true positives”

Booth JCL et al (2001)

Gut 49 (Suppl 1) i4 column 1 Section 3.1 lines 23-27

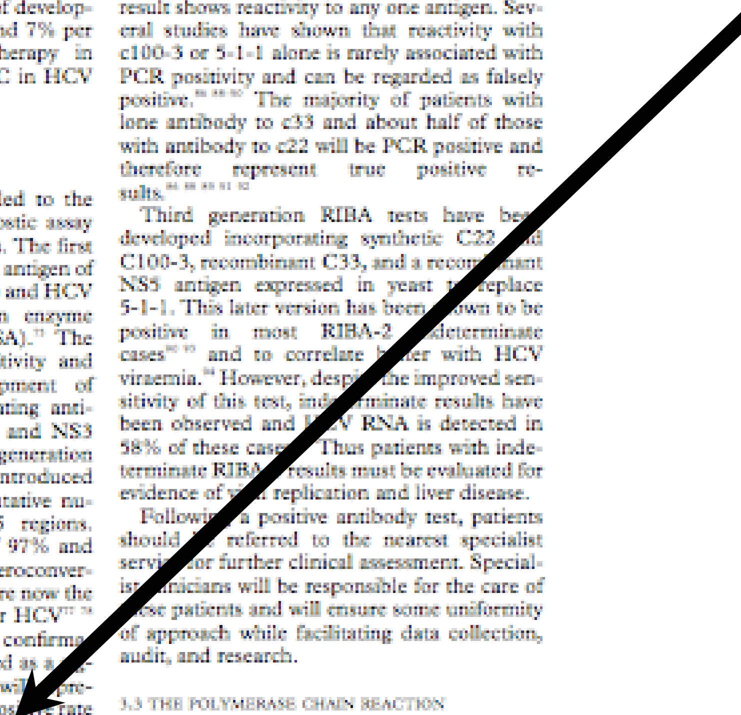
HCV infection is associated with a large proportion of HCCs. In southern Europe and Japan, 50–75% of HCCs are associated with HCV. HCV may cause HCC as a consequence of cirrhosis or as a result of chronic necroinflammation rather than having any direct carcinogenic effects. Unlike HBV, HCV does not integrate into the host's DNA. The majority, if not all, of patients with HCV associated HCC have established cirrhosis. Both HBV coinfection and excess alcohol seem to have an additional effect on the development of HCC.

The natural history of disease progression is slow in HCV related liver disease with estimates of 20–30 years' duration of infection prior to the development of HCC. In patients with established cirrhosis the rates of development of HCC range between 1% and 7% per year. The role of antiviral therapy in preventing the development of HCC in HCV infected cirrhotics is controversial.

## 3.0 Diagnosis

### 3.1 DIAGNOSTIC SEROLOGICAL ASSAYS

The discovery of HCV in 1989 led to the development of an antibody diagnostic assay based on viral recombinant peptides. The first generation tests incorporated a fused antigen of human superoxide dismutase (SOD) and HCV polypeptide (C100–3) used in an enzyme linked immunosorbent assay (ELISA). The first generation assay lacked sensitivity and specificity prompting the development of second generation assays incorporating antigens from the nucleocapsid (C22) and NS3 (C33) genomic regions. Third generation assays (ELISA-3) have since been introduced incorporating antigens from the putative nucleocapsid, NS3, NS4, and NS5 regions. ELISA-3 tests have a sensitivity of 97% and have shortened the mean time to seroconversion by 2–3 weeks. ELISA-3 tests are now the most widely used screening tests for HCV but despite the improved specificity, confirmation of positive results is still required as a significant proportion of positive tests will represent false positive results. The false positive rate is especially important in low prevalence settings where the number of false positives may exceed the number of true positives.



What it really looks like

A positive ELISA test in a patient with chronic liver disease is probably enough to diagnose HCV infection and a confirmatory antibody test may not be needed. Confirmatory PCR testing of serum for HCV RNA is suggested for this group of patients.

- Patients with suspected HCV infection should be tested for anti-HCV by an up to date (currently third generation) ELISA

results. A first recombinant immunoblot assay (RIBA-100) was developed with separately immobilised C100-3, 5-1-1, and SOD antigens.

Second generation RIBA tests were developed with antigens from nucleocapsid (C22) and NS3 (C33) in addition to C100-3 and 5-1-1. Both chimpanzee and human studies have suggested that second generation tests allow earlier detection of HCV infection in acute cases and are more frequently positive in chronic cases. A positive second generation RIBA result is associated with HCV viraemia by PCR in 88–98% of cases.

A positive RIBA test is associated with reactivity with two or more of the antigens, and in the majority (63%) of cases reactivity to all four antigens is detected. An indeterminate result shows reactivity to any one antigen. Several studies have shown that reactivity with c100-3 or 5-1-1 alone is rarely associated with PCR positivity and can be regarded as falsely positive. The majority of patients with lone antibody to c33 and about half of those with antibody to c22 will be PCR positive and therefore represent true positive results.

Third generation RIBA tests have been developed incorporating synthetic C22 and C100-3, recombinant C33, and a recombinant NS5 antigen expressed in yeast to replace 5-1-1. This later version has been shown to be positive in most RIBA-2 indeterminate cases and to correlate better with HCV viraemia. However, despite the improved sensitivity of this test, indeterminate results have been observed and HCV RNA is detected in 58% of these cases. Thus patients with indeterminate RIBA-3 results must be evaluated for evidence of viral replication and liver disease.

Following a positive antibody test, patients should be referred to the nearest specialist service for further clinical assessment. Specialist clinicians will be responsible for the care of these patients and will ensure some uniformity of approach while facilitating data collection, audit, and research.

### 3.3 THE POLYMERASE CHAIN REACTION

Initial PCR for HCV detection used primers derived from heterogeneous non-structural regions of the virus. The development of primers from the highly conserved 5' non-coding region greatly enhanced the detection of HCV RNA by PCR. The sensitivity of PCR detection was further enhanced by the development of PCR primers producing shorter PCR products. The sensitivities of most PCR assays is in the range of 500–1000 equivalents per ml.

Direct detection of the virus using PCR is needed in patients recently infected with the virus and in immunosuppressed individuals who may be antibody negative. In addition,

# Royal Cornwall Lab Service

Muir Gray 21/06/1944 NHS number 400 186 6897

ELISA25.5

Hepatitis C is of low prevalence in Cornwall. National guidance is that diagnosis should be confirmed by PCR test in low prevalence populations
For PCR test click here

For access to full text of guidance click here
To test your knowledge in one minute click here

# PATIENTS 2012

- The Clinician was the driving force in the 20th Century , the patient will be the driving force in the 21st century

eRosetta Press

# The Resourceful Patient

J A Muir Gray

Muir Gray has familial hypercholesterolaemia

Every six months he receives an email reminder from the lab to have a blood test

He receives 2 SMS reminders if no blood sample is received within 2 weeks

If no specimen is received his GP receives a copy email

If there is a result is sent to the GP and to his Healthspace where it is stored in sequence

Appropriate advice and support is automatically generated

Professionals and patients need clean clear knowledge for decision making just as they need clean clear water for hand washing

Water may look clear but be polluted and poisonous

At present people simply hold out a basin to collect knowledge, or dip a bucket in the sea of PubMed, one of the wonders of modern healthcare but peer review is no guarantee of freedom from pollutants - bias and errors due to chance- or poison due to the deficiencies of the peer review and editorial process

©GiardiaClub.com