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WHICH URINE TEST?

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insight

- A spot urine with creatinine correction is the preferred method of urine collection rather than a 24 hour urine collection due to its ease and better reproducibility.
- eGFR is preferred to 24 hour urine creatinine clearance. The only exceptions are when a patient's muscle mass is unusual for their age or sex (ie. cachexia or athletes).
- The preferred sample for urine albumin is an untimed, first morning urine for albumin creatinine ratio, not a 24 hour urine collection.

Introduction

The examination of urine to detect or monitor disease is an ancient medical skill that is still effective today. Urine testing is primarily used to detect diseases of the urinary tract, however it can also be valuable in testing for other diseases.

The main obstacle with urine testing is that analyte concentration depends largely on the patient's fluid intake. This can result in a substantial variation of the amount of a particular substance in the urine.

Standardising urine concentration is important to allow for the variable amount of water in urine.

There are two common approaches to standardising urine concentration (1) collecting a spot urine and measuring creatinine and (2) collecting urine for 24 hours.

Spot Urine Reference Intervals

	Men	Women	Pregnant Women
Albumin/Cr (mg/mmol)	<2.5	<3.5	n/a
Protein/Cr (mg/mmol)	3-20	4-25	<30
Calcium/Cr (mmol/mmol)	<0.5	<0.7	n/a

Collecting a spot urine and measuring creatinine

The standard approach to correcting an analyte concentration for the rate of water excretion is to express the result as a creatinine ratio (eg. albumin/creatinine ratio or calcium/creatinine ratio). The underlying principle is that creatinine is produced constantly throughout the day because it is a spontaneous by-product of creatine metabolism in muscle.

It is important to acknowledge that men have more muscle than women, so men have a higher urine creatinine than women. Therefore the albumin creatinine ratio in men is lower than for women because men's creatinine is typically higher. This principle applies to all urine creatinine ratios.

Timed/24 hour urine collections

By collecting urine for a defined time interval, we can compare the rate of analyte excretion rather than the concentration of the analyte. For example 24 hour catecholamine excretion (umol/day) or overnight (10hr) albumin excretion rate (ug/min).

The major criticism of timed collections is that some patients may not be very good at performing them. A patient's sense of timing may not be as thorough as required; and some patients (particularly the elderly) may get confused about when they must empty their bladder, and what urine should be discarded or kept.

Furthermore, some factors are out of the patient's control. For example, the patient may think they have emptied their bladder but residual bladder volume can vary between 10-50mL. Furthermore, higher residual bladder volume may be more common in clinical practice due to prostatism in elderly men and diabetic neuropathy. It is also important to note that a higher residual bladder volume increases the patient's predisposition to bacteriuria and urinary tract infections (UTI's).

Common Urine Tests	Optimal specimen
Urinary Tract Infection (UTI)	Spot mid stream urine. Cervical swab still best detection for chlamydia
Diabetes Hypertension	Spot first morning urine – for albumin creatinine ratio
Renal Disease	Spot first morning urine – for protein creatinine ratio
Urine Drug Screen (UDS)	Spot urine. Australian Standard AS 4308 - supervised collection. Avoid excessive water consumption
Polyuria	Spot first morning urine for osmolality
Myeloma	Consider serum test for free light chains
Phaeochromocytoma	Consider plasma metanephrines
Cushing's Disease	Consider midnight salivary cortisol
Carcinoid Syndrome	24 hour urine for 5HIAA
Gout	24 hour alkaline urine for uric acid
Calcium disturbance	24 hour acidified urine for calcium

Mid Stream Urine (MSU)

When collecting a urine sample for bacterial culture it is very important to avoid contamination due to skin commensals by the simple techniques involved in obtaining a mid-stream urine sample (MSU).

Red cells can gradually lyse (especially in dilute urine), so optimal examination of erythrocyte morphology requires urine that is as fresh as possible (preferably less than two hours old).

First stream urine samples are much better for detecting Neisseria gonorrhoeae or Chlamydia trachomatis by PCR; however cervical swabs have a greater sensitivity for the detection of Chlamydia than a urine sample.

Albuminuria

The term 'microalbuminuria' is being replaced with the simpler term 'albuminuria' because we are testing for small amounts of albumin, not for a small form of albumin. Even normal kidneys leak a small amount of albumin every day – usually less than 10mg. Albumin excretion increases with exercise and protein meals and therefore overnight collections are more accurate. Furthermore, because the laboratory is better at performing a creatinine measurement and correction than the (usually diabetic) patient is at completing their overnight collection, **the preferred sample for urine albumin is an untimed, first morning urine for albumin creatinine ratio.**

Proteinuria

Proteinuria is usually defined by its detection with a urine protein dipstick. The levels of protein loss are greater than albuminuria (which is not detectable by protein dipstick). **For both accuracy and convenience, the preferred sample for urine protein is also the first morning urine for protein creatinine ratio.** Proteinuria that is only present during the day (orthostatic proteinuria) is usually of no clinical concern.

Urine Drug Screen (UDS)

This method of testing for drugs of abuse is becoming increasingly common for medicolegal and occupational purposes.

It is important to realise that for urine drug screen results to 'stand up in court', the collection and analysis of the urine must be done according to the Australian Standard AS4308. Melbourne Pathology is one of the few laboratories in Victoria that is accredited to this Standard, and supervised urine collections can be performed at many of our specialised collection centres. To locate one of these collection centres, call 9287 7700.

The most common query about this test also relates to creatinine measurement. A low creatinine value (defined as < 1.8mmol/L), according to the Standard, defines a urine sample which is unusually dilute and unreliable as the subject may be deliberately providing dilute urine to avoid detection. It is possible to reach these low concentrations, particularly in subjects with low muscle mass, by drinking a litre of water before the test – therefore excessive water consumption should be avoided in order to eliminate any doubt being cast on the subject's motives. One glass (300-400mL) an hour before the test is usually adequate to avoid difficulties in producing a urine specimen.

24 Hour Urine for Creatinine Clearance

These are rarely necessary as the calculation of eGFR from the serum creatinine level (and the patient's age and sex) is more reliable. The underlying reason for this is that an estimate of the patient's muscle mass, based on their age and sex, is more accurate than the patient's ability to collect an accurate 24 hour urine sample. **The only exceptions are when a patient's muscle mass is likely to be unusual for their age or sex** (ie. body builders or elite athletes, or a decrease in muscle mass in cachexia or significant causes of muscle atrophy).

Polyuria

The measurement of urine osmolality is the best test of a patient's ability to concentrate urine. Frequently, patients who complain of polydipsia and polyuria are suspected of having diabetes insipidus (especially when diabetes mellitus has been excluded). The easiest way to screen for the inability to concentrate urine is to collect the first morning urine and test for urine osmolality. This is because when we are lying asleep there is less blood flow to the kidneys, and the first morning urine is typically the most concentrated urine we produce all day. Diabetes insipidus is not rare, especially when you consider its most common cause is hypercalcaemia.

Myeloma

The presence of free immunoglobulin light chains in urine is a poor prognostic sign in paraproteinaemia and multiple myeloma. Although the testing of urine has been used for over a century, the detection of free light chains in serum has superceded urine measurement and is now rebateable in myeloma, plasma cell dyscrasias and amyloidosis.

Phaeochromocytoma

For patients with severe or unexpected hypertension, the simplest method of screening for a noradrenaline producing tumour (phaeochromocytoma) is by the detection of noradrenaline in a 24 hour urine. In this case a spot urine is less useful because the urine may not be collected during a paroxysmal episode of hormonal excretion. **A test which is proving increasingly popular in these cases is plasma metanephrines.** These blood borne metabolites are generally a good sign of both increased catecholamine production and the altered metabolism of phaeochromocytoma.

Other conditions

24 hour urine cortisol testing for Cushing's disease has generally been superceded by the midnight salivary cortisol test, which is much more convenient for patients. 24 hour 5-hydroxy indole acetic acid (5HIAA) is the screening test for carcinoid syndrome, particularly when symptoms of skin flushing and diarrhoea are present. Uric acid excretion requires an alkaline urine collection and urinary calcium collections should be acidified, otherwise precipitation will lead to an underestimate of these analytes.

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