HARMONIZATION PROPOSAL FOR SYNACTHEN TESTING BASED ON AN AUDIT OF OVER 1100 TESTS AND LITERATURE REVIEW

Kay Weng Choy1, Nilika G Wijeratne1,2,3, Kevin TK Lee2, James CG Doery1,2
1 Monash Pathology, Monash Health and 2 Department of Medicine, Monash University, Clayton, 3 Dorevitch Pathology, Heidelberg, Victoria
Kw.choy@monashhealth.org

A Short Synacthen Test (SST) is widely accepted as the best first line procedure to definitively exclude adrenal insufficiency but many differences exist in all aspects of the test. Can we define a path to greater harmonisation? Harmonisation involves two key steps; harmonisation of the testing protocol and harmonisation of the cut-off to define sufficiency.

METHOD
We have analysed our extensive data base of >1,100 serial Synacthen tests to establish:
• Relationship between 30 & 60 minute cortisol responses
• Effect of age and
• Effect of gender on cortisol response
We have also evaluated selected recent pertinent literature to highlight current obstacles to a harmonised protocol and consensus cut-offs for adrenal insufficiency. We have only considered the 250 ug IM test.

RESULTS
Based on our data1 and that of Chitale et al2 we have produced evidence that a Synacthen test is best rationalised to only 2 samples; baseline and 60 minutes. Notwithstanding this view we and Chitale have confirmed a consistent correlation between the 30 and 60 minute responses with 16% further rise at 60 minutes.

REFERENCE
Chitale A et al 2013
Choy KW et al 2014
Mean

Table 1. Relationship between 30 & 60 min cortisol response

<table>
<thead>
<tr>
<th>Method</th>
<th>50 min cut-off</th>
<th>60 min cut-off</th>
<th>Proposed 60 min cut-off</th>
</tr>
</thead>
<tbody>
<tr>
<td>GCMS</td>
<td>418/421</td>
<td>486/490</td>
<td>490</td>
</tr>
<tr>
<td>Abbott</td>
<td>430/416</td>
<td>500/484</td>
<td>490</td>
</tr>
<tr>
<td>Advia</td>
<td>448/446</td>
<td>521/519</td>
<td>520</td>
</tr>
<tr>
<td>Beckman Access</td>
<td>459/455</td>
<td>534/529</td>
<td>530</td>
</tr>
<tr>
<td>Siemens</td>
<td>469/478</td>
<td>545/556</td>
<td>550</td>
</tr>
<tr>
<td>Roche</td>
<td>574/524</td>
<td>668/609</td>
<td>640</td>
</tr>
</tbody>
</table>

Table 2. Proposed method dependant cut-offs at 60 min

CONCLUSION
The SST should be standardised to:
• 250 ug IM dose of Synacthen
• 60 minute post Synacthen cortisol.
• 30 min cortisol samples are not necessary

DISCUSSION
There is general consensus that a 250 ug test is the preferred dose of Synacthen with a growing acceptance of a 60 minute cutoff. Much work remains to be done by the IVD industry to obtain alignment of immunoassays with isotope dilution MS methods.

REFERENCES
1. Choy KW, Lee KTK, Wijeratne N, Doery JCG. Synacthen testing: Do we need a 30- or 60-minute sample or both? J Endocr. 2014
3. Choy KW, Wijeratne N, Lee KTK, Doery JCG. Influence of age and gender on cortisol response using a data mining approach to over 1,000 sequential short Synacthen tests. JACC: 2016, P329
   
   A high level working party is indicated to provide ongoing review of new literature and development of consensus Guidelines for Synacthen testing.