The treatment of RA has been one of the great success stories of the past 20 years. A condition that to many was a life sentence - with no chance of parole - has become one which in most cases can be well-managed, some can even enter remission, enabling them to lead a normal life of work, family and private enjoyment, mobile and out of pain.

Yet this success is not fully appreciated by the public, nor celebrated by the National Health Service (NHS) as it deserves. The revolution has come about as a result of improving drug treatments and a radical change in strategy, which links early detection of the condition to prompt treatment. When all goes well, the results are good, with as many as half of patients going into remission: to all outward appearances, cured.

But all does not invariably go well. Patients with painful joints are too reluctant to go and see their doctor, while those GPs poorly-trained in the diagnosis of RA may only send them away with a prescription for painkillers. It can take several visits to get a referral to a specialist who then has to make the best of an imperfect situation. The window of opportunity for achieving remission is too often slammed shut by delays that could be avoided.

But all does not invariably go well. Patients with painful joints are too reluctant to go and see their doctor, while those GPs poorly-trained in the diagnosis of RA may only send them away with a prescription for painkillers. It can take several visits to get a referral to a specialist who then has to make the best of an imperfect situation. The window of opportunity for achieving remission is too often slammed shut by delays that could be avoided.

Nor are specialists allowed as much freedom of action as they would like. The biological drugs that have helped make the treatment revolution possible come at a higher cost than other treatment options and patients must often go through a trial by treatment in order to gain access to them. Some are lucky enough not to need them, in which case the guidelines in place work well: there is nothing the NHS is happier to prescribe than a cheap drug that works.

But for those that do need biologics - and even more for those who go on to need more than one in succession - a series of hurdles have been erected that, when taken in the round, are out of step with current clinical practice. It is right that NHS resources should be prudently accounted for, but to judge the impact of the biologics only in terms of the individual patient's cost and benefit is to see the issue through a distorting lens. The majority of RA patients are of working age, and to keep them at work, generating wealth, paying taxes, off benefits and able to look after their families, creates an economic return that dwarfs the narrow focus on costs of medicines versus quality life years saved.

The battle is not won. There are still some patients who do not benefit from the existing biologics and depend on future research to generate new products tailored to the small print of a disease that varies so much from patient to patient. Patients, public, and the profession need to unite to ensure that today's success is not allowed to slip away, but provides a springboard for tomorrow's.
For many years, RA was a disease in the shadows. Doctors did not understand its causes and lacked the means to treat it effectively, many wrongly believing that with bed rest and pain-killers the majority of patients got better. The public saw it as a disability of the old with vague and sometimes disbelieved symptoms, while a lot of patients persuaded themselves it was a consequence of age which they must bear with as much stoicism as other aches and pains. Many spent their lives out of sight, unable to work and trapped in their homes, with occasional respite visits to hospital. “There was no talk about remission, or even getting your disease under control” says Ailsa Bosworth, founder of the National Rheumatoid Arthritis Society, who was diagnosed with RA in her early 30s. “It was very much about ‘yes, how can we relieve your pain?’”

Since RA was first given a name in the mid-19th century, many theories about its origins have been advanced, some favouring an infectious cause, others believing there to be a genetic link. Today it is known that the symptoms of RA are caused by friendly fire, when the body’s immune system turns its energies into attacking itself - it belongs to the class known as auto-immune diseases. What triggers this misdirected attack remains unknown, but it could be an infection, an injury, stress, a genetic predisposition, or other factors yet to be discovered.

The immune system is complex and exquisitely specific. Normally it is marshalled into action by the presence of an invader, such as a virus, a bacterium, or a tumour. It recognises the invader as foreign, and attacks it using weapons designed to defeat the invasion without damaging anything else, desisting as soon as the battle is won. To pull this off, it has to distinguish between “self” and “non-self”, between its own tissues and those of the invader. In RA and other auto-immune diseases something goes wrong. The tissue of the joints is mistakenly seen as “non-self” and a concentrated attack is launched. And because the joint tissue never goes away, the attack continues: acute inflammation becomes chronic, damage multiplies (including pain and swelling), and the joints are eroded.

RA is not a rare condition. There are 690,000 affected people in the UK and 26,000 new diagnoses every year, which makes it more common than multiple sclerosis or leukaemia. Nor is it restricted to older people; 12,000 children under 16 suffer the juvenile form of the disease. Although the joints are the principal focus, RA can affect many other organs as well. There is considerable variation in the symptoms. Professor Ali Jawad, Consultant Rheumatologist at the Royal London Hospital says: “Two thirds of patients present with arthritis affecting mainly the small joints of the fingers on both hands. Quite often the wrists are affected and the knees, the feet to a lesser extent. Then in decreasing order it would be the elbows and the shoulders and the hips.”

I was worried about how my life would pan out.”

Women are around three times more likely to develop RA than men and it runs in families, but not especially strongly. “It is not a genetic disease as such, but there are genetic factors” says Dr David Walker, consultant rheumatologist at Newcastle upon Tyne NHS Foundation Trust. Once the immune system begins to misdirect its fire, the damage it does can be extensive. While disease progression varies greatly from patient to patient, if left untreated RA will cause irreversible damage to the joints, which may need to be pinned or replaced. Unlike osteoarthritis, which affects only the joints, RA can also cause inflammation elsewhere and damage the lining of the heart and lungs, as well as the blood vessels and eyes.

The effects can be crippling, both physically and psychologically. When Mary Cowern was diagnosed with RA at the age of 20, her first reaction was disbelief. “I think my first words were “You must have got that wrong – I can’t have RA, I’m too young.” But disbelief quickly turned into despair as her symptoms worsened and her work as a shop manager became more and more difficult for her. “I was worried about how my life would pan out” she says. “I could see myself becoming more disabled and then wondering where this would end. I was only in my 20’s and my life seemed to be quite over.”

Women are around three times more likely to develop RA than men.
In the middle of the Ashdown Forest in Sussex, a leading centre for hip and knee replacement surgery operates with great success far from the great centres of medicine – quite a long way, indeed, from any other hospital. The Horder Centre is remote because it started its life as a centre for hip and knee replacement surgery operates. (It was the success of these drugs that caused the Horder Centre to switch from RA to hip and knee implant surgery for osteoarthritis.)

Many patients then spent part or all of their time in hospital. The 1993 edition of the Primer on Rheumatic Diseases, the leading professional title on the subject, said hospital. The 1993 edition of the Primer on Rheumatic Diseases, the leading professional title on the subject, said: “When I first started that job, it was a shock to the system to say the least because there were people with extremely advanced joint disease that wasn’t being properly controlled. They were awfully disabled – they came in wheelchairs, or with walking sticks or Zimmer frames. It was a huge, massive problem for them all.”

Ailsa Bosworth remembers the period without any hint of nostalgia. “I was diagnosed in the days when all you had were NSAIDs and painkillers and they waited until you were disabled before they gave you anything faintly useful.”

But the prospects for many patients remained poor. “We used to wait until patients had bone erosions on their X-rays before we would intervene with the odd DMARD that we had, so it was late and inadequate treatment with potentially toxic and not very effective drugs.”

The use of steroids such as cortisone to reduce inflammation and suppress the immune response had been hailed as a huge advance, but experience showed that the side-effects were severe and in some cases fatal. Steroids provided no permanent answer, but continue to have a role in damping down flares. Gold-based medicines and penicillamine were more encouraging, the first to have an effect on the progress of the disease rather than merely its symptoms. “Some of the happiest patients are the ones that respond really well to gold” says Dr Walker. Sulfasalazine, one of the anti-bacterial sulfa drugs, had been tried in the 1950s because of suspicions that RA might be caused by an infection, and it proved moderately effective. Hydroxychloroquine, an anti-malarial drug, was found to have immune-suppressing qualities and joined the armoury. Most importantly, a cancer drug, methotrexate, was found to work surprisingly well. This group of disease modifying anti-rheumatic drugs (DMARDs) formed the basis of treatment in the pre-biologic era. (It was the success of these drugs that caused the Horder Centre to switch from RA to hip and knee implant surgery for osteoarthritis.)

The use of biologics every two years in case it was damaging the liver. We were very anxious about using it because of that, because a liver biopsy has a mortality attached to it.” Caution was the watchword. The pyramidal approach meant starting slowly, one drug at a time, then trying another if that failed, and slowly building up to the more potent but potentially more toxic drugs such as methotrexate. Dr Louise Warburton, a GP with a special interest in rheumatology, recalls her first job at the Robert Jones and Agnes Hunt Hospital in Oswestry, in 1992. “We just had the basic DMARDs – I don’t even think we used methotrexate then, because it wasn’t around, so we used sulfasalazine as one of them, and hydroxychloroquine, and there was something called penicillamine. They were fairly basic drugs. They are not very effective in aggressive disease and they have lots of horrible side effects, really. When I first started that job, it was a shock to the system to say the least because there were people with extremely advanced joint disease that wasn’t being properly controlled. They were awfully disabled – they came in wheelchairs, or with walking sticks or Zimmer frames. It was a huge, massive problem for them all.”

Alison Kent, a rheumatology nurse specialist at Salisbury NHS Foundation Trust, began work at about the same time as Dr Warburton. “The treatment goals were about trying to keep patients’ disease as quiet as you possibly could, and keep them pain-free. The treatment pyramid was to start slowly and build up, so as your disease progressed you received higher treatment. I would spend a lot of time doing counselling and education and supporting, because it was helping people to live with the condition. We hardly ever used the word ‘remission’ at all.”

Pamela Adams, an RA patient from Worcester, was diagnosed with the disease more than 30 years ago, when she was 29. She had never heard of RA: “My understanding was old people got it. It was a bit of a shock at the time because my first thought was that I was going to end up in a wheelchair. The main thing that was affected were my knees – walking the older children to school and pushing the pushchair. I was struggling. I shuffled a lot because my feet and my fingers started to swell.

“And it didn’t just affect your joints, it affected everything.”

Professor Jawad carried out an audit of the time RA inpatients spent at the Royal London in 1999, and discovered it totalled 2,400 bed days – equivalent to 240 patients each spending an average of ten days in the hospital during the course of the year. At that time, the London employed four surgeons who operated on the hands of the RA patients – two orthopaedic surgeons and two plastic surgeons. Professor Peter Kay, consultant orthopaedic surgeon at Wrightington Hospital near Wigan, who is National Clinical Director for Musculoskeletal Services, says that it used to be commonplace to see people with RA who were really quite crippled, with deformities – twisted hands and fingers, and in wheelchairs. “We still do joint replacements in RA patients, but it is less common than it used to be,” he says. “The really bad deformities that you used to get, particularly affecting the hands and upper limbs, that was a major problem but you see an awful lot less of that.”
half the patients prescribed methotrexate were still getting it, compared to a third given antimalarials or injected gold, 30% given penicillamine, 25% sulfasalazine and 18% oral gold. The authors of the study called these results disappointing but concluded that methotrexate was the best of the bunch.

Despite the high drop-out rate, however, it was clear for the first time that it might be possible to stop the disease developing and prevent the erosion of the joints; some patients might even go into remission. Emboldened by this, the old concept of a slow build-up in treatment intensity was abandoned in favour of a strategy of hitting the disease hard and early.

“Fifteen years ago we used to say you start with one drug, maybe start with hydroxychloroquine, if the patient is not better within six weeks then add in another one and then add in another one” says Professor Jawad. “The problem was we noticed the effect on the bones. The reason why we have to treat the patients early is because of the time of diagnosis, let’s say around half the patients will have holes in the bones, erosions. If you don’t treat effectively then within two years 80% will have these erosions and once they happen they are very difficult to treat.”

“If we attack with vigour at the beginning you are more likely to stop the erosions from happening. Early diagnosis is important, early intervention is important.”

“While a large dose of methotrexate kills cells, lower doses given weekly have an immune-modulating effect, with a much lower risk of serious side-effects. Many patients do well on methotrexate. “Roughly a third go into remission so yes, they do very well” says Dr Walker.

Pamela Adams is one patient who has responded positively to methotrexate. “It’s worked OK for me” she says. “I can still work part-time as an administration clerk, four to six hours a day. You do get your days with this complaint – there are days when it flares up and you just feel sore and it is difficult to move. But without methotrexate I would be worse."

But her daughter Donna Saunders, who also has RA, takes a different view. She is on biologics and believes her mother should be, too. She says her mum is too stoical and underrates the pain she feels. “Although she is saying she manages, I do think she could be better and on biologics that would make a difference. But she doesn’t meet the criteria."

Mrs Adams takes methotrexate once a week by self-administered injection. “The next day I feel sick and poorly, really drained, but that will wear off. For the rest of the week it works. Without it you would really be struggling to do anything but with the medication you can get about a bit more than you would without.”

Dr Walker is taking part in a national survey of methotrexate. “We just did 100 patients who are on a stable dose of methotrexate and planning to continue and asked them what they were putting up with, and 56 had something; fatigue for a day, and nausea which can be very unpleasant as it is almost anticipatory. They look at a bottle and start retching. Patients sometimes describe it as a ‘methotrexate day’, it’s really very unpleasant. Women also complain about hair loss.”

A retrospective study of almost 2,300 patients treated between 1985 and 1994 showed that methotrexate was better tolerated than other DMARDs. Fewer patients discontinued taking it, and a lower proportion of those who did blamed inefficacy. While many did give up, complaining of side effects and poor results, even larger numbers abandoned the other DMARDs. After roughly three years half the patients prescribed methotrexate were still getting it, compared to a third given antimalarials or injected gold, 30% given penicillamine, 25% sulfasalazine and 18% oral gold. The authors of the study called these results disappointing but concluded that methotrexate was the best of the bunch.

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““What we did as a result is that we found if we attack with vigour at the beginning you are more likely to stop the erosions from happening. Early diagnosis is important, early intervention is important. Hit it on the head.”

This marked a big change in treatment, turning the old treatment pyramid upside down. Guidance from the National Institute for Health and Care Excellence (NICE) now says that newly-diagnosed patients should be treated with a combination of three drugs right from the start, of which methotrexate should be one, together with at least one other DMARD, plus short-term steroids. 
The key ingredients of most drugs are chemicals in the form of small molecules able to penetrate almost any part of the body through the bloodstream. They work by interfering with the activity of the protein molecules, a thousand times larger, that make up the organs. But this is not how the body’s own defences work; the immune system does not generate tiny active substances akin to drugs, but instead mobilises large proteins called antibodies to attack invaders. These are tailored to the precise job they have to do, and switched off when that job is done. Matching this precise and specific mode of action has long been a dream of drug developers. The key sign that it might be possible came in 1975, when César Milstein and Georges Köhler at the Medical Research Council’s Molecular Biology Laboratory in Cambridge devised a way of creating an endless supply of antibodies in a test tube. Building on the work of many previous researchers, they did this by taking immune system cells from the spleen of a mouse that had been challenged by a foreign protein (sheep red blood cells) to stimulate the production of antibodies. The problem that had stumped earlier researchers was that such cells, grown outside the mouse in a culture medium, do not continue producing antibodies for very long.

Milstein and Köhler had the bright idea of immortalising the immune system cells by fusing them to mouse tumour cells. Tumours do not die off as normal cells do, but continue proliferating indefinitely. The two scientists hoped this fused hybrid cell would produce an single line of identical antibodies, they became known as monoclonal antibodies.

Their advantage was that they could be produced in vast quantities, to target almost any antigen. Their disadvantage was that they were based on mouse, not human cells, and would be recognised as foreign by any patient into whom they were injected and attacked by the patient’s own immune system. Producing human monoclonal antibodies proved difficult, but there were ways to “humanise” mouse monoclonal antibodies, also pursued at Cambridge, using recombinant DNA methods. While Milstein (who shared the 1984 Nobel Prize for Medicine with Köhler and a third scientist, Niels Jerne, for the discovery) did not at first realise the economic potential, it has proved enormous: the market for monoclonal antibody drugs now exceeds $50 billion a year.

The potential for monoclonal antibody medicines in RA emerged with the discovery that a naturally-occurring protein, tumour necrosis factor (TNF) is a major regulator of the inflammation process. TNF (which acquired its misleading name from experiments showing it could destroy tumour cells in test tubes) is a cytokine, a class of small proteins that act as messengers. Of these, a form of TNF called TNF alpha is the most important in RA, acting as a ringleader encouraging other cytokines such as interleukin-1 (IL-1) and interleukin-6 (IL-6) to produce the enzymes that actually destroy cartilage and bone. In 1983 a study at the Kennedy Institute at Hammersmith Hospital in London demonstrated that a monoclonal antibody drug targeted at TNF alpha produced a marked reduction in inflammation (9). The drug was infliximab, developed in the US.

Biologics reached the clinic in the late 1990s, producing compelling results in many patients. Mary Cowern had her first injection on a Tuesday. She had read about the new drugs and admits it was quite a scary moment for her. Not only was she terrified of needles, but she worried that this was her last chance and that it might not work.

The effect was swift, and took her by surprise. “A couple of days later I had got up, gone downstairs and was making a cup of tea, and I suddenly thought ‘Oh my God, that was my last chance and that it might not work. The effect was swift, and took her by surprise. “A couple of days later I had got up, gone downstairs and was making a cup of tea, and I suddenly thought ‘Oh my God, that was my last chance and that it might not work. The effect was swift, and took her by surprise. “A couple of days later I had got up, gone downstairs and was making a cup of tea, and I suddenly thought ‘Oh my God, that was my last chance and that it might not work. The effect was swift, and took her by surprise. “A couple of days later I had got up, gone downstairs and was making a cup of tea, and I suddenly thought ‘Oh my God, that was my last chance and that it might not work. The effect was swift, and took her by surprise. “A couple of days later I had got up, gone downstairs and was making a cup of tea, and I suddenly thought ‘Oh my God, that was my last chance and that it might not work. The effect was swift, and took her by surprise. “A couple of days later I had got up, gone downstairs and was making a cup of tea, and I suddenly thought ‘Oh my God, that was my last chance and that it might not work. The effect was swift, and took her by surprise. “A couple of days later I had got up, gone downstairs and was making a cup of tea, and I suddenly thought ‘Oh my God, that was my last chance and that it might not work. The effect was swift, and took her by surprise. “A couple of days later I had got up, gone downstairs and was making a cup of tea, and I suddenly thought ‘Oh my God, that was my last chance and that it might not work. The effect was swift, and took her by surprise. “A couple of days later I had got up, gone downstairs and was making a cup of tea, and I suddenly thought ‘Oh my God, that was my last chance and that it might not work. The effect was swift, and took her by surprise. “A couple of days later I had got up, gone downstairs and was making a cup of tea, and I suddenly thought ‘Oh my God, that was my last chance and that it might not work. The effect was swift, and took her by surprise. “A couple of days later I had got up, gone downstairs and was making a cup of tea, and I suddenly thought ‘Oh my God, that was my last chance and that it might not work. The effect was swift, and took her by surprise. “A couple of days later I had got up, gone downstairs and was making a cup of tea, and I suddenly thought ‘Oh my God, that was my last chance and that it might not work. The effect was swift, and took her by surprise. “A couple of days later I had got up, gone downstairs and was making a cup of tea, and I suddenly thought ‘Oh my God, that was my last chance and that it might not work. The effect was swift, and took her by surprise. “A couple of days later I had got up, gone downstairs and was making a cup of tea, and I suddenly thought ‘Oh my God, that was my last chance and that it might not work. The effect was swift, and took her by surprise. “A couple of days later I had got up, gone downstairs and was making a cup of tea, and I suddenly thought ‘Oh my God, that was my last chance and that it might not work. The effect was swift, and took her by surprise. “A couple of days later I had got up, gone downstairs and was making a cup of tea, and I suddenly thought ‘Oh my God, that was my last chance and that it might not work. The effect was swift, and took her by surprise. “A couple of days later I had got up, gone downstairs and was making a cup of tea, and I suddenly thought ‘Oh my God, that was my last chance and that it might not work. The effect was swift, and took her by surprise. “A couple of days later I had got up, gone downstairs and was making a cup of tea, and I suddenly thought ‘Oh my God, that was my last chance and that it might not work.
Trial results of five biologics (infliximab, etanercept, adalimumab, golimumab and certolizumab) confirm his view that all fall within a similar range of effectiveness. Benefits have included far fewer inpatient stays. At the Royal London they fell from 2,400 bed days in 1999 to just 180 in 2006, after biologics became established. "That is a dramatic impact," says Professor Jawad. The number of surgeons who operate on damaged joints at the hospital has fallen from four to one. "Really you could say we have shifted the expectations," he says. "Now we are achieving remission in RA, we are preventing an accumulation of damage and we are preserving quality of life."

A diagnosis of RA has in the past generally led sooner or later to leaving the job market. But many patients on biologics can continue in work, or return to it like Mary Cowern. She now works as the Welsh Director of the charity Arthritis Care. "I am back working full time which I never thought I would be able to do ten years ago. I am in a relationship and I have a step-daughter so I have family life. All the things I thought had been taken away from me, I got back. It might sound a bit corny but I have got the old me back, because I am a lot more positive. It is really phenomenal for me the difference it has made."

Life expectancy in RA patients is lower than in matched control populations, so better control of the disease ought to reduce that difference. A study published in 2007 found that after adjusting for disease severity treatment with TNF-blockers was found to be associated with reduced death rates in women, though not in men at that time. Longer-term studies may show both sexes gain some years of life.

For arthritis nurse specialist Alison Kent, biologics have changed the whole dialogue of the clinic. "My job has changed dramatically because we are now talking to patients about remission, and keeping them in work. In the past a lot of our work was about counselling and supporting and pain control, whereas now it is a lot more about disease assessment, education about the medication, side effects and self-management. It is more of a positive message to be able to give to people because you can say: 'Well, if this one doesn't work then there is another one' whereas it used to be 'If this doesn't work we are at the end of our possibilities.'"

GP Louise Warburton says a major change has been that it is now often impossible to tell that a patient has RA. "A patient would come in with no sign of disease and you would think 'Why are they in this clinic?' It wasn't until you looked back at the notes that you saw they had had very active disease and that it was much better."

While the NAO found that healthcare costs for treating RA are large, at £560 million a year, they are dwarfed by the costs in sick leave and disability payments of £1.8 billion. The NAO does not attempt to estimate the cost to the economy of the lost productivity of RA patients but the NRAS puts it at £8 billion a year.

EYE WITNESS REPORT
BILOGICS IN RHEUMATOID ARTHRITIS

SECTION FIVE RA CARE IN THE NEW ERA

The biologics come at a higher cost than other treatment options and so need to justify their cost by the outcomes they achieve. In the NHS this calculation is the responsibility of NICE, which has issued guidance both on the individual medicines and, in NICE clinical guideline 79, on the management of RA as a whole, in adults. This guidance calls for the urgent referral of patients if the small joints of the hands or feet are affected, more than one joint is affected, or there has been a delay of three months or longer between onset of symptoms and seeking medical advice.

"Patients delay, up to three months or even longer; and then GPs delay in referring them."

The first treatment option, says the NICE guidance, should be conventional DMARDs, which must include methotrexate and at least one other DMARD, plus short-term steroids. This should be done as soon as possible, ideally within three months of the onset of symptoms. That is a hard target to meet, and it is not being met, the NAO found in its 2009 report. "I quote this report all the time when I am lecturing GPs" says Dr Warburton. "Patients delay, up to three months or even longer; and then GPs delay in referring them. The net effect is that it takes an average of nine months for patients to be put on the right treatment."
If having these drugs enables somebody to go back to work and start paying tax instead of claiming benefits, that has a direct impact on the wider society and on government.

If patients do not respond to conventional DMARDs within six months, and their DAS28 score is greater than 5.1 on at least two occasions one month apart, they may then be prescribed biologics, normally in combination with methotrexate. Biologic treatment should only be maintained if there is an improvement of at least 1.2 in the DAS28 score at six months, and if it is sustained at subsequent six-monthly appointments. If the first biologic fails, patients may move on to rituximab plus methotrexate, which should also be subject to the same six-monthly checks.

Ailsa Bosworth of NRAS does not believe that this guidance ensures that all patients who should be on biologics actually are. She argues that the threshold is too high and the sequencing has more to do with the order in which the drugs were introduced than it does to their clinical benefits. “The threshold was cautiously set, quite rightly at the time, because we didn’t know what the long-term outcomes would be, and we were concerned about greater cancer risk, so it was right to be cautious. But term outcomes would be, and we were concerned about the direct impact on the wider society and on government.

These findings were supported by a 2010 report by Professor Sir Mike Richards, the former National Director for Cancer, and now Chief Inspector of Hospitals. Charged by the Health Secretary with investigating the international variation in the use of drugs in 14 countries, he concluded that the UK came tenth out of 14 in its use of RA drugs – two places worse than in its overall ranking, which was eighth.

The UK approach to biologics has found a doughty opponent in Sal Brinton, Liberal Democrat health spokesperson in the House of Lords, who suffers from RA. Baroness Brinton has found accessing biologics difficult and their effect limited. Diagnosed eight years ago, she is one of the unlucky ones who do not respond well, and she is now in a wheelchair. Her blood tests were negative – “therefore I don’t get an automatic route to biologics until a whole string of other things have been tested” she says. “It took quite a while even to get on to methotrexate. I also had ten DMARDs before moving on to biologics.”

A comparison of the variations in guidelines in use across Europe, funded by Merck Sharp and Dohme, found little consistency in the 12 countries studied. “The potential to tackle RA and limit the burden of disease is now well-established, but the will to do so in some countries appears to be weak”, the report concluded. “Of the 12 countries studied this seems to be too little, too late.”

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The rigid interpretation by her Clinical Commissioning Group (CCG) of the NICE guideline forced her to take rituximab with methotrexate when she failed on her first biologic, against her wishes and those of her consultant because it was contraindicated. “The CCG insisted that the pathway be followed, even though NICE says that you must also look at the patient’s response”, she says. “I am not alone. I am on the RA bulletin boards, on Facebook, on NRAS; it is a repeated problem.”

Like others, she is critical of delays in referral. “Some GPs (but not mine!) are woefully ignorant - the problem is that they receive very little musculoskeletal and auto immune disease training. This needs to be remedied.” It is a criticism echoed by Dr Warburton: “GP training schemes don’t spend much time on RA, and the problem is that GPs will probably only see one case every two years of new rheumatoid in their surgery. The obvious cases are obvious, but even some of those are not referred promptly”. Ailsa Bosworth believes that occasions where patients are being referred as rapidly as the guidelines suggest are “very rare”, despite evidence that if you can treat somebody within that 12-week window of opportunity you have a much better chance of getting them into remission. The NAO report found that people with RA visit a GP four times on average before being referred – and 18% of them visit eight times before a referral.

Peter Kay, with overall responsibility for musculoskeletal conditions for NHS England, says: “These are expensive drugs but the response is quite impressive. Obviously if you consider the societal costs, they are not as expensive as they seem. I regard it as being really important that people present early, are diagnosed early, and receive treatment early.”

The danger, as Ailsa Bosworth sees it, is that NICE’s remit is drawn so narrowly that it leaves too much out of consideration. “NICE has done a lot of good, but is only looking at half the picture. If having these drugs enables somebody to go back to work and start paying tax instead of claiming benefits, that has a direct impact on the wider society and on government. Not to take that into account when you are evaluating the health economic benefit of these drugs is completely illogical and misleading.”
EYE WITNESS REPORT
BIOLOGICS IN RHEUMATOID ARTHRITIS

BY NIGEL HAWKES

THE WITNESSES

Professor Ali Jawad, Consultant Rheumatologist, The Royal London Hospital
Professor Peter Kay, National Clinical Director for Musculoskeletal Services for NHS England and Consultant Orthopaedic Surgeon, Wrightington Hospital
Pamela Adams and Donna Saunders, RA patients (mother and daughter), Worcester

Dr David Walker, Consultant Rheumatologist, Freeman Hospital
Dr Louise Warburton, GP with Special interest in Rheumatology: Telford Musculoskeletal service; and GP Board member Telford and Wrekin CCG
Mary Cowern, Director, Arthritis Care Wales

Alison Kent, Rheumatology Nurse Specialist, Salisbury NHS Foundation Trust
Baroness Brinton, Liberal Democrat Health Spokesperson, House of Lords
Alisa Bosworth, Founder and Chief Executive, National Rheumatoid Arthritis Society

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