

The GAG layer in the bladder

Miss M F Eylert

Consultant Urologist with Special Interest in Female, Neurological and Urodynamic Urology, Aneurin Bevan University Health Board

The bladder appears to be a simple organ, which can fill and empty. Nevertheless, the actual function is very complex, and bladder conditions are common. The bladder is lined with cells, and protecting these cells on the inside is a barrier called the glycosaminoglycan layer (or simply “GAG layer”). This is a kind of special lining which provides protection to the bladder cells. If this layer becomes damaged for any reason, symptoms such as pain, frequency and urgency of urination can occur.



Pain can be felt with little bladder filling and increases with filling. Pain does not cause urine leakage.



Urgency is a sudden desire to pass urine which is difficult to defer. Urgency may be accompanied by leakage or fear of leakage of urine.



Increased urinary frequency is caused by either pain or urgency, requiring the need to be near a toilet. Often therefore, increased urinary frequency results in limitations on the person’s work and social life.



Bacteria can also gain entry through the broken GAG layer and cause a urinary tract infection.

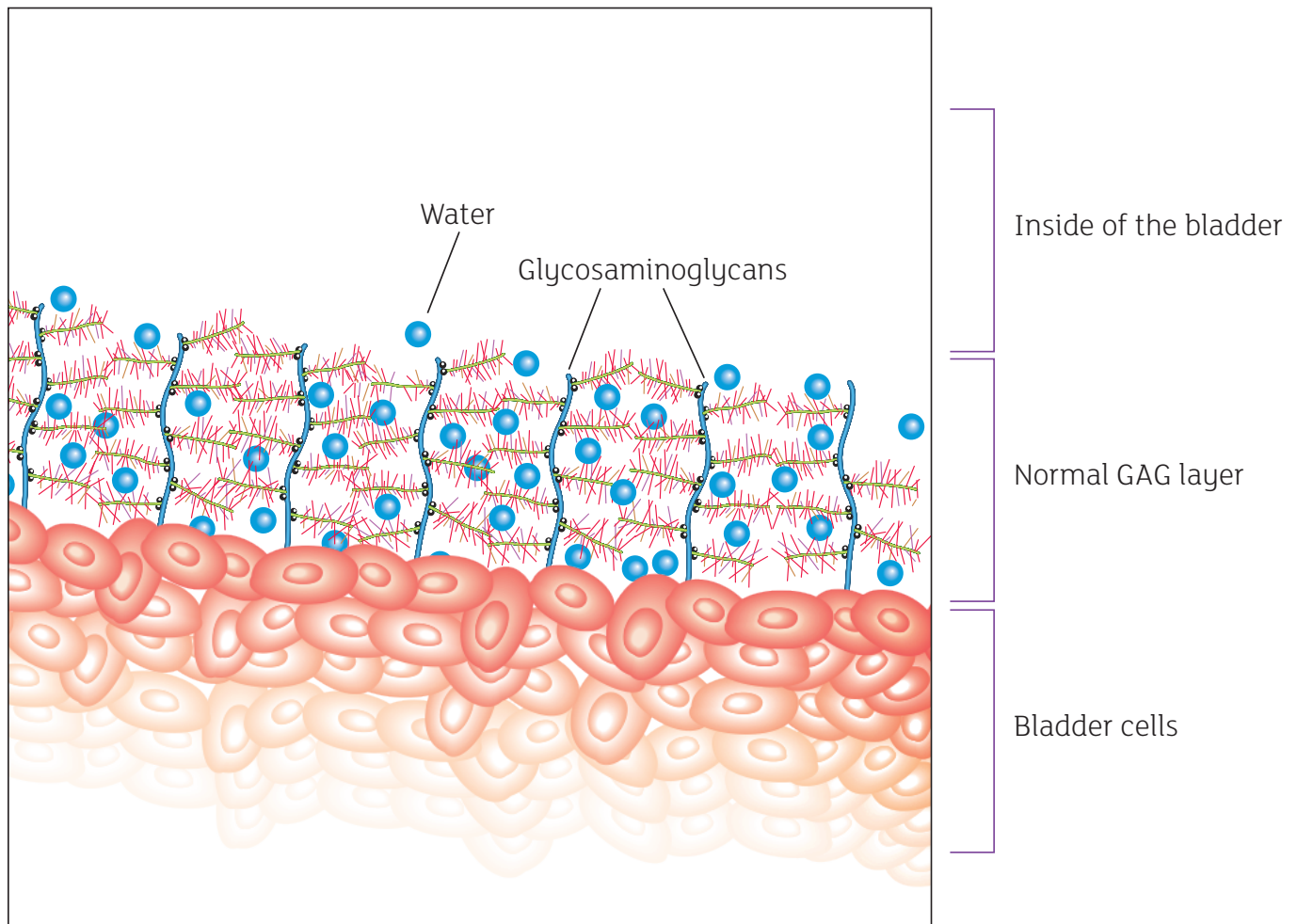
It is possible to replenish this damaged GAG layer, and by doing so, make the bladder more resistant to irritation and infection. Most patients will see their symptoms resolve or improve over time.

What is the GAG layer?

The GAG layer is a mucus-like layer on the inside of the bladder, protecting the bladder cells. There are many components that make up the GAG layer, but the main ones are chondroitin sulphate, hyaluronic acid and heparin sulphate. The GAG layer holds water firmly within it, without interacting with the urine; therefore, creating a waterproof barrier which protects the bladder cells.

Urine is a solution of waste products and toxins, ready for excretion from the body. The contents of the urine are not meant to come into direct contact with bladder cells. The main purpose of the GAG layer is to protect the bladder cells from these irritants. It also creates an additional barrier against bacteria.

A healthy GAG layer



Changes and damage to the GAG layer

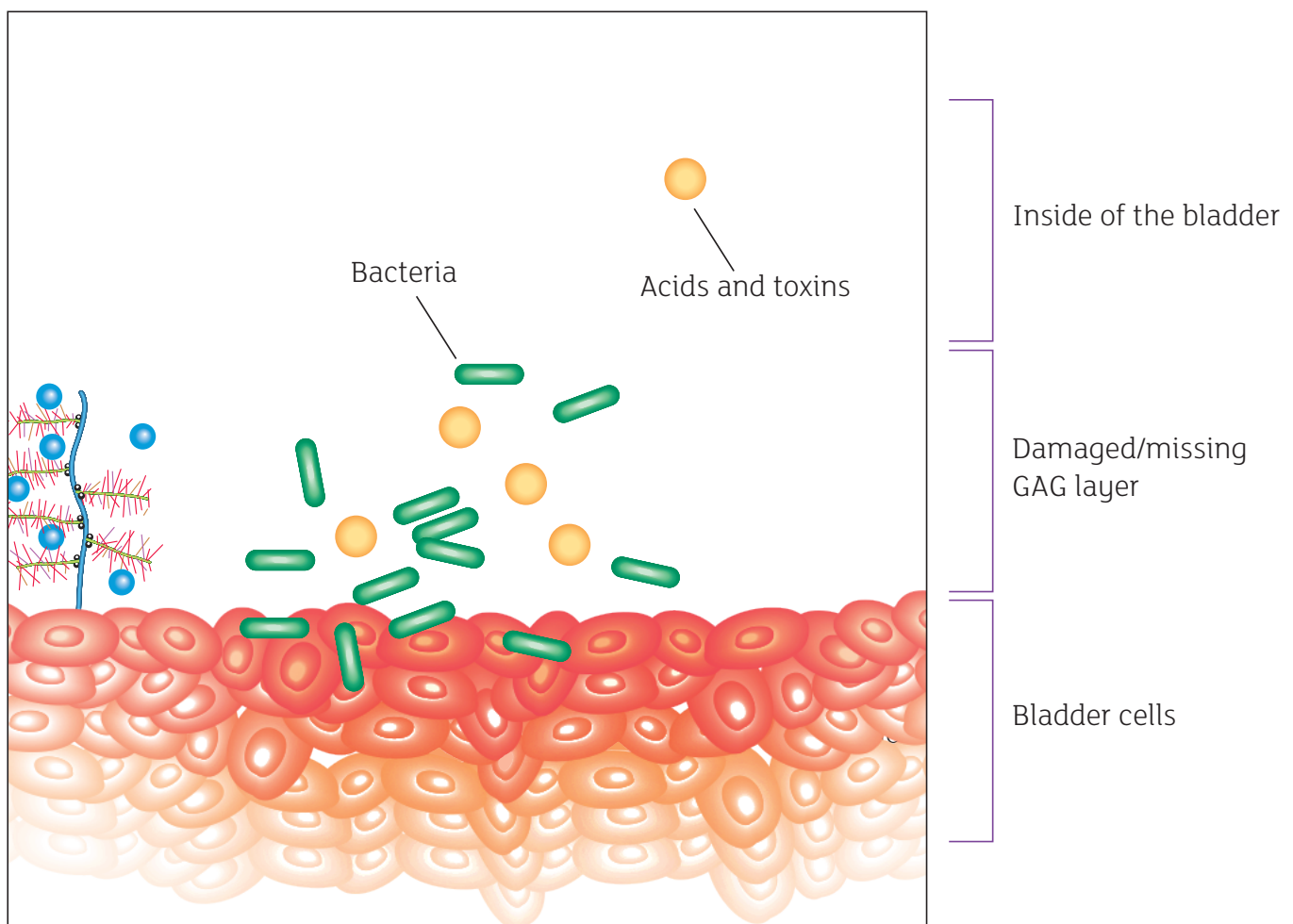
Damage to the GAG layer causes the acids and toxins found within the urine to reach bladder cells directly. This in turn can cause sensations of urgency and pain as well as cause inflammation; it may even result in bleeding. GAG layer damage also reduces the protective effect against infection by bacteria. The more concentrated the urine, the higher the potential for irritation and infection through any breach of the GAG layer.

The precise events that cause GAG layer damage and prevent natural replenishment of it are not fully understood. However, such damage appears to play a role in chronic inflammatory disorders (bladder pain syndrome/ interstitial cystitis, chemical cystitis, radiation cystitis) and recurrent bladder infections (urinary tract infections). Once the damage has occurred and natural healing is disturbed, the symptoms get ever worse and then infections and other chronic inflammation may occur together. More acids and

toxins reach the bladder cells, this causes more urgency and pain signals to be sent. Inflammation causes cells from the immune system to move to the bladder to fight the problem.

Sometimes the body succeeds in replenishing the damaged GAG layer itself, but sometimes it does not. This explains why many patients suffer periods of symptom “flare-up” with relatively better symptoms or even resolution of symptoms in between. In some patients, the inflammation fails to resolve the problem, and the bladder cells become more and more exposed - the symptoms worsen over time. We do not understand what causes the balance between damage and repair, and why some flare-ups continue for longer than others. However, the understanding of the structure of the GAG layer and the protection it offers gives us a direct option for treatment.

Damaged or absent GAG layer



How GAG layer replenishing therapy works

Artificial replenishment of the GAG layer can help in a variety of clinical situations. These include:

- Recurrent bladder infections (rUTIs)
- Bladder pain syndrome (BPS) which is also called interstitial cystitis (IC)

- Chemical cystitis (such as after BCG (Bacillus Calmette-Guérin) treatment for bladder cancer)
- Radiation cystitis (after previous radiation treatment for any pelvic cancers).

Restoring the GAG layer reduces inflammation in the bladder and reduces symptoms as a result, as toxins and acids from within the urine can no longer reach the bladder cells directly. Natural healing is supported and excess cells from the immune system leave the bladder again. Pain and urgency messages are no longer triggered as frequently or as strongly; reducing these symptoms and helping psychological and quality of life recovery.

A replenished GAG layer also restores the natural barrier to bacteria, making bladder infections less likely to occur and easier to fight off again.

Changes in the GAG layer can contribute to and interact with other functional changes within the bladder; driving symptoms further. Such other changes include changes in the way the bladder cells function, changes in the transmission of messages from the bladder to the brain, changes in the reactions of the immune system, and interaction with psychological symptoms. These multiple issues explain why GAG layer replenishment can take some time to help symptoms, and also why in some patients GAG layer replenishment fails to improve symptoms.

GAG layer replenishing therapy

Different GAG layer replenishing treatments are available and your Consultant or Nurse will discuss the most suitable ones for you. This article will serve as a general summary of bladder instillations as a GAG replacement therapy.

Bladder Instillations

There are many different types of bladder instillations. They can be used for all clinical situations mentioned in this article (bladder pain syndrome / interstitial cystitis, chemical cystitis, radiation cystitis and recurrent urinary tract infections). Different instillations contain different amounts of the component parts of the GAG layer which help to physically rebuild it. The treatment is administered directly into the bladder; in most cases this will be through a catheter, but catheter-free options are also available. There are usually no common side effects in other parts of the body, but a small number of patients will feel pain and pressure during administration due to a very small bladder. Most people can hold the 40-50ml of solution contained within the treatment for at least 30 min in their bladders without side effects. The solution is excreted by peeing it out. Generally, all courses start with 4 individual instillations over a month. The requirement and frequency of further instillations vary by condition, product and prescriber. Only bladder pain syndrome patients may require the treatment long-term, as their GAG layers appear to be damaged more easily and frequently long term.

Personal recent data regarding bladder instillations from a high-volume centre included 74 patients; 9 times as many females as males and all ages were represented. 65% of patients found benefit during the initial 4 treatments (over 1 month), and 70% of patients found improvement once the course was completed or they were converted to long-term treatment.* The benefit was similar in all bladder conditions. Pain due to a very small bladder capacity occurred in 3 patients.

Restoring the GAG layer reduces inflammation in the bladder and reduces symptoms as a result, as toxins and acids from within the urine can no longer reach the bladder cells directly. Natural healing is supported, and excess cells from the immune system leave the bladder again. Pain and urgency messages are no longer triggered as frequently or as strongly; reducing these symptoms and helping psychological and quality of life recovery. GAG layer replenishing treatment is usually directly instilled into the bladder. Such treatment can be very effective.

There is still a lot we don't know about damage and healing of the GAG layer, or how to predict in advance which patients will benefit from GAG layer replacement. Nevertheless, many patients benefit from it and it can transform their lives.

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