



# Fasting with adrenal insufficiency: Practical guidance for healthcare professionals managing patients on steroids during Ramadan

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## Summary

There are limited recommendations for fasting in many chronic diseases such as adrenal insufficiency (AI). Research in such situations highlights potential for complications and need for education for patients with AI undertaking fasting during Ramadan. This article aimed to provide up-to-date guidance for healthcare professionals to educate, discuss and manage patients with AI who are considering fasting in Ramadan and is religiously compatible. Latest guidance on this topic and the evidence base for steroid dosing are reviewed and discussed. Risk stratification for patients with AI and optimal strategies for management, including steroid dosing, are detailed. Our review highlights that patients with AI wishing to fast should undergo a thorough risk assessment ideally several months before Ramadan. 'High risk' and 'Very high risk' patients should be encouraged to explore alternative options to fasting discussed below. Prior to the commencement of Ramadan, all patients must receive up-to-date education on sick day rules, instructions on when to terminate their fast or abstain from fasting, carry steroid warning information and must have a valid intramuscular (IM) hydrocortisone pack and know how to administer this. Switching patients with AI desiring to fast from multiple daily hydrocortisone replacement to prednisolone 5 mg once daily at dawn (during Suhoor or Sehri) is recommended and discussed. Patients on fludrocortisone for AI should be advised to take their total dose at dawn. We provide practically relevant case-based scenarios to help with the application of this guidance. Future efforts need to focus on healthcare professional awareness and further research in this setting.

## KEYWORDS

ACTH deficiency, Addison's disease, adrenal insufficiency, fasting, Ramadan, steroids

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## 1 | INTRODUCTION

During the month of Ramadan, the majority of Muslims globally observe the religious obligation of fasting (abstaining from food and drink) from dawn till sunset for 29 or 30 consecutive days.<sup>1,2</sup> As the timing of Ramadan is based on the lunar calendar, Ramadan falls 11 days earlier annually and over a 33-year period, passes through all four seasons, with consequential shorter fasts in winter and longer fasts in the summer months.<sup>3</sup> Fasts can therefore stretch to up to 20 hours in temperate regions, such as in the summer in parts of the UK. It is common practice to have one meal (known as Suhoor or Sehri) just before dawn and another (known as Iftar) after sunset. Taking medicines orally and intranasally is considered breaking a fast.<sup>4</sup> Therefore, oral agents should be taken before dawn or after sunset if the patient wants to fast. Patients with AI who partake in fasting may, therefore, be at risk of dehydration and an adrenal crisis.

Adrenal cortisol secretion has a circadian rhythm with peak levels at around dawn and levels that decline during the day with low levels at night (when asleep). AI can result from primary (adrenal disease including Addison' disease), secondary (anterior pituitary disease) and tertiary (being on suppressive doses of exogenous steroids for another condition) causes. Depending on the type of AI, different approaches in management may be needed; however, all patients with AI need glucocorticoid replacement to try and mimic the natural circadian rhythm of cortisol secretion.<sup>5</sup> Religious fasting could be at odds to the multiple daily dosing mandated with the standard treatment regimen associated with hydrocortisone replacement. Furthermore, changes in daily routine and behaviour, with some individuals staying up late into the night, may alter cortisol rhythm and therefore dosing and timing requirements during this month.<sup>6-8</sup> Predicting how to manage this group needs further research, as unnecessary excessive steroid doses may be harmful and inadequate steroid cover may result in an adrenal crisis. Risks of adrenal crisis may be even higher in primary AI with mineralocorticoid deficiency, or secondary AI with concomitant pituitary (diabetes) insipidus as compared to other forms, due to the greater risk of electrolyte imbalance and hypovolaemia.<sup>9,10</sup>

With up to 1.8 billion Muslims throughout the world and 3.4 million Muslims in the UK, it is estimated that approximately 450 000-750 000 people worldwide and 850-1450 people in the UK are likely to be considering fasting with AI during the month of Ramadan.<sup>11-15</sup> Given the rising incidence as well as other aetiologies for long-term steroid dependence, this figure is likely to be higher in the UK. Fasting with AI can result in complications, especially if the patient's understanding of their health condition is low.<sup>16</sup> Furthermore, there is evidence to suggest that many patients continue to fast despite complications occurring.<sup>16</sup> Therefore, it is vital that people on glucocorticoid replacement wishing to fast are educated on the nature of their condition as well as the requirements of fasting, to empower them to make an informed decision about fasting and how to minimize the potential risks to themselves.

Patients on long-term glucocorticoid replacement wishing to fast need a thorough clinical assessment, ideally some months

before Ramadan, which includes a review of their regular medications, complications, co-morbidities and social and lifestyle factors to help determine what is best for them. Guidance on safe fasting and education on sick day rules combined with instructions on when to urgently terminate their fast is essential. For example, patients who are unwell enough to contemplate sick day rules ought not to fast that day. Despite such advice, some patients may choose to fast against medical advice, and it is important then to try and ensure this happens safely.

Healthcare professionals (HCPs), in particular endocrinologists, can play a key role in optimizing patients with AI to fast and help them to make the correct decisions with regard to their health and fasting. At present, there is a brief consensus of South Asian guideline on this topic.<sup>10</sup> However, given the emergence of recent evidence and the longer duration of fasts in many temperate countries, further guidance is needed which this article intends to address.

## 2 | METHODS

This guideline aims to provide guidance for HCPs managing patients with AI who wish to partake in religious fasting. Given the paucity of formal guidance and consensus of professional opinion on this important topic, the Society for Endocrinology commissioned the authors to undertake a review of the evidence and provide experience-based guidance for HCPs in the UK and abroad. The authors used a combination of the limited published literature on fasting with AI, available research on fasting with other long-term conditions and clinical experience in this setting to help inform this guidance. Furthermore, existing experience with once-daily steroid options as an alternative to multiple hydrocortisone dosing in AI was reviewed.

Finally, the guidance and advice that is proposed by the authors in this review is for a nonpandemic or prevailing mitigating circumstances. Where appropriate, any additional or specific guidance, for example pertaining to COVID-19, has been clearly outlined.

### 2.1 | Section 1: Glucocorticoids for primary, secondary or tertiary adrenal failure and considerations for fasting

#### 2.1.1 | Standard glucocorticoid replacement regimens

Patients may be on hydrocortisone, which owing to its short half-life needs to be taken twice or thrice daily, prednisolone which has a longer half-life and can be taken once daily on waking, cortisone acetate which is taken twice daily or modified-release preparations of hydrocortisone which are typically taken once a day.<sup>17-19</sup>

Additionally, patients with secondary AI may be on other pituitary hormone replacement including thyroxine, growth hormone, sex steroids (testosterone or oestrogen) and desmopressin, and those with primary AI may also be on fludrocortisone. Whilst

these hormone replacements have briefly been discussed, this article aims to focus on glucocorticoid replacement in patients with primary or secondary AI. It is crucial, however, that clinicians consider the impact fasting may have on patients requiring multiple hormone replacements when advising them on how to take their medications during a fast and whether indeed it is safe for them to fast at all.

### 2.1.2 | Ramadan-specific steroid regimens for consideration

Although twice-daily hydrocortisone is a potential option, the doses will need to be administered at dawn and sunset. If the day is long, such as during the long summer days in the UK, cortisol levels are likely to fall significantly before sunset and so patients on this regimen need to be advised to terminate their fast if they become unwell before sunset. A typical replacement dose is 15–25 mg taken at higher doses in the morning, noon and lower dose in early evening. There is no available evidence to suggest that the 'stress' of fasting warrants a dose increment in steroids; however, this is something that should be individualized and could form part of future research. Furthermore, stress from partaking in activities such as optional evening prayers (called Tarawih) which last approximately 1.5–2 hours may need additional consideration.

Once-daily prednisolone is an easier alternative and is used at doses of 3–5 mg in most patients outside fasting.<sup>17–19</sup> There has been one randomized double-blinded controlled trial comparing prednisolone 5 mg in the morning and placebo at sunset, to twice-daily hydrocortisone (10 mg + 5 mg) that showed no difference in any markers of well-being or risk of adrenal crisis.<sup>20</sup>

Another potential option are modified-release hydrocortisone preparations.<sup>21</sup> These are currently very rarely prescribed in the UK.<sup>22</sup> Whilst patients taking modified-release hydrocortisone preparations can theoretically fast without any dose adjustments, their very high costs, poor availability worldwide and no reported experience in this setting do not make them a suitable option as a first-line recommendation for Ramadan-specific steroid dosing.

A single tablet of prednisolone 5 mg has the advantage of being widely available throughout the world and is the only glucocorticoid available in many countries. It may also offer a theoretical advantage in temperate countries such as the UK, which are further from the equator and where the current duration of fasts is longer than in North Africa where this trial was undertaken.<sup>18</sup> The option of lower doses such as 3 or 4 mg daily would be interesting to study in Ramadan, but 1 mg tablets of prednisolone are not widely available. The EU-AIR study highlighted that majority of patients are on hydrocortisone and some patients are over-replaced which may be responsible for the adverse cardiometabolic profile in these individuals.<sup>23</sup> Prednisolone has a longer half-life than hydrocortisone, so the dose equivalence is not linear. The dose equivalence ratio for hydrocortisone is between 6:1 and 8:1.<sup>24</sup> A full replacement dose of prednisolone is between 2.5 and 5 mg once daily.<sup>17,19</sup> Further

randomized controlled trials to determine whether lower doses are sufficient are needed to determine optimum replacement strategies.

Mineralocorticoid replacement should be continued at the same dose. Fludrocortisone is usually taken as 50–100 µg once daily; however, doses may be higher in some individuals. Synthetic glucocorticoids such as prednisolone have lower mineralocorticoid activity as compared to hydrocortisone.<sup>25</sup> Given their relatively modest contributions towards mineralocorticoid replacement, hydrocortisone to prednisolone conversions do not usually need additional fludrocortisone doses.

Most patients with primary AI should therefore take 5 mg prednisolone and their usual morning dose fludrocortisone at dawn (during Suhoor or Sehri) if they choose to partake in fasting. Conversion from hydrocortisone to prednisolone can occur immediately before the month of Ramadan starts.<sup>20</sup>

Patients with secondary AI should preferably have all their replacement hormones including the choice of steroid, thyroxine, growth hormone and sex steroids optimized prior to Ramadan. Patients who are on higher doses of steroids for other conditions should consult their specialists about whether fasting is safe and should continue their steroid treatment at the same dose if over an equivalent of prednisolone 5 mg.

Pregnant and breastfeeding women are discussed in more detail in the case-based scenario section of this review (Section 4). In relation to pregnancy, a low threshold to not fast should be advocated, particularly when there is clinical uncertainty in relation to outcomes or there is a genuine or legitimate fear of harm as outlined in the following section. However, if mothers were insistent on fasting, essentially these women could also be managed with once-daily prednisolone (3–5 mg depending upon the stage of pregnancy). During lactation, this results in negligible amounts of prednisolone in breast milk and is unlikely to cause any systemic effects in the infant.<sup>26</sup>

## 2.2 | Section 2: Health considerations relating to fasting in Ramadan and adrenal insufficiency

### 2.2.1 | General principles and considerations

At its core, Islamic law, the Shari'ah, aims to protect integral values including an individual's life, well-being and health.<sup>27</sup> A degree of difficulty as a means of encouraging virtues such as patience is expected in Ramadan for those partaking in it; however, religious law encourages the pre-emption of potential harm to health and well-being and provides exemptions and alternatives in place of the usual rituals.<sup>28</sup> Islamic rulings make several exceptions to lift the obligation of fasting for those in whom it may entail hardship such as the elderly, those who are travelling, those with significant mental health illness and pregnant women (if there is known, or potential risk, or an appropriate HCP has legitimate concern to the health of the mother and/or foetus).<sup>29,30</sup> At present, there is some evidence that fasting during pregnancy may have negative effects on the unborn foetus.<sup>31–33</sup>

**TABLE 1** Risk stratification for fasting with adrenal insufficiency

Low/Moderate risk (Decision to not fast based on discretion of medical opinion and ability of the individual to tolerate fast)	Stable and well-controlled adrenal insufficiency (low) No significant co-morbidities (low) Treated concomitant mineralocorticoid deficiency (moderate)
High risk (Advice should NOT fast)	Recent diagnosis of steroid dependence within the last 3 mo Pregnancy
Very high risk (Advice MUST NOT fast)	Multi-morbidity: major organ system involvement Concomitant diabetes mellitus on insulin treatment Concomitant pituitary (diabetes) insipidus Adrenal crises in the last 12 mo Untreated concomitant mineralocorticoid deficiency Untreated TSH deficiency

### 2.2.2 | Terminating a fast and use of medication when fasting

Islam supports those with appropriate ailments to terminate the fast or be exempted from fasting if there is reasonable expectation that a person will become ill (eg those with pre-existing or current physical illness which may be significantly exacerbated by fasting are permitted to not fast), or that their health would be compromised such that they would not be able to function in a safe or responsible manner due to physiological compromise.<sup>34</sup> In such a circumstance, the two main alternative options to fasting are as follows<sup>1,3</sup>:

- Making up the missed fast when their health permits them to do so—either when the illness is no longer present, such as in acute illness, or when the illness is not worsened by fasting at another point in time in relation to chronic illness, for example fasting in the winter when the days are shorter.
- An exemption from fasting in those whose illness will not permit them to keep fasts indefinitely, this being replaced by a requirement to feed the poor (fidyah).

Reasonable expectation of illness or compromise would be determined by applying one of the three following criteria: (a) prior experience of what fasting does to the ailment; (b) common knowledge (eg effect on a person with Addison's disease who does not take their latter doses of hydrocortisone tablets); and (c) the opinion of a qualified physician on the matter.<sup>29</sup> Appropriate ailments can also include old age, or a condition which is stable, but through fasting the condition can adversely affect health or increase the risk of doing so especially with abstaining from use of medications, for example steroid replacement in adrenal failure. A more detailed exposition pertaining to the religious obligation of fasting and considerations in relation to health and illness has been published elsewhere by authors of this review.<sup>35</sup>

It should be highlighted that although unanimous opinion exists on certain issues, there is a breadth of opinion on a variety of issues and healthcare providers may encounter Muslims with differing viewpoints on these issues. Furthermore, a significant number

of people who have been advised not to fast by their HCP may still choose to do so.<sup>16,36</sup>

### 2.3 | Section 3: Practical guidance for healthcare practitioners when approaching this situation in clinic

Whilst all patients with AI have a higher probability of complications during prolonged fasting than the general population, it may be useful for clinicians to risk stratify patients when discussing the implications of fasting on their patient's health. This risk stratification should take into consideration not only the patient's endocrine condition but also their other co-morbidities, medications and overall frailty. Patients, as well as clinicians, may find this approach beneficial when making informed decisions about partaking in fasting during Ramadan. Such an example of risk stratification has been utilized in authoritative international diabetes guidance (International Diabetes Federation endorsed Diabetes and Ramadan [DAR] Guidelines) and has been approved by the Islamic Organization for Medical Sciences and the International Islamic Fiqh Academy.<sup>1</sup>

Thus, the authors propose the following categorization for risk stratification as outlined in Table 1, using the same type of categorization and definitions applied by DAR. Patients in the 'low and moderate' risk category could be supported through religious fasting with appropriate education and counselling whilst those in the 'high' risk and 'very high' risk category should be encouraged and supported to explore alternative options to fasting. However, this list is not exhaustive and should assist and does not replace the clinician's overall judgement. Each patient's scenario should be assessed based on their own individual clinical and social circumstances; however, the list in Table 1 provides a general guide.

In the context of prevailing mitigating circumstances, for example the current COVID-19 global pandemic, the authors advise upgrading the patient's baseline categorization to the next categorization, for example moderate risk becoming high risk. Further details are available in resources developed specifically for this setting.<sup>37</sup> Such a recommendation is based on current expert advice given in relation to patients with adrenal insufficiency (AI) being at increased

risk of severe illness from COVID-19.<sup>38,39</sup> Given the significant burden on healthcare services from the current COVID-19 pandemic, the recommendation also attempts to minimize the strain on health services given possible requirements for access to HCPs for education or prescription changes. However, the authors acknowledge that such prevailing circumstances are evolving, and the latest advice and evidence can also change. Therefore, HCPs are advised to check appropriate national specialist bodies websites for latest guidance.

### 2.3.1 | General education and emergency management plans

- All patients with AI wishing to fast should receive up-to-date education on steroid sick day rules (verbal and written) and must have a valid intramuscular (IM) hydrocortisone pack with training on how to administer this prior to the commencement of Ramadan.
- Patients should be warned of the symptoms of acute AI and should be advised to urgently terminate the fast and administer IM hydrocortisone if they develop these symptoms.
- All patients should always also be given and advised to carry a steroid warning card with details of their local endocrine unit.<sup>40</sup>
- In addition, patients with concurrent mineralocorticoid deficiency should be advised to avoid prolonged sun exposure to minimize salt and water losses.
- Adrenal crisis needs to be managed urgently in hospital, with intravenous fluids. Patients should not delay hospital admission for fear of contracting COVID-19.

Figure 1 is a flow diagram which HCPs are encouraged to follow when discussing fasting in patients with AI (modified from Ref. 35), and Table 2 provides a summary. Table 3 provides sick day rules guidance for Ramadan and covers guidance during intercurrent illness, in

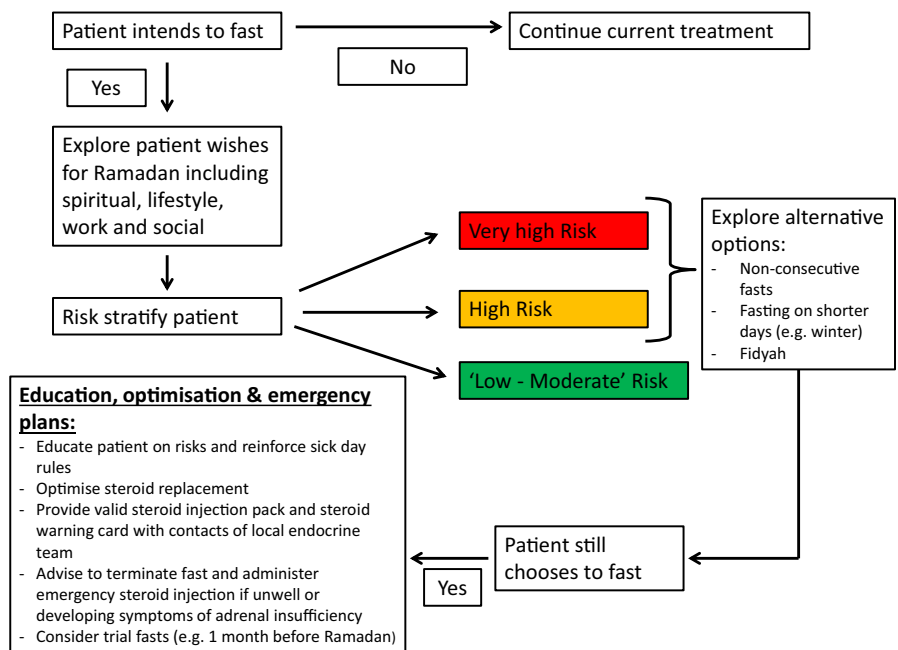
line with previous guidance.<sup>41</sup> Any situation that requires doubling of glucocorticoid doses or emergency hydrocortisone injections warrants immediate breaking of the fast and abstinence from fasting until complete recovery.

### 2.3.2 | Hydration advice

It is extremely important that all patients ensure adequate hydration with noncaffeine containing fluids between dusk (Iftar) and dawn (Suhour or Sehri). Given the presence of concomitant mineralocorticoid deficiency, patients with primary AI may be at increased risk of hypovolaemia and dehydration especially if their condition has not been adequately treated.<sup>9,10</sup> As a general precaution, patients with primary AI may be advised to rehydrate with electrolyte replacement (fluids with added salt) whilst those with secondary AI with pituitary (diabetes) insipidus are likely to require more free water.

### 2.3.3 | Patients on exogenous glucocorticoids for other conditions

Patients on oral steroids for other conditions should consult their specialists regarding safety of fasting. In most scenarios, where someone is well enough to undertake fasting and is on exogenous glucocorticoids, long-acting formulations, such as prednisolone, are typically used. For patients who are on a tapering dose of prednisolone for other conditions, with no underlying AI, there is no evidence that a change in dose is required during fasting. These should be continued during fasting at the same dose. Further dose reductions should be discussed with their physicians and may be delayed until Ramadan is over.



**FIGURE 1** Flow diagram for healthcare professionals to help with decision-making, discussions and management of patients with adrenal insufficiency (AI) who are intending to fast [Colour figure can be viewed at wileyonlinelibrary.com]

**TABLE 2** Summary of guidance for the management of patients with adrenal insufficiency who wish to fast during the month of Ramadan

Patients on long-term glucocorticoid replacement wishing to fast should undergo a thorough risk assessment ideally several months before Ramadan

'High risk' and 'Very high risk' patients should be encouraged to explore alternative options to fasting, which may require input from family members and/or the appropriate religious authority

All patients must receive up-to-date education on sick day rules combined with instructions on when to terminate their fast or abstain from fasting

The above point is of particular importance in the context of any prevailing unique and mitigating circumstances, for example the COVID-19 pandemic

Patients must have a valid intramuscular (IM) hydrocortisone pack and know how to administer this prior to the commencement of Ramadan

All patients should be advised to carry a steroid warning card with contact details of their next of kin and local endocrine unit at all times

Patients who use their IM hydrocortisone and are still unwell should go directly to hospital for intravenous fluids, which are lifesaving especially with the COVID-19 pandemic

Switching patients with adrenal insufficiency (AI) who are wishing to fast from multiple daily hydrocortisone replacement to once-daily prednisolone at dawn (during Suhoor or Sehri) is recommended. In most cases, such as patients who are on a total daily hydrocortisone dose between 15 and 30 mg daily, a dose of prednisolone 5 mg once daily will be sufficient

Patients on fludrocortisone for AI should be advised to take their total dose at dawn (during Suhoor or Sehri) and avoid prolonged sun exposure

Patients on steroids for other conditions with no concerns regarding adrenal insufficiency should consult their specialists about whether fasting is safe and should continue their steroid treatment at the same dose

Pregnant and breastfeeding patients with AI should be advised against fasting. This should be more strongly stated if there are concerns around absorption of steroids or other complications during pregnancy and in the post-partum period

## 2.4 | Section 4: Examples of case-based scenarios with potential treatment options discussed for patients with adrenal insufficiency intending to fast

The following scenarios cover a range of likely cases HCPs are likely to encounter in relation to patients with AI and intending to fast and possible options that can be offered to facilitate safe fasting. These scenarios assume the absence of prevailing mitigating circumstances (at the time of publication, such as the COVID-19 global pandemic). It must be made clear from the outset that regardless of any advice offered by the HCP, the final decision to fast or otherwise rests with the patient and clear documentation of relevant discussions and outcomes should be documented or mentioned in relevant clinical letters. Further in any of the following scenarios or the like, if it becomes apparent that patients are struggling to fast (including

**TABLE 3** Sick day rules for Adrenal Insufficiency in Ramadan

Type of illness	Actions
Mild intercurrent illness	<ol style="list-style-type: none"> <li>1. No further actions needed, however, if symptoms worsen, have a very low threshold to undertake actions listed below and maintain good hydration between Iftar and Sehri/Suhoor</li> </ol>
Moderate intercurrent illness	<ol style="list-style-type: none"> <li>1. Break your fast immediately and abstain from fasting</li> <li>2. Double your usually daily glucocorticoid dose (eg if you are on prednisolone 5 mg once-daily, increase this to 10 mg once daily)</li> <li>3. Rehydrate by drinking plenty of fluids</li> <li>4. Always carry your steroid warning card with contact details of your local endocrine team</li> <li>5. Ensure you have a valid steroid injection pack and that you or your carer or cohabitants are aware on how to administer this</li> <li>6. Resume fasting only when you are completely well—if you are unsure, then seek medical advice before resuming your fasts</li> </ol>
Severe intercurrent illness or persistent vomiting	<ol style="list-style-type: none"> <li>1. Break your fast immediately and abstain from fasting</li> <li>2. Give an emergency hydrocortisone IM injection (100 mg)</li> <li>3. Seek urgent medical attention immediately as emergency management in hospital with intravenous fluids and hydrocortisone infusion is very likely to be needed</li> <li>4. Resume fasting only when you are completely well—if you are unsure, then seek medical advice before resuming your fasts</li> </ol>

having to prematurely terminate the fast) or health or safety concerns emerge by ongoing fasting, then terminating the fast and not fasting the rest of the month of Ramadan is the default clinical and religious standpoint.<sup>1,30,35</sup>

### 2.4.1 | Scenario 1—Fasting with ACTH deficiency

Mrs A is a 45-year-old lady with partial ACTH deficiency following transsphenoidal surgery and external beam radiotherapy for acromegaly. She takes hydrocortisone once a day on waking and has done so for many years. She is well-versed with sick day rules. Both she and her husband are trained in administering IM hydrocortisone. She would like to fast during Ramadan and has in fact been doing this for the last few years but has never discussed this before. She reports taking hydrocortisone at Suhoor (dawn). She is able to fast

but finds herself feeling very low in energy by Iftar (sunset) time. She has struggled to take part in evening prayers (tarawih) after breaking her fast.

#### Discussion

Mrs A is in the low-risk category and has a good understanding of her condition. As she is receiving once-daily hydrocortisone, she could continue to take this during Ramadan prior to commencing her fast at Suhoor. However, an additional evening dose of hydrocortisone (eg 5 mg) can be considered particularly if she wishes to partake in evening prayers. Alternatively, temporarily switching to prednisolone 5 mg at dawn should be considered.

### 2.4.2 | Scenario 2—Fasting with primary adrenal insufficiency

Mr M is a 60-year-old gentleman with a long history of primary AI due to Addison's disease for which he takes hydrocortisone (10 mg on waking, 10 mg at midday and 5 mg at 5 PM) and fludrocortisone (100 µg on waking and 50 µg in the evening). Although he has been discouraged from fasting in the past, he would like to attempt fasting during Ramadan this year and would like to discuss this.

#### Discussion

Given Mr M has primary AI, the risk of an acute adrenal crisis should be discussed. Patients with primary AI are likely to be at higher risk of adrenal crisis, than patients with secondary or tertiary AI, due to higher risks of dehydration and hypovolaemia from concomitant mineralocorticoid deficiency.<sup>9</sup> Alternatives to fasting during the summer months should be discussed (as detailed in Section 2). If the patient still chooses to fast during Ramadan, nonconsecutive fasts and trial fasts should be encouraged.

To support fasting, hydrocortisone should be switched to once-daily steroid replacement (eg prednisolone 5 mg at Suhoor) and he should be advised to take all of his fludrocortisone at this time as fludrocortisone has a long half-life, and splitting the dose has no advantage. Although not necessary, if the HCP or patient have unfamiliarity or uncertainty with this regimen, a trial on this new steroid regimen of prednisolone 5 mg and fludrocortisone 150 µg every morning combined with an assessment of Mr M's BP and electrolytes prior to the start of Ramadan is encouraged where possible. Steroid education and emergency management, as outlined in Section 3 above, should be reinforced. Importance of hydration should be reinforced and considering fluids with electrolyte replacement (or added salt) should be considered.

### 2.4.3 | Scenario 3—Fasting with multi-morbidity and adrenal insufficiency

Mrs Y is a 75-year-old lady with congestive cardiac failure requiring daily diuretics, type 2 diabetes mellitus on multiple daily insulin

injections and secondary adrenal deficiency on replacement doses of hydrocortisone. She is aware of the risk of life-threatening adrenal crises, fluid overload and electrolyte disturbances through delaying and/or omitting her medications to partake in fasting during Ramadan. As her clinician, she would like to discuss whether fasting would be exempt given her multi-morbidities with you.

#### Discussion

Mrs Y is in the high-risk category and should be actively discouraged from fasting given the potential adverse effects on her health. She should be advised not to observe longer fasts, and even shorter fasts (eg in the winter months) as it is likely to cause harm to her health. Thus, as a perpetual circumstance to debarring safe fasting exists, Mrs Y would be advised to pay fidyah to the poor as an alternative. Where possible, input from other family members or the local imam should be considered.

### 2.4.4 | Scenario 4—Fasting with panhypopituitarism (secondary AI)

Miss Z is a 26-year-old lady with ACTH, TSH and gonadotrophin deficiency. She is currently well managed on hydrocortisone (10 mg on waking, 5 mg at midday and 5 mg at 5 PM), levothyroxine (75 µg once daily) and sequential combined transdermal HRT. She would like to resume fasting which she undertook prior to her diagnosis 2 years ago.

#### Discussion

Given that Miss Z is well managed, she is low risk. For steroid replacement, as outlined previously, education, optimization and emergency plans should be discussed. As in case 2, once-daily steroid dosing with prednisolone should be considered to give adequate steroid coverage through the day.

Fasting with well-controlled hypothyroidism is safe. Although levothyroxine can be taken at any time where it is permissible to eat and drink, it may be difficult to adhere to taking this as per usual recommendations (30 minutes before food to maximize its absorption) given the short window to eat and drink during the long summer fasts in Ramadan. Therefore, it is possible that during the month of Ramadan the absorption of levothyroxine may be reduced. This is unlikely to have a significant impact in most situations; however, depending on the patient's practices, best options to time the intake of levothyroxine can be discussed. In most cases, this is immediately on waking for Suhoor or immediately after breaking fast at Iftar.

Transdermal medications are permitted during fasting.<sup>4</sup> However, if the patient wishes to consider oral options which they can take when it is permissible to eat and drink, a switch can be considered ideally at least a month before Ramadan.

Whilst undergoing menstruation (naturally, or iatrogenically induced), patients are exempt from fasting. However, they will have to make up for their missed fasts at a later date. However, as menstrual

bleeds in this situation are iatrogenically induced, patients, if they desire to, could be managed with a continuous combined HRT option, or continue back-to-back COCP usage if they would prefer to avoid menstrual bleeds during the month of Ramadan and revert to sequential combined options thereafter.

#### 2.4.5 | Scenario 5—Fasting with panhypopituitarism (secondary AI) including pituitary (diabetes) insipidus

Mr X is a 54-year-old gentleman with panhypopituitarism secondary to a pituitary adenoma managed with 10 mg of hydrocortisone on waking and 5 mg at lunchtime, Nebido 1 g every 4 months, levothyroxine 100 µg and desmopressin 10 µg nasally twice daily.

He expresses a desire to fast during the month of Ramadan. He asks you about the practicalities of doing this.

##### *Discussion*

Given Mr X has pituitary (diabetes) insipidus along with cortisol, thyroid and gonadotrophin deficiency, he is in the high-risk category and the clinician should explain the risks of severe dehydration, electrolyte imbalance along with risks of adrenal crisis to the patient. The patient's anterior hormone deficiencies can be managed as discussed in previous cases. However, given the prolonged fasts and disruption in regulating fluid and electrolyte homeostasis in pituitary (diabetes) insipidus, there are no safe management strategies that can be considered. Thus, fasting should be strongly discouraged on health grounds. Furthermore, the intake of desmopressin (oral or intranasal) is not permissible during a fast.<sup>4</sup> Even nonconsecutive fasting or winter fasts would be risky in this situation. The HCP should discuss alternatives to fasting such as fidyah. To help aid discussions, input from other family members or the local imam can be considered.

In patients with mild pituitary (diabetes) insipidus on once-daily desmopressin (morning or evening) who insist on partaking in Ramadan despite HCP recommendations and high risks of dehydration, clinicians *could* consider supporting the patient if the fasts are <12 hours in duration and during the winter months; however, all other options of not partaking in fasts should be considered first. If faced with this situation, we would strongly encourage that the patient first undergoes a supervised trial fast with close fluid balance and electrolyte monitoring, prior to the commencement of Ramadan. That said, it is likely that most hospitals would not be able to support this, in which case fasting would not be recommended. If the patient still chooses to proceed with fasting, then they should be counselled on the potential risks, including very high risks of dehydration and hypernatraemia, particularly if they wish to partake in consecutive fasts during the summer days. Ensuring good hydration with water, rather than electrolyte-rich fluids, should be encouraged. They should be strongly advised to have a low threshold to terminate the fast and encouraged to hydrate themselves well.

#### 2.4.6 | Scenario 6—Pregnant mothers and considerations for breastfeeding

Mrs B is a 28-year-old lady with adrenal suppression due to long-term steroids for inflammatory bowel disease (IBD). Her IBD is now in remission; however, her adrenal axis did not fully recover and as a result she was commenced on hydrocortisone 10 mg on waking and 5 mg in the early afternoon by her endocrinologist. She appropriately increased the dose of hydrocortisone at the start of the third trimester to 15 mg on waking and 10 mg in the early afternoon. She is 24-week pregnant, and her obstetrician is happy with both her and her baby's progress.

She would like to fast during Ramadan which falls in her final trimester and early post-partum phase. She would like to discuss the safety of this with you.

##### *Discussion*

Pregnant patients are best advised to defer their fasts and make up for them after pregnancy if there are concerns of risk to the mother and/or foetus, as outlined earlier, by the pre-empting criteria to avoid fasting in mitigating circumstances.<sup>29</sup> However, despite this, if a pregnant mother is considering fasting, important and relevant risks of causing harm to the mother and/or foetus should be communicated clearly, particularly where medical or scientific evidence is available. In this scenario, there are no specific additional risks from AI. Concomitant type 1 diabetes mellitus which can coexist with Addison's disease would be an example of where a pregnant mother would be told unequivocally not to fast.<sup>30</sup> This patient and others choosing to fast in the long summer period during pregnancy despite medical recommendations can be supported with standard pregnancy advice for AI, which for prednisolone treatment is 5 mg daily.

In the nonfasting individual, the dose of steroid replacement is unchanged in the first and second trimesters and is increased by 20% to 40% in the third trimester. In the first trimester, prednisolone 3-5 mg once daily or hydrocortisone 20 mg divided into three doses is commonly used. Both are inactivated by 11-betaHSD type 2 in the placenta (to prednisone and cortisone, respectively), so that neither has any effect on the foetus. Fluorinated steroids (such as dexamethasone) are not inactivated by 11-betaHSD type 2 and also do not have mineralocorticoid activity.<sup>25</sup> They should not be used as steroid replacement during pregnancy, but of course can be used where the aim is to treat the foetus, as with lung maturation.

Outside pregnancy, the evidence is that 3-4 mg daily is optimum, so the dose of 5 mg in the third trimester would be appropriate. The only evidence on dosing available at present suggests that 5 mg daily is safe and effective during Ramadan, although lower doses may be appropriate, further studies need to be undertaken to confirm this.<sup>20</sup> Patients must be advised to have a very low threshold to terminate fasting if they are unwell. Pregnant patients with AI should be advised against fasting if there are concerns around poor absorption of steroids, nausea, vomiting, hyperemesis, other complications during



pregnancy or intermediate or high risk of fasting with AI (Table 1). In this situation, the patient can make up for their fasts missed after pregnancy if deemed safe.

Similarly, during breastfeeding, patients may choose to defer their fasts and make up for them after breastfeeding, particularly if there is concern regarding milk production diminishing or the mother is unable to meet the necessary calorific demand in the short period available to eat between fasts. However, if they consider fasting and are low or intermediate risk, they can be supported with prednisolone 5 mg once daily. This results in negligible amounts of prednisolone in breast milk and is unlikely to cause any systemic effects in the infant.<sup>26</sup>

### 3 | CONCLUSION

This review presents a summary of research, guidance and consensus of professional opinion from authors on the practical management of AI in Ramadan. It highlights the importance of education and optimization of steroid replacement in this setting. As outlined in Ramadan guidance in relation to diabetes, there is a strong need for patient and HCPs and religious/community figureheads such as imams to engage with each other and discuss these contemporary medical issues.<sup>30,35</sup> Finally, future research work to explore unanswered questions and expand on the limited evidence base is needed.

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### CONFLICT OF INTEREST

Nothing to declare.

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