Diagnostic tests for RA now and in the future

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As many patients know Rheumatoid Arthritis (RA) can be difficult to diagnose as its signs and symptoms mimic so many different diseases. It also can be frustratingly elusive – often hiding itself away as soon as you have that vital appointment:

Over the years there have been many developments in diagnosing RA and the future looks brighter still. We are seeing improvements in diagnostic testing that will have far reaching implications including the ability to predict the course of the disease (prognosis) and the identification of which treatment will have the best result early on in the disease, removing the unacceptable trial and error endured currently by most patients as they 'hope' a particular drug works for them.

This is summarised below:

It was here a moment ago Doctor!!

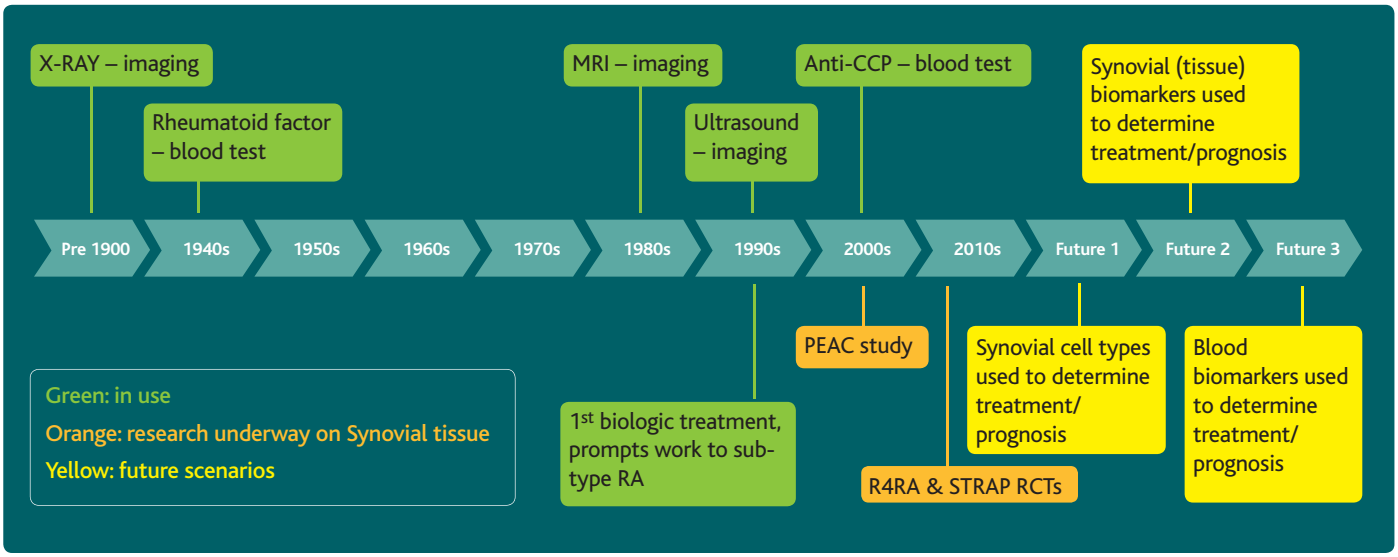


Figure 1 – Diagnostic tests, current and future

Current testing

Patients attending a rheumatology clinic with suspected RA currently undergo a thorough physical examination. They are asked questions about their symptoms and family history, blood samples are taken to measure a number of markers and they are offered tests that provide images of joints through x-rays, ultrasound and MRI. Each test can help support or eliminate a diagnosis so that eventually, with the help of skilled clinicians, many of us do reach a definitive diagnosis. Following a diagnosis, these tests continue to be used to monitor the progression of the disease, helping a doctor to recognise when treatment alteration or change is required.

Throughout this process there are uncertainties for the patient: What is my prognosis? Will I end up with significant disability if I don't take immunosuppressant therapy? And probably the biggest question of all which drug(s) are going to work best for me?

Biological Therapies

Since the 1980s there has been the introduction of a number of biologic therapies for RA. These are monoclonal antibodies that target very specific parts of the immune system (the NRAS ***Medicines in Rheumatoid Arthritis*** booklet is a great source of information on these important treatments). Researchers hope to be able to identify what part of the immune system isn't working well for an RA patient and match the treatment to the patient. This is known as personalised or stratified medicine and has the potential to help clinicians and patients make more effective decisions about treatment. In this article we would like to tell you about the use of tissue biopsies as an important and exciting new development in this field of research.

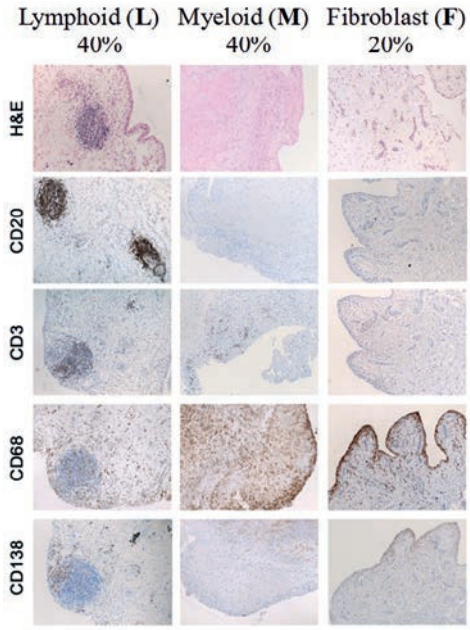
What is a biopsy?

A biopsy is the taking of a tissue sample so it can be examined. In RA a small piece of inflamed tissue from the lining of a joint (synovium) is retrieved using a needle under a local anaesthetic with ultrasound guidance

The synovial tissue can then be stained and examined under a microscope to determine the cell type, this is known as the pathotype.

Different pathotypes > Stratified medicines

Three main pathotypes (predominant cell types in the tissue) Lymphoid, Myeloid and pauciimmune-fibroid have been identified each with different cell composition. These are being investigated to enable stratification of the patients (a way of grouping) so that individuals receive the treatment most likely to work for them.



Three types of pathotypes

Professor Costantino Pitzalis from Queen Mary University of London is leading several trials in this area including:

1. ***The Pathobiology of Early Arthritis Cohort*** (PEAC), collecting clinical, imaging and biological data on patients from the time they are diagnosed, and start treatment on DMARDs. **www.peac-mrc.mds.qmul.ac.uk**
2. ***A Randomised, open labelled study in anti-TNFa inadequate responders to investigate the mechanisms for Response - Resistance to rituximab versus tocilizumab in RA*** (R4RA) this study has completed recruitment and the results will be available next year. **www.r4ra-nihr.whri.qmul.ac.uk**
3. ***Stratification of Biologic Therapies for RA by Pathobiology*** (STRAP) is a randomised clinical trial recruiting patients for whom DMARDs are or have become ineffective and are moving onto a biologic medicine for the first time. **www.matura-mrc.whri.qmul.ac.uk**

We know the lymphoid pathotype contains a greater proportion of B-cells than the other pathotypes and because the biologic treatment rituximab targets and reduces B-cells we predict that rituximab will work better in patients with this pathotype. This is being tested in STRAP and is running at seventeen hospitals across the UK see. You can find out if your hospital is one of those 17 at **www.matura-mrc.whri.qmul.ac.uk/strap_recruiting_centers.php**

Research in this exciting field is suggesting it may soon be possible for all RA patients to have a biopsy, that will inform clinicians as to which drugs are going to work best for the patient first time. As well as looking at the cells in tissues, researchers are also looking at the molecular/genetic picture so that further in the future it might be possible to replace the biopsy with a simple blood test.

The vision for the future is that a simple test will make getting it right first time a reality. The right drug for the right person at the right time.

If you'd like to know more about this exciting research email **g.hadfield@qmul.ac.uk**