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Please read this bit first

The HPCSA and the Med Tech Society have confirmed that this clinical case study, plus your routine review of your EQA reports from Thistle QA, should be documented as a "Journal Club" activity. This means that you must record those attending for CEU purposes. Thistle will **not** issue a certificate to cover these activities, nor send out "correct" answers to the CEU questions at the end of this case study.

The Thistle QA CEU No is: **MT00025.**

Each attendee should claim **THREE** CEU points for completing this Quality Control Journal Club exercise, and retain a copy of the relevant Thistle QA Participation Certificate as proof of registration on a Thistle QA EQA.

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Misdiagnosis of patient results: The possibility of error

Factors that may lead to errors and inappropriate application of laboratory-derived results include:

- Misuse of the reference range
- Analytical error
- Artefactual results

Reference range

A reference range (or reference interval) is a statistically derived set of figures which indicates the range of values, for a given analyte, found in the majority (e.g. 95%) of the so-called 'normal' (or reference) population. There are several methods for deriving these figures but most describe 95% of the given population, e.g. mean value plus/minus two standard deviations (2SD) of the values found. Therefore at the outset at least 5% (1 in 20) of 'normal' people will, by definition, have a value outside the given reference range. Reference ranges are often expressed by defining the upper and the lower limits.

Most laboratories supply only one set of reference values for a given analyte, but it is important to realise that there are a number of biological factors that influence the reference range. The most important of these are *age, sex, physical size, pregnancy, and time of sampling*.

Age: e.g. *plasma alkaline phoshatase* – high in infants, children, and young adults up to 20 years of age (upper limit approximately 2.5 times the adult level);

Sex: e.g. *plasma gamma-glutamyl transferase (GGT)* – lower in women (male, <45 U/L; femaile, <30 U/L);
plasma testosterone – lower in women;
plasma urate – lower in women

Physical size: e.g. *plasma creatinine* – lower in infants, children, and small women (since it relates to muscle mass)

Pregnancy: e.g. *plasma thyroxine binding globulin (TBG)* – higher in pregnancy and may result in a high plasma total thyroxine

Time of sampling: e.g. *plasma cortisol* exhibits a circadian rhythm – higher in the morning

All of these factors should be considered when interpreting a given result. A good example is provided by the influence of muscle mass on the plasma creatinine value. The reference range for this analyte in an adult is about 60 – 120 mmol/L. If the glomerular filtration rate falls, e.g. due to hypovolaemia of dehydration, the plasma creatinine value may increase two-fold (e.g. to 100 µmmol/L) and yet still remains within the reference range.

Analytical error

If an analyte is re-analysed a number of times on the same sample, different values will be obtained because of the inherent error of the method. This is called the precision (or imprecision) of the method and reflects the ability of the laboratory to achieve the same result every time the sample is analysed.

This analytical error may be expressed in absolute units or as a percentage e.g for plasma sodium it may be 3 mmol/L or 2%. This means that for a measured plasma sodium concentration of 135 mmol/L, the true sodium level lies somewhere between 135±3 mmol/L, or 132-138 mmol/L

Knowledge of this type of error is important when considering two values on the same patient, taken at different times. For example, in a patient treated for hypernatraemia, if the original sodium level was 170 mmol/L and the level after treatment was 165 mmol/L then it follows that:

- the original value lies between 167-173 mmol/L
- the second values lies between 162-168 mmol/L

The overlap between these two values suggest that there has been no actual change in the plasma level. Had the second value been 163 mmol/L (160-166 mmol/L) then it is probable that there has been a significant change in the plasma sodium concentration.

Artefactual result

Most abnormal laboratory results are expected in that they reflect some known, or suspected, pathophysiology. Occasionally a value may be totally unexpected or not, suggested by the patient's disease processes. In these circumstances artefactual causes should be considered before taking any action, and it is a wise course to obtain another specimen from the patient for re-analysis.

Whenever an unexpected result (abnormal ot normal) occurs, it should be re-evaluated with respect to: the patient, the specimen, the container and the method of transport.

Patient

- **Clinical condition**: e.g. the high plasma acetoacetate levels found in diabetic ketoacidosis interfere with the Jaffẽ reaction for the measurements of plasma creatinine giving fasely high values.
- **Diet:** e.g. high plasma levels of glucose and triglycerides occur in the early postprandial state
- **Drugs:** e.g. prednisolone cross-reacts with cortisol in most radioimmunoassay methods giving falsely high values
- **Exercise:** e.g. severe unaccustomed exercise increases the plasma levels of lactate and creatine kinase

Specimen sampling

- **Time of day:** e.g. plasma cortisol is higher in the morning (circadian rhythm)
- **Site :** e.g. venous samples taken proximal to IV infusions reflect the infused material
- **Technique:** e.g. blood gas samples containing air bubbles result in a low Pco^2 and a high Po^2
- **Tourniquet:** e.g. prolonged use of a tourniquet can result in abnormalities such as high plasma calcium and albumin levels.

Container

- **Lack of preservative:** e.g. the glucose level in samples not containing fluoride decreases with time
- **Wrong preservative:** e.g. blood samples taken into potassium-EDTA tubes will show high potassium and low calcium levels.

Sample transport

- **Delayed separation:** e.g. prolonged contact between blood cells and plasma will result in high plasma potassium and phosphate levels.

CPD Questions:

1. List and discuss the biological/factors influencing reference range.
2. Detail and consider your lab's policy with regard to what this article calls 'artefactual' results. Do you consider the factors mentioned as being potential causes?