

# HbA1c REVISITED: CHANGE OF UNITS AND INTERPRETATION

by Dr Bevan Hokin

HbA1c is one example of a 'glycated haemoglobin' – a term covering a number of chemically different modifications to the haemoglobin molecule, resulting from the binding of glucose to various amino groups in the haemoglobin molecule. This reaction occurs between glucose and all blood and blood-cell proteins that have free amino groups.

The effect on haemoglobin is marked, as the red cell membrane is particularly permeable to glucose. While the extent of formation of HbA1c depends on the plasma glucose concentration, other factors such as temperature, pH, ion concentrations and the duration of the exposure, influence the reaction.

The glycation of haemoglobin is irreversible. The removal of HbA1c from the blood is linked to the average life of red blood cells (about 120 days). Consequently the HbA1c reflects plasma glucose levels over the preceding few weeks.

The measurement of glycated haemoglobin has become an important test to assess metabolic control in diabetics and in retarding the progress of complications.

## THE LABORATORY MEASUREMENT OF HbA1c

Until recently there have been several potential problems that could confound the interpretation of glycohaemoglobin results:

- Four different assay principles
- Twenty different methods
- Measuring different glycohaemoglobins (total glycated haemoglobin, HbA1 and HbA1c)
- Different standardisation of the methods resulting in different results for the same patient sample
- Reproducibility of some methods
- Difficulty in comparing results from different laboratories.

## PROGRESS TOWARDS STANDARDISATION

Standardisation is critical to allow comparisons between methods and laboratories. A working

party of the International Federation of Clinical Chemistry (IFCC) and the American Association for Clinical Chemistry (AACC) that included international (including Australian) input has co-ordinated an international project by which all methods are standardised. Further, Glycohaemoglobin analyser manufacturers and all reagent manufacturers have their assays standardised by Reference Laboratories established by the IFCC/AACC working party.

Consequently all laboratory methods will report their HbA1c results in units which have been standardised against the reference method. The new unit is mmol of glycated haemoglobin per mole of haemoglobin.

As part of this standardisation process, terminology and units have changed:

- The terminology to be used for the assay is glycohaemoglobin (GHb) assay
- The unit of measurement for GHb is mmol/mol
- Other units such as %GHb, %HbA1 should not be used
- Assay methods must have a coefficient of variation (CV%) better than 5% and preferably better than 3%.

## INDICATIONS FOR REQUESTING GHb

- Monitoring diabetic metabolic control
- Improving patient compliance
- Primary diagnosis of diabetes (although Medicare do not have an item number for this use of GHb (HbA1c) results).

## TARGETS AND REFERENCE RANGE FOR GHb

- The old target for HbA1c being <7% and preferably <6.5% will now be 53 and 48 mmol/mol respectively for GHb.
- The now out-of-favour "Change therapy" level of 8.0% becomes 64 mmol/mol.
- The old GHb (HbA1c) reference range of 4.0 to 6.0% becomes 20-42 mmol/mol.

Note that most laboratories will be reporting both old and new units for up to two years to allow clinicians to become familiar with the new units. However, the "Estimated Average Glucose" (eAG) result will be discontinued shortly.

## WHAT CONCLUSIONS CAN BE DRAWN FROM THE GHb VALUE?

The GHb value provides information about the average blood glucose concentration during the past several weeks, compared with serum glucose, which reflects the momentary situation. Good diabetic control may be inferred from a GHb result of <48 mmol/mol. Consistent values >64 mmol/mol suggest that treatment should be considered.

Elevated GHb is also a predictor of the risk of progression to diabetic complications.

## SENSITIVITY OF GHb MEASUREMENT

A newly diagnosed and treated diabetic should experience a drop in GHb of about 11 mmol/mol every 10 days until normoglycaemia is achieved. (e.g. from 86 to 75 in first 10 days etc.).

Biological and analytical variability suggests that a change in GHb of 5 or 6 mmol/mol indicates a clinically significant change in metabolic control. Three consecutive smaller changes in the same direction also suggest a clinically significant change in control.

## CONCLUSIONS

Clinicians and patients alike can have confidence in the reliability and clinical utility of the new improved GHb results. It is now possible for patients and their doctors to directly compare their level of glycaemic control against international standardised data.

*Information sourced from consensus/position papers published by AACB, ADEA and RCPA*

SAN Pathology uses an approved Reference method for GHb and has imprecision data of < 2%.



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# IS THERE ANY LIFE LEFT IN MODERN FLUOROSCOPY?

By Dr Martin Davis

Fluoroscopy has been available since the beginning of radiology.

Until the 1960s fluoroscopy depended on very faint images which were directly visualised on fluorescent screens which were illuminated directly by x-rays and used a form of geometric and analogue electronic image intensification dependent on minification of the image. During the 1960s television cameras were utilised to provide further electronic amplification and image intensification and also allowed recording. The technology used in the 1960s through to the late 1990s was very bulky, complex to manufacture and maintain, using large glass vacuum tubes, and prone to drift in image quality. The bulkiness of the image intensifier chain and of the generator unit made this equipment quite threatening to patients, and it was difficult to work with patients who were very sick or had multiple intravenous lines or drains in situ following major surgery.

Clinical utilisation of fluoroscopy started to reduce in the 1980s with the widespread adoption of computed tomography and ultrasound. However usage of fluoroscopy remained strong in the 1980s and early 1990s in the area of gastrointestinal imaging, with large daily lists of barium meal and barium enema examinations in most radiology departments. Since endoscopy has become much more widely available it has largely replaced fluoroscopy as examination of first choice for both upper and lower GI examination apart from special cases. As a result most radiology practices established in the last decade have not made the investment in fluoroscopic equipment and those practices with equipment which has come to end of life have often not replaced the machinery.

During the last decade however there has been significant technology advancement in flat panel detectors which convert x-rays directly into an electrical signal which can be amplified and displayed on a liquid crystal

display monitor. This results in a significantly smaller receiver component for fluoroscopic system which increases flexibility in patient positioning and movement. Although they cost approximately twice the price of a current image intensified analogue system, these new digital flat panel detectors provide significant advantages which include: larger field of view, no introduced image distortion, wider dynamic range, reduced image flaring, and usually significantly reduced radiation dose. Modern computer technology coupled with these detectors has allowed fast acquisition of sequential images and these flat panel detectors have gained wide acceptance in angiography and cardiac catheterisation. The price however has limited the usage of these systems in the general fluoroscopy arena, in view of the reduced clinical demand.

Fortunately the new flat panel detector technology coupled with modern computer systems and the experience of manufacturers with modern flat panel cardiac catheterisation and angiography and digital radiography equipment has broadened the options for equipment replacement.

While it is apparent that there will not be a significant demand for routine barium meal or barium enema examinations there remains a few specialised areas where these examinations are required for best practice support for difficult clinical problems. These include oesophageal resection or gastric resection, bariatric preoperative and post-operative assessment, and post-operative colonic resection assessment.

The last decade has seen increasing demand for upper gastrointestinal procedural endoscopic support including ERCP, biliary and gastrointestinal stenting, all of which require increasingly detailed imaging, and in some cases prolonged procedure time where a reduction in patient and operator radiation dose is important and significant.

Additionally there will be a requirement for low-dose paediatric fluoroscopy particularly in gastrointestinal tract and urinary tract assessment as well as image guided joint injection.

The development of flat panel detector workflows from cardiac catheterisation and angiography has enabled some of these procedures to be performed on a flat panel detector fluoroscopic unit with only minimal software enhancement. Thus a modern flat panel fluoroscopic unit can be designed to perform procedures such as peripheral line insertion or simple angiography.

Flat panel detector technology such as used in a modern digital fluoroscopic unit shares many features in common with a modern digital detector standard radiographic room. This equipment can therefore be utilised for many standard radiographic projections and is particularly advantageous in those examinations which require precise positioning for interpretation. Thus this equipment is seeing increased utilisation in the post operative assessment of metallic joint prostheses, and in specialised projections of certain complex anatomic regions such as the shoulder or ankle.

Sydney Adventist Hospital Radiology department has invested recently in a state-of-the-art radiographic/fluoroscopic unit with flat panel detector and basic angiography capability. This will allow San Radiology to satisfy the fluoroscopic needs of the specialist referral base for ERCP, complex upper and lower GI surgery assessments, and paediatric cases as necessary. The unit can also be used for vascular access and other simple angiography procedures as the anticipated demand for complex angiographic and interventional procedures increases beyond the capacity of the current new facility. Additionally the unit can also be used where appropriate for standard radiography.



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