MDRTB/XDRTB depends on drug sensitivity test (DST) results to the remaining first-line and reserve drugs.

We have previously demonstrated that our national ‘fastrack’ molecular tuberculosis and rifampicin resistance identification service significantly reduces time for detection compared with bacteriological culture. Overall, Mycobacterium tuberculosis complex is detected 15.2 days earlier than gold standard automated liquid culture methods and detected 15.2 days earlier than gold standard DST results to relevant clinics, reducing the need for the introduction of genotypic tests for MDRTB. DST results to relevant clinics, reducing the need for the introduction of genotypic tests for MDRTB.

Table 1 MDRTB and additional drug resistances: years 2008 and 2009 (complete drug profiles)

<table>
<thead>
<tr>
<th>Drug</th>
<th>2008+2009</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total MDRTB strains with complete DST profile</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MDRTB (R+H)</td>
<td>107</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>MDRTB (R+H) + resistance to any reserve drug*</td>
<td>51</td>
<td>48</td>
<td></td>
</tr>
<tr>
<td>MDRTB (R+H) + sensitivity to all reserve drugs*</td>
<td>17</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>Group 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MDRTB (R+H) +/or E +/or Z</td>
<td>56</td>
<td>52</td>
<td></td>
</tr>
<tr>
<td>MDRTB (R+H) +/or E +/or Z + resistance to any drugs*</td>
<td>34</td>
<td>61</td>
<td></td>
</tr>
<tr>
<td>MDRTB (R+H) + sensitivity to all reserve drugs*</td>
<td>22</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>Resistance to first-line drugs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethambutol</td>
<td>48</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td>Pyrazinamide</td>
<td>30</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Resistance to reserve drugs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injectables†</td>
<td>6</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Quinolones‡</td>
<td>21</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Prothionamide</td>
<td>41</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>Streptomycin</td>
<td>68</td>
<td>64</td>
<td></td>
</tr>
<tr>
<td>XDR</td>
<td>3</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

In multidrug-resistant tuberculosis (MDRTB) isolates the rate of resistance to any reserve drug was significantly greater when accompanied by resistance to another first line drug (group 2 vs group 1) (Fisher’s exact test p=0.0065). Our findings justify a policy of using the ‘fastrack’ approach and, when rifampicin resistance has been detected and a culture obtained, of setting up DST to all first and reserve drugs immediately and simultaneously (rather than the conventional approach of DST for reserve drugs only when MDRTB is detected phenotypically). The NMRL has recently added a similar test for resistance to isoniazid and the introduction of genotypic tests for XDRTB would be highly desirable. This policy would greatly accelerate the return of DST results to relevant clinics, reducing the time for the instigation of appropriate management, helping to reduce any increasing prevalence of MDRTB.

Acknowledgements The authors owe grateful thanks to all staff of the NMRL for their expertise and unfailing cooperation. FAD was responsible for policy development and is the guarantor. DCSh and NS developed the database for assessing the drug resistance patterns in MDRTB cases. All authors contributed to the study design, had full access to all of the data and take full responsibility for the integrity and interpretation of the results and writing of the manuscript. All authors approved the final manuscript.

Concluding remarks None.

Contributors SLM was responsible for the drug sensitivity tests. FAD was responsible for policy development and is the guarantor. DCSh and NS developed the database for assessing the drug resistance patterns in MDRTB cases. All authors contributed to the study design, had full access to all of the data and take full responsibility for the integrity and interpretation of the results and writing of the manuscript. All authors approved the final manuscript.

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A randomised trial of domiciliary ambulatory oxygen in patients with COPD and dyspnoea but without resting hypoxaemia

We read with great interest the recently published article by Moore et al1 and we would like to make the following remarks.

Desaturation with exercise is still a hotly debated issue, and the papers that deal with the effectiveness of oxygen therapy during exercise in patients with chronic obstructive pulmonary disease who desaturate have not shown any benefit.2 3 It should nevertheless be pointed out that there are different types of desaturating patients with exercise. Indeed, we recently published a paper4 the results of which clearly show that only patients who desaturate before 1 min—early desaturators—during the 6-minute walking test are associated with an important desaturation during daily life activities. This is why we believe that desaturation with exercise research has to take into account whether the patients are early or late desaturators in order to reach sound clinical conclusions. Along the same lines, the effectiveness of oxygen therapy in these patients can differ according to the type of patients (early or late desaturators).
Peripheral airway/alveolar nitric oxide concentration in asthma

We read with great interest the paper by Gelb and colleagues1 who suggest that peripheral airway/alveolar nitric oxide (NO) concentration after correction for axial NO back-diffusion (CalvNO\textsubscript{corrected}) is normal during asthma exacerbation (with a hypothesis of an incidence of >50% of its increase). If one admits that an exacerbation constitutes the ultimate expression of loss of asthma control, their results are in line with ours demonstrating that CalvNO\textsubscript{corrected} is not a marker of asthma control.2 Nevertheless, some of their patients with an exacerbation had an increase in CalvNO\textsubscript{corrected} since one can see in their figure 5 that almost 20% of their patients are above the 95th percentile of healthy subjects (>7 ppb). The small size of their cohort (n=15) is an obvious limitation that is acknowledged by the authors. We therefore reanalysed the results of our multicentre trial to evaluate the prevalence of increased CalvNO\textsubscript{corrected}. When using an upper normal limit of 25% for CalvNO\textsubscript{corrected} (that corresponds approximately to their upper normal value), the prevalence of its increase is 23% (41/175) in our population of adults and children with asthma. In our study we further demonstrated a negative relationship between CalvNO\textsubscript{corrected} and mid forced expiratory flow (FEF\textsubscript{50–75%}), which may suggest that peripheral NO could be associated with airway remodelling.2 This latter result was in line with the demonstration that peripheral airway/alveolar NO concentration, after correction for axial NO back-diffusion, can be increased in some patients with asthma (~25%). Whether peripheral NO helps to identify a specific 'phenotype' of asthma which may be more closely linked to severity than to control warrants further studies.

Gelb and colleagues also show that 2/15 subjects with an exacerbation had normal exhaled NO values.1 Similarly, we have previously shown in a multicentre trial that patients with acute asthma admitted to the emergency department can have normal exhaled NO levels (2/65 patients in our study).2 In conclusion, the clinical usefulness of techniques to discriminate NO gas exchange between large central airways and peripheral smaller airways/alveolar compartments in patients with asthma remains to be established, and the factors governing the increase in exhaled NO remain partly determined.

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Competing interests CD has received a free NO analyser (ENDONO 8000) from SERS (Aix en Provence, France) for the development of their software for NO analysis at multiple exhaled flow rates. BM has no competing interests.

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Author’s response

We thank Garcia-Talavera et al for their interest in our paper.1 We acknowledge their findings, in a group of chronic obstructive pulmonary disease patients with only mild hypoxaemia, of a correlation between early oxyhaemoglobin desaturation during the 6-minute walk test (6MWT) and desaturation over 24 h.2 The 6MWTs performed in our study were carried out according to American Thoracic Society guidelines.3 Given their recommendations that oxygen saturation measured by pulse oximetry (Sp\textsubscript{O}2) should not be used for constant monitoring during the test and that the technician must not walk with the patient to observe Sp\textsubscript{O}2, saturation in our study was measured at rest and immediately at the end of the 6-minute period. We are thus unable to comment upon the presence or absence of early as opposed to late desaturation in our cohort of desaturators. Nonetheless, it is likely that our group of 80 ‘end test’ desaturators would have included both early and late desaturators, according to the definition of Garcia-Talavera et al. We found no association between the degree of desaturation at the end of the 6MWT and our primary or secondary outcome criteria. Others have similarly found an absence of association between the degree of desaturation and improvement in exercise capacity with supplemental oxygen.4 Whether or not early desaturation during the 6MWT correlates with desaturation during activities of daily living or nocturnally, it remains unknown whether such early desaturation correlates with degree of dyspnoea or whether treating it with supplemental oxygen would improve this symptom.

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Competing interests None.

Ethics approval This study was conducted with the approval of the Human Research Ethics Committee, Austin Health, Heidelberg, Victoria, Australia.

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