Chronic UTI @ The Portland

Chronic UTI Patient Information

What is a chronic UTI?

A chronic UTI usually develops after an acute episode or episodes of UTI. Unfortunately, it reflects a situation where a patient has persistent symptoms that never go away. They may reduce in intensity from time to time, but the patient is always suffering with some sort of symptom and they don't feel their normal selves. Some patients also describe periods of time where the symptoms increase in intensity or 'flare'. Symptoms of a chronic UTI may include pain, the need to pass urine a lot more (frequency), be getting up at night, find it difficult to feel like they have completely emptied their bladder or feel as though they urgently need to pass urine (urgency).

Why does chronic UTI happen?

It is well-established that multiple bacteria responsible for UTI, including E. coli, Enterococcus, Staphylococcus and Klebsiella, have an intracellular phase where they form persistent reservoirs in the bladder. They can invade the cells which line the bladder (urothelium) and hide inside these cells. Human biopsy samples show these reservoirs can persist very deep in the bladder wall. This invasive behaviour partly explains why traditional short course antibiotic treatment frequently fails, even for uncomplicated UTI in otherwise healthy young women as these short courses cannot penetrate inside the bladder cells.

Studies show high UTI recurrence rates and many women require long-term prophylactic antibiotics. With the normal urothelial cell turnover, it is thought that intracellular reservoirs will eventually be expelled and killed by antibiotics in the urine.

In addition , we now understand the problems with the diagnostic tools used in the field of UTI and their flaws. Our ongoing programme of work aims to test an easy to use bedside diagnostic that can be used to diagnose and manage ongoing patient care. This can only be done through rigorous investigation by studying the urine from patients over time and looking at how a patient's immune systems responds to the urinary bacteria and bladder environment. . Current tests, and most developmental tests, only look at abundance and identification of bacteria. Our understanding of the bladder environment has now moved on and we know that the urine is has its own microbiome (community of bacteria) that in the majority of people does no harm. However we need to develop a better understanding what has happened to that urinary environment and to the immune response in patients with UTI and Chronic UTI. We can then better understand treatment and prevention options.

What is your treatment protocol?

Our treatment protocol involves assessing a patient by taking a history and using a 39 point symptom score which was devised in our translational research unit at UCL-Whittington under Prof. James Malone-Lee. When indicated we would also conduct a physical examination of our patients . It is usual that, before a patient comes to see us, they have had many investigations and sadly failed treatments. If any further investigations are needed we can then request theses. We would test the urine as described below at each visit. We monitor progress by assessing the patients symptoms and urine whilst under treatment every months.

We test the urine using fresh microscopy of a sample of urine and count the white cells and epithelial cells, generating a plot of the white cell count and epithelial cell count. Along with the symptom score, this allows us to monitor disease activity. We do not use urine culture or dipstick tests to inform our management. This is because we have studied these tests in depth as part of our research and are aware of their shortcomings. In particular, the urine culture can be misleading which we will come on to. The white cells and epithelial cells found in the urine are a sign of infection and inflammation produced by the body during a urine infection and so inform us on how the immune system is responding to the urinary environment.

The treatment regimes we use are outside national guidelines (NICE) and have been developed through observational studies and small randomised controlled studies. We have published our studies on these regimes (see references) and the treatment protocols are used in our NHS Whittington Tertiary clinic. In brief, we aim to use a first generation, narrow spectrum antibiotic in the highest dose tolerated and we tailor the regimes to the patient's response and tolerance. The patient's description of their symptoms and the urinary microscopy are very important in assessing response and progress. We also use methenamine hippurate which is a urinary antiseptic, in addition to the antibiotics. Methenamine hippurate (Hiprex) is an old antibacterial agent that turns the urine into a disinfectant. It acts in the urine on planktonic bugs that break out of cells and stops them from colonising fresh cells. It has potential for treating the situation during the weeks spent waiting for the bladder to clear itself of colonised cells by shedding them from its surface. Whilst on treatment some patients may experience oscillations in their symptoms or an acute worsening of symptoms which is commonly referred to as a 'flare'. Flares are to be expected and this does not mean that your treatment is not working. Our research has shown that during a flare you may experience more shedding of the bladder lining and so and increase in white blood cells and free bacteria in the urine. Most flares are short lived and settle within 24-72 hours and you may need to take some pain relief during this time. If the flare is not settling then we recommend increasing the dose of your antibiotic for a short period for 3-7 days and the reduce the dose of the antibiotic back down once the flare symptom have resolved. Over the course of your treatment the flares will reduce in frequency, duration and intensity. We offer the service of urine microscopy, known as a urinalysis, that can be done in between review appointments. This can be requested by emailing the administration team. You can attned for a urine sample and then we write to your with the results. If the patient is having any severe side effects then we recommend stopping the antibiotic and emailing in to uti.portland@hcahealthcare.co.uk for advice.

In your treatment plan we also carefully consider other factors that play a role in chronic urinary infection such as the menopause and the vaginal microbiome. We will give you advice on how to manage these factors and how this can improve your symptoms and outcome. In addition, managing pain is very important and we try and use a multi-disciplinary approach to pain, including lifestyle advice, physiotherapy, psychological support, medications and onward referral to a pain specialist.

What is the average duration of treatment?

The average duration of treatment in our patient group is 383 days and we try not to change the treatment regime which requires a determined persistence from our patients. We have, in the past changed our regime too quickly in response to a flare, with regret. It is expected that patients will have symptom exacerbations along the way. A smaller proportion of our patients require one of our second line regimes involving a more broad spectrum antibiotic and an even smaller proportion are on a combination of antibiotics. We aim is to achieve a situation where the symptoms are stable on methenamine alone and then to eventually withdraw the methenamine also. We tailor our treatment to the individual patient and we try and reduce antibiotic exposure as much as we can.

Why do I need a blood test?

We ask our patients to have a blood test done every 3 months to assess their liver and kidney function due to exposure to antibiotics. All patients on long term antibiotics are asked to have blood tests every three months, either through the private clinic or their GP to ensure patient safety. If indicated by the result of tests carried out, you may be asked to stop treatment.

Treatment with long-term antibiotics is not licenced in the UK. For this reason, we ask that you follow your treatment plan diligently and adhere to our safety guidance relating to the reporting of side effects. You will be monitored very carefully with a clinic review every 3 months.

Why you do not consider broth cultures, rigorous culturing or next generation sequencing analysis in general of importance when you are treating patients?

One of the problems that troubles us the most is knowing what microbes are causing the symptoms. It is very important to understand that just because you detect the presence of an organism through culture of the urine; be it in a routine NHS laboratory, a broth culture, culture of the urinary sediment or through sequencing, it does not mean that the bacteria isolated or found is the cause of the infection. It might be that it is just easy to grow and that it exists without harm in the bladder. This is becoming all too evident from our current laboratory work. There appears to be no reliable method for implicating an isolate as the ‘cause’ of the symptoms. The normal bladder is not sterile and has a polymicrobial microbiome of well over 450 different species. We can still see presumed

pathogenic species in the urine of patients who have recovered and in our healthy volunteers. For years it has been widely assumed that if you detect a microbe in the urine, obtained from someone with lower urinary tract symptoms, then it must be the cause of the symptoms. It is difficult to accept this given modern evidence. This is why we put so much emphasis on the symptoms and the plots of the urinary urothelial cell counts and pyuria. We see patients who have sent urine to the USA and elsewhere, seeking special cultures. All too often, the data obtained do not help matters but do encourage people to focus on specific bugs without necessarily knowing whether they are relevant.

Is there any way to cure embedded infection, or is it a case of managing symptoms? Can you give us an idea of your success rate?

Yes, on average our treatment regime takes 383 days after which time 80% of patients have successfully stopped antibiotics. 20% of patients require a longer treatment time. Within this 20% group, we have a few patients that we find difficult to manage off antibiotics and they have had to continue with close monitoring. We do not know why this group behave in this way and it is one of areas of interest for our research. There may well be factors related to the individual, the medication or the bacterial populations in the bladder that cause this response.

How do you address any potential gut issues which may arise during or after treatment. Are there any particular probiotic regimes that you suggest?

We do not advocate any particular probiotic regimes as there is currently limited evidence in the area but we base our management on an individual basis. We are very careful to highlight potential bowel side effects and ask the patients, in particular, to read the information leaflets on taking the medication. Often, taking the antibiotic correctly with or without certain foods is very helpful. Some of our patients have found it very helpful to use gastro-resistant capsules which they can buy over the internet. We do not know for sure whether probiotics help or not. They do no harm, other than some are expensive: Some patients report benefit and others do not. We have no objection to patients using them. We do recommend using probiotic foods such as Kefir and refined starches.

Why do flares occur despite being on antibiotics?

Symptom flares are common in this condition. A good response can be interrupted by an eruption of unpleasant symptoms. In addition, if you have been feeling better, the symptoms can feel more severe than at the outset despite the disease activity being less. Many of these flares settle without there being a need to do anything different. The recovery involves a series of oscillations of decreasing amplitude so that we expect these ups and downs. If treatment is necessary we usually respond by increasing or doubling the dose of one (or more) of the antibiotics that are being used to treat the chronic infection. If you have been on an effective regime we are reluctant to change the antibiotic as we have understood that this does not help in the long term. We are keen not to rotate

antibiotics. We do not normally consider changing the prescription without doing a urine microscopy and identifying a change in the urinary white cells. The majority of the time the best course is to wait for the flare to settle of its own accord.

What should I do if I have a flare up?

The first thing to do is use some simple methods to calm down inflammation. You can use some simple pain killers, take rest, reduce any stressors and make sure you are hydrated (but don't drink excessively). If this is not helpful and there is pain, you can consider using bicarbonate of soda (a teaspoonful in a glass of water) which can reduce pain. Failing this, you can escalate your treatment safely for a few days in the following way, which should be cut back down after systems resolve. If the symptoms do not abate with an increased dose after 7 days, please email us for advice as below.

Cefalexin may go up to 1 gm three or four times a day

Amoxicillin may go up to 1g three times a day

Co-amoxiclav may go up to 625 mg three or four times a day

Nitrofurantoin may go up to 100 mg three times a day

Trimethoprim to 200 mg three times a day

Doxycycline to 100 mg three times a day

Oxytetracycline 1 gm three times a day

Azithromycin to 500 mg once a day

Clarithromycin to 500 mg twice a day

Pivmecillinam 400 mg three times a day

Lymecycline 408 mg three times a day

Methenamine can be increased to 1g three or four times daily

What should I do if I have a side effect on an antibiotic?

Please make sure you have read the information leaflet that comes with the antibiotic carefully and the information that we provide. Please stop the antibiotic immediately if the side effect is a rash or any kind of swelling, shortness of breath, then please report to us and do not take it again. If the side effect is milder but not tolerable, such as tummy upset, nausea or others, please stop the antibiotic and try again after a couple of days. If the same occurs again, please email us and we should consider an alternative therapy.

What is the relationship between the vaginal microbiome and UTI?

There is growing evidence that the vagina is an important site in the development of UTI, it can serve as a potential reservoir for bacteria ascending from the rectum. The vaginal microbiome can be positively affected to try and reduce the risk of UTI. The microbiome in the vagina is dynamic and often a critical factor because changes in the characteristics of the vaginal bacterial ecology resulting in the loss of normally protective Lactobacillus bacteria increase the risk of UTI. These changes may result from oestrogen deficiency, antibiotic therapy, contraceptives, and episodes of UTI itself. Interventions designed to maintain homeostasis of the vaginal ecology can be helpful in preventing UTI. We often recommend using vaginal boric acid pessaries to reduce the vaginal pH. We would recommend using 600mg twice weekly. The patients favour the website siaderma.co.uk. We would also recommend using tea tree oil vaginal pessaries to act as an anti-fungal and may help to acidify the vaginal flora and reduce over growth of certain types of lactobacillus and vaginal thrush. Another alternative is topida spray.

We may recommend vaginal oestrogen after discussion and examination. Alternatively, a good vaginal moisturiser can be helpful such as 'Victory oil' or 'YES'.

Why do the symptoms sometimes persist but the white cells in the urine get better?

The symptoms typically lag behind the urine in relation to resolution so it is necessary to sustain the antibiotics or the Methenamine until these have resolved, which may be some time after the urine has cleared. This is because an inflammatory reaction can exist in the tissues without white cells and epithelial cells leaking into the urine in significant numbers.

Pain is a particularly difficult symptom as the mechanisms of how pain occurs are complex and may require not only our treatment protocol but a holistic approach to consider the up regulation of the nervous system from constant inflammation in the bladder and urethra and from a reactionary tension in the pelvic floor muscles. Your doctor may advise specific pain medications or pelvic floor desensitisation.

Contact us:

Chronic UTI Clinic
Practice Manager – Ms Ali Parkes
uti.portland@hcahealthcare.co.uk
The Portland Hospital Consulting Rooms
HCA Healthcare UK
212 Great Portland Street
London
W1W 5QN

Useful Resources:

The Whittington Health LUTS clinic
https://www.whittington.nhs.uk/default.asp?c=42456#locations

UTI Global Support
https//www.chronicutiglobalsupport.com

Bladder Health UK Chronic UTI
https://bladderhealthuk.org/cystitis-utis-fowlerssyndrome

Chronic Urinary Tract Infection Campaign
https://cutic.co.uk/

Live UTI free
https://liveutifree.com/

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