

a) WHAT IS AVAILABLE AND WHAT IT DOES¹

1 In the UK, people with Addison's disease are entitled to free NHS prescription medication, by asking their GP to authorise a Medical Exemption Certificate for them.

HYDROCORTISONE is prescribed to replace the cortisol steroid normally produced by your adrenal glands. Lack of cortisol is what causes the muscle weakness, low blood sugar and loss of concentration commonly experienced by Addisonians. There are several substitutes for hydrocortisone, the most common ones being prednisone, dexamethasone and cortisone acetate.

FLUDROCORTISONE is prescribed to replace the aldosterone steroid normally produced by your adrenal glands. Lack of aldosterone causes the electrolyte balance in the body to become destabilised as the kidneys retain potassium, the body loses salt and fluids, leading to low blood pressure and dehydration.

“I was on cortisone acetate for a few years and didn't think too much about it. When I switched to hydrocortisone I felt 100% better. It made me feel more 'normal' also when my endocrinologist added fludrocortisone. I got rid of the lower back pain I had had for so many years.” SUE

The adrenal hormones, cortisol and aldosterone, are essential for life. Their technical description is steroid hormones. Your steroid medication aims to replace them in a manner that approximates the natural rhythms of the body.

Most Addisonians are prescribed a combination of hydrocortisone and fludrocortisone to replace the cortisol and aldosterone hormones. The exact dose depends on the size and metabolism of the individual, as well as how advanced their condition is. In the early stages of the disease many individuals are still able to produce some cortisol and enough aldosterone. Getting it right depends on collaboration between you and your medical practitioners; they must monitor your blood tests and you must monitor your well-being in response to different levels of medication. In the end, a large part of your mutual success will be due to a considered process of experimentation.

Over time, an individual's need for each medication may alter slightly. If you feel a return of any of your former Addison's symptoms, or start to identify the symptoms of being over-medicated, you will need to review this with your doctor.

Cortisol replacement

Hydrocortisone is usually taken in three or two small doses over the course of the day. You may find it helpful to adjust the timing and amount of each divided dose to match changes in your lifestyle.

Hydrocortisone is the preferred drug because it is quickly absorbed and the closest mimic of what the body would naturally produce. A hydrocortisone tablet has been almost totally absorbed by the stomach and is active in the bloodstream within 30 minutes of being swallowed on an empty stomach.

Hydrocortisone has a further advantage over other types of steroid: the amount of it in your bloodstream can be accurately measured. This makes it easier to monitor your dosage and adjust it up or down if necessary.

3 MEDICATION

Prednisone and dexamethasone are longer-acting steroids and take longer to become active in the bloodstream after being swallowed. Prednisone and dexamethasone are normally taken less often and in larger single doses. Individuals who switch to these drugs from hydrocortisone may find they need to increase their fludrocortisone dose.

Cortisone acetate is an older version of hydrocortisone and less readily absorbed. It is also slower acting, as it must first be processed by the liver into a form the body can use.

Each of these other drugs has a different strength to hydrocortisone; roughly equivalent doses are shown in the table below.

ROUGHLY EQUIVALENT DOSES OF STEROIDS*

*Hydrocortisone	20mg
*Prednisone	5mg
*Dexamethasone	0.75mg**
*Cortisone acetate	25mg

* Each of these drugs has slightly different properties, which should be discussed with your endocrinologist.

** See Glossary for a more thorough discussion of the potency of dexamethasone.

Why is hydrocortisone the preferred drug?

Although it is a synthetic drug, hydrocortisone is indistinguishable from the cortisol naturally produced by the adrenals. It is also fast acting and can be measured in the blood. For these reasons, hydrocortisone is the preferred drug for most Addisonians. But it may not suit everyone. Some individuals find they do better on a longer-acting steroid.

In the UK, the 1996 survey found that around 89% of all Addisonians were taking hydrocortisone. Of the rest, 6% were taking prednisone and 5% were taking cortisone acetate.

Medical prescribing patterns do vary by country. In the US, the 1997 survey found that 65% of Addisonians were taking hydrocortisone. The remainder were taking either prednisone (20%) or cortisone acetate (15%) while just 1% was taking dexamethasone.

“I did terribly on hydrocortisone (roller coaster days) and terribly on dexamethasone (too potent and I became Cushingoid). I felt pretty good on prednisone. That was the best until my latest endocrinologist put me on cortisone acetate. I’m happy to say it is the one for me! I did find I needed differing amounts of fludrocortisone on the different corticosteroids. I needed more on prednisone than I did on hydrocortisone. And now I need less on cortisone acetate.” KELLY

Aldosterone replacement

Fludrocortisone is usually taken as a single daily dose, first thing in the morning. It is slower acting than cortisol-replacement steroids, so people who only require a small amount can take it every second day. There is a wide variation in how much fludrocortisone individuals need to take. A small number of Addisonians find they do not need fludrocortisone once their hydrocortisone medication is stable.

85% of Addisonians who took part in the 1996 UK survey were taking fludrocortisone. The amounts taken by individuals ranged from 0.025mg every other day up to 0.4mg per day, while most people were taking a standard dose of 0.1mg per day (equal to 100mcg).

Too much fludrocortisone can lead to a potassium deficiency which, in severe cases, causes an irregular heartbeat or other cardiac symptoms. Too little fludrocortisone can lead to a potassium overload, which also causes cardiac symptoms.

You will need to monitor your own response to your fludrocortisone dose and inform your medical practitioner if you experience new symptoms, which you think may be related. It is important not to modify your fludrocortisone medication before checking with your doctor.

People with secondary adrenal failure usually keep their adrenal production of aldosterone so, in almost all cases, do not need to take fludrocortisone. Similarly, individuals who are experiencing steroid-induced adrenal suppression do not usually need any fludrocortisone.

“I recently started taking fludrocortisone after my latest renin test showed that my aldosterone output is waning. I only have to take it every other day so far, and supplement with a little extra salt here and there. I have taken salt tablets when I have been in the heat.” KARLA

“I take fludrocortisone at 0.2mg a day. It helps with my sodium retention and keeps my blood pressure up. But the main reason it’s such a high dose is that my potassium wants to climb to near fatal levels without it.” TRACEY

b) THE NATURAL DAILY CYCLE OF ADRENAL HORMONE PRODUCTION

In a person with healthy adrenals, cortisol levels start to rise around 4am, are at their maximum around the time you wake up in the morning and then gradually taper off during the day. That is why you will be advised to take your largest divided dose first thing in the morning.

Cortisol levels are naturally at their lowest shortly after going to sleep, so it is best to take your last divided dose of the day by early evening. Taking

steroid medication too late in the evening can cause sleeping difficulties. Around 6pm, or at least four hours before going to bed, is best.

Aldosterone production follows a similar pattern to cortisol, with the highest levels naturally occurring around the time you wake up. That is why fludrocortisone is usually taken with the morning medication.

c) HOW DO I KNOW WHAT IS THE RIGHT DOSE FOR ME?

Some medical textbooks still refer to the standard practice of prescribing a single dose of hydrocortisone for both men and women irrespective of size and bodyweight. In practice, most endocrinologists and Addisonians now believe this is inappropriate.

Most women do not need as much as 30mg hydrocortisone while some large, well-built men do need more. Some small, lightly-built women can live comfortably on a dose of less than 20mg. Similarly, lightly-built men need less than 30mg.

■ *A rough rule of thumb is that both women and men should start with a daily dose of 20mg hydrocortisone².*
 ■ *Then if you still feel noticeably unwell, gradually increase your daily dose in increments of 2.5mg until you feel well enough to live a normal daily life.*

² Some petite women may, in fact, be able to start on a dose of 15mg hydrocortisone per day, particularly if they are also taking contraceptives or other female hormone replacement therapy.

Some Addisonians find that adjusting the timing and amount of each divided dose can be just as helpful as taking a larger daily dose.

IT IS IMPORTANT that you do not take any than the smallest possible daily dose of hydrocortisone suitable for your symptoms. Over a period of years too much can lead to damaging side-effects such as glaucoma and osteoporosis.

As a general rule, taking more steroid than your body strictly needs for a day or two is not harmful. Taking too much steroid for longer periods of time is harmful. So you can prudently increase your dose for a short time if you think you are developing a serious illness. But for your everyday medication, the aim should be to keep your dose as low as possible.

“When I was first diagnosed in 1979 I was put on 15mg hydrocortisone as I am quite petite. This dosage gradually increased to 30mg over many years. Then, about six years ago, there were other health problems. After that I slowly reduced my dose so that, for the past two years, it has been just 12.5mg a day.” SUSAN

d) TIMING YOUR DIVIDED DOSE

Some medical textbooks still refer to the standard practice of taking hydrocortisone twice a day, early morning and evening. In practice, many endocrinologists and Addisonians agree that taking a smaller, divided dose more frequently has real benefits. For example, if you commonly experience an energy-lag in the afternoon, it may help to switch from taking your medication twice a day to taking it three times a day.

It prevents the energy lag that many Addisonians experience in the afternoon when their cortisone levels are at their lowest. Some people describe this energy lag as a kind of ‘brain fog’, while others describe it as feeling low on blood sugar, faintly dizzy, or just irritable.

For people taking prednisone or dexamethasone, the timing of divided doses is usually less critical, as the medication stays in the bloodstream for longer. This can be useful for individuals whose lifestyle makes it difficult for them to take medication during the day. However, these drugs also take longer to become active after being swallowed, which can be a disadvantage at times.

“I find it important to split my medication up into three daily doses to avoid those highs and lows. Doing this I am able to continue with my physical and usually stressful work. Don’t be afraid to take your medication in smaller, spread-out doses. Taking it with food helps to slow the body’s absorption rate.”

JAMES

“The morning dose is the most important for me to take on time. But I can tell the difference with the afternoon one if I am more than an hour late. The timing can change with how the day goes, if there are a lot of stresses. Once I got up at 4am and by 7am I was on the way out. I learnt then that once I start my day I need my medication.” **ALAN**

NICK is in his mid-thirties and a keen runner. He used to take his 30mg hydrocortisone in two divided doses, 20mg before breakfast and 10mg at 6pm. Following a day curve analysis he now takes 40mg hydrocortisone in three divided doses:

- 20mg on waking
- 10mg with lunch
- 10mg at 6pm

CATHARYN is in her early forties and a full-time mother. She used to take 30mg hydrocortisone in two divided doses. After switching to three divided doses she found she could cut down her total hydrocortisone dose to 25mg:

- 12.5mg on waking
- 7.5mg with lunch
- 5mg at 6pm

MIKE is a senior civil servant. For many years he took 15mg hydrocortisone in two divided doses. Since introducing a low dose of prednisone in the evening, he has been able to reduce his total daily dose to the equivalent of just 12mg hydrocortisone. He takes:

- 7.5mg hydrocortisone on waking
- 1mg prednisone at 6pm

KAREN is in her late thirties and runs her own business as well as bringing up a young family. Before her day curve she was taking 20mg hydrocortisone a day in two doses: 15mg on waking and 5mg with dinner. Following her day curve, she now takes it three times a day:

- 10mg on waking
- 5mg with lunch
- 5mg with dinner

e) MONITORING YOUR MEDICATION: BLOOD TESTS

Thorough blood tests are available in the UK to help you determine the right daily dose of medication for you. Remember that these are tests to monitor your ongoing medication, not tests to determine whether you still have the disease. Some of these tests can be done by your GP while others need to be conducted at a hospital laboratory.

TESTS FOR HYDROCORTISONE	TESTS FOR FLUDROCORTISONE
8am plasma cortisol	Plasma renin
8am plasma ACTH	Electrolytes (potassium and sodium)
Day curve analysis	Blood pressure

The most comprehensive test of hydrocortisone medication is known as a day curve and is usually done through the endocrinology department of a major hospital. If you have not had a day curve done, you may wish to ask your GP if they could refer you to a suitable hospital.

The most widely used test of how well the adrenals themselves are functioning is the *ACTH stimulation test*. Most Addisonians will have undergone an ACTH stimulation test to confirm their diagnosis with the disease. A few Addisonians are asked to repeat this test over time to assess any further deterioration in their adrenal function.

Some endocrinologists do not offer a full day curve analysis, preferring to use a combination of 24 hour urine analysis and mid morning/mid-afternoon blood samples recording cortisol and ACTH levels.

If you cannot travel to a major hospital for a day curve, it is still possible for your GP to monitor the adequacy of your hydrocortisone dose in consultation with an endocrinologist. The 24 hour urine sample and the mid morning/mid afternoon samples of cortisol and ACTH can be administered by a GP.

Day curve analysis

Different hospitals have different procedures for a day curve, although all follow the same general principles. Most are done on an out-patient basis.

The most comprehensive day curve analysis involves taking blood samples over an 11 hour day starting early morning before you take your first divided dose of medication for the day. Repeated blood tests during the day track the medication entering your blood stream when you take each dose and record how long it lasts. The amount of hydrocortisone in your bloodstream during the day can then be compared to the ideal for a healthy individual, and the amount and timing of each dose adjusted as necessary.

“It took me a while to get the medication into a good balance after my diagnosis. It really took me a couple of years to get it right. For a while I was still so exhausted I couldn’t even walk to the letterbox and back.” JAMES

When you go for a day curve do remember to check if you are allowed to eat breakfast before you arrive. Make sure you bring all your normal daily medication with you including any medication you take for other conditions.

Following a day curve analysis, your specialist may advise you to reduce or increase your current daily dose or to try taking it in smaller, more frequent amounts. A specialist should advise you to reduce your dose if the day curve showed that your

blood levels of cortisol were significantly higher than those of a healthy person for long periods of time.

Most specialists agree that Addisonians do not need to have a repeat day curve done unless there are major changes in their general health or weight. For example, if you were to develop a further endocrine problem - such as a thyroid disorder - you should probably request a repeat day curve, once your thyroid medication had been stabilised.

f) DRUG INTERACTIONS

Most prescription and over the counter drugs will not affect your steroid medication, although it is always wise to check this with your doctor or pharmacist. However, there are a few prescription drugs that influence the way hydrocortisone and other steroid medications are metabolised by the body, either slowing down or speeding up the rate at which the steroids are metabolised. This means that anyone taking these drugs will probably need to adjust their steroid medication.

Contraceptive pills and Hormone Replacement Therapy (oral oestrogens) slow down the rate at which the body metabolises hydrocortisone by around one-third. This means a woman taking the pill or HRT is usually comfortable on a hydrocortisone dose that is one-third less than she would otherwise need. If she continues taking her previous hydrocortisone dose, she may develop mild signs of over-medication, such as a puffy face and little fat deposits on the tummy, above the collar bones and on the back of the neck.

Anyone who is taking drugs to treat tuberculosis (such as Rifampicin and Rifabutin) will typically need to increase their dose of both hydrocortisone and fludrocortisone by up to double the normal dose, as anti-tuberculosis drugs speed up the rate at which the body metabolises its steroid medication. These anti-tuberculosis drugs are highly potent, so you will need to make sure your condition is being thoroughly monitored by your doctors throughout your treatment.

Anti-epileptic medications (such as phenytoin) can also speed up the metabolism of steroids. Growth hormone treatment can lower blood levels of cortisol, by reducing the amount of cortisol-binding globulin available.

If you should need ulcer-healing drugs (such as carbenoxolone) you may need to reduce your fludrocortisone, as these drugs can lower potassium levels. If you should need to take anti-depressants, you may need to ask your doctor to monitor your electrolytes, as some types can cause the body to lose more sodium than usual.

g) MEDICATION AND FOOD

Hydrocortisone prescriptions are usually issued with instructions to take this medication with food. In practice, most Addisonians can take their tablets with just water without experiencing indigestion. This is because the amounts of steroid we swallow are smaller than those taken by individuals with medical conditions needing supplementary steroids (pharmacological doses).

If you find you do experience indigestion taking your steroid medication with water, a glass of milk (or milk substitutes such as soy, rice milk) is usually all that is needed to prevent indigestion. As a general rule, individual doses of 20mg hydrocortisone or less do not need to be taken with food.

Swallowing your tablets just with water makes it easier to take your first dose for the day as soon as you wake up. Waiting to take your first tablet with breakfast means a delay in getting the steroid into your bloodstream, during which time you will feel less well with no hydrocortisone in your blood.

It is also advisable that, if you wear contact lenses, you should put these in before taking hydrocortisone tablets, so that there is no risk of getting any traces of the medication in your eyes.

h) REPLACEMENT OF OTHER ADRENAL HORMONES?

Addisonians are usually lacking in one other major group of adrenal hormones: DHEA and its related compounds. DHEA is not available in the UK at present. However, during the late 1990s several clinical trials in the UK and internationally concluded that there were moderate benefits for most Addisonians from taking small quantities of DHEA. These benefits included protection against osteoporosis, greater energy, enhanced levels of libido and lean muscle, and relief from dry skin. Side effects noted by some individuals were acne, greasy skin and moderate weight gain. Two of the three clinical trials involved very small numbers of women

only, and none of the trials lasted longer than four months. A follow-up study in the UK is taking place during 2001/2 and this will last a full 12 months.

Anyone who is considering taking DHEA is advised to discuss this with their doctor and have their blood level measured before they do. Although clinical trials to date have recommended a daily dose of 25-50mg, not all Addisonians will need as much as this. A few individuals have reported that doses as low as 10mg brought their levels up to the normal range. Bear in mind that some endocrinologists are cautious about prescribing DHEA in advance of the results from longer-term clinical trials, while others are already doing so.

“I have been taking part in trials of DHEA over the past two years. The first study was a double blind study taking the real McCoy for three months and a dummy for three months. I knew when I was on the real tablets as I had more energy but the side effects were acne on my face, chest and scalp. I lost weight but that may have been down to more horse riding.” JANE

i) ALTERNATIVE AND COMPLEMENTARY THERAPIES

Liquorice root has stimulatory properties similar to aldosterone. If you eat real liquorice in addition to your fludrocortisone medication, you risk over-medication. Liquorice root is not recommended as a substitute for fludrocortisone as it is not possible to predict the strength or consistency of the product. Most liquorice sweets are, in fact, only liquorice-flavoured and can safely be eaten - but do check the list of ingredients. Some cough mixtures also contain real liquorice.

There are no herbal therapies available which can mimic the effects of natural human cortisol. Until steroid medication became available in the 1950s, Addison's disease inevitably resulted in death over a period of time. Addisonians who experiment with 'natural' alternatives to their normal medication risk the same fate.

Complementary therapies such as meditation, massage and yoga can offer benefits. Meditation can be a useful way of dealing with a build-up of fatigue, tension or irritability during the day. Massage and yoga can help with the joint and muscle aches which a number of Addisonians experience. Regular physiotherapy can also bring real relief for joint and muscle aches.

"I know of another male Addisonian who lived 20 miles north of here, but he was 'cured by faith' and threw away his medication. He dropped dead in his house three days later." JAMES

j) STORING YOUR MEDICATION

Most prescription medication is stable when stored between 0° and 25° Celsius (32° and 77° Fahrenheit). Always check the expiry date on your medications, especially your injection kit, and dispose of any medication that reaches its expiry date. Many medications have a shelf-life of around two years, so it is seldom worth keeping more than six months' supply at home.

At temperatures higher than 30° Celsius (85° Fahrenheit), most medication will reach the end of its shelf life more rapidly than the stated expiry date and may start to deteriorate (lose its effectiveness). For this reason, any medication that you carry close to the body in a pocket or bag should be used within a few days, unless you are storing it inside an insulated travelling container. Insulated travelling containers can be ordered through most pharmacists. If you are carrying an injection kit with you in this kind of hot weather, it should be discarded after 12 months, or sooner if

the contents become cloudy or coloured. Injection kits are discussed more fully in sections 9 and 10: *Travel and Crisis Management*.

MEDICATION: A SUMMARY

A combination of hydrocortisone and fludrocortisone is the most usual treatment for Addison's disease.

A variety of blood tests are available to help you and your doctors establish your correct baseline dosage.

You may feel better splitting your daily hydrocortisone medication into three divided doses.

Taking the first dose of the day on waking is recommended.

Individual doses of 20mg or less do not usually need to be taken with food.

The last dose should be taken no later than 4 hours before bedtime.