Ofloxacin and Pulmonary Tuberculosis

To the Editor:

We read with great interest the article by Kohno et al published in the December, 1992, issue of *Chest* concerning the comparison of ofloxacin and ethambutol in the treatment of pulmonary tuberculosis.1 We wish to supplement and reiterate on several issues concerning the potential role of ofloxacin for the treatment of pulmonary tuberculosis.

As referenced by the authors, ofloxacin has distinct activity against intracellular *Mycobacterium tuberculosis*.3 It is also well known that ofloxacin, like other fluoroquinolones are well concentrated within alveolar macrophages.3 Thus it is likely that ofloxacin like pyrazinamide has sterilizing capacity, which is a drug characteristic that contributes to the success of short-course chemotherapy. Indeed, this issue has been explored in another study, though comparing ciprofloxacin (rather than ofloxacin) with pyrazinamide.4 In that study, all patients received 6 months of daily rifampicin and isoniazid with either 2 months of ethambutol and pyrazinamide or 4 months of ciprofloxacin. There has been a rapid fall in culture positivity in the standard regimen group and a more gentle decline in the ciprofloxacin group. However, this does not reach statistical significance. The other aspects that warrant investigation are the early bactericidal effects and the prevention of emergence of resistance.4 Concerning adverse reactions, from the finding of Kohno and coauthors,1 it does seem that ofloxacin is as well tolerated as ethambutol with particular reference to the liver. We have lately reported the relatively good tolerance of ofloxacin in 29 patients with hepatic dysfunction and pulmonary tuberculosis.5 This property might be unique to ofloxacin because it is normally handled almost exclusively by renal clearance though changes secondary to hepatic dysfunction have not been completely unraveled.6 We also concur with Kohno and co-authors that ofloxacin might have a place in the treatment of multidrug resistant pulmonary tuberculosis. In addition to our earlier report,7 we have treated another 12 patients with bacilli resistant to at least streptomycin, isoniazid, and rifampicin *in vitro* with ofloxacin. Two patients received 400 mg ofloxacin once daily. Ten patients received 600 mg to 800 mg ofloxacin once daily. Other accompanying drugs used included kanamycin, ethionamide, cycloserine, ethambutol, and pyrazinamide depending on guidance provided by *in vitro* susceptibilities. All 12 patients achieved culture conversion within 4 months of commencement of chemotherapy.

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6 Todd PA, Faulds D. Ofloxacin: a reappraisal of its antimicrobial activity, pharmacology and therapeutic use. Drugs 1991; 42:825-76

Assessing Exercise-induced Bronchospasm

To the Editor:

We read with great interest the study by Haas et al,1 which appeared in the January 1993 issue of *Chest*. The authors advocate the use of the entire maximum expiratory flow volume (MEFV) curve in determining presence or absence of exercise-induced bronchospasm (EIB). There are several points we would like to emphasize and comment on.

Haas et al1 state that it is misleading to use an arbitrary reduction in a single forced expiratory airflow parameter (for example FEV1 or PEFR) to diagnose EIB. Furthermore, the use of arbitrary criteria has already been condemned as unacceptable.2 In

Table 1—Response to Exercise in the Group of 70 Atopic Asthmatic Children

<table>
<thead>
<tr>
<th></th>
<th>FVC</th>
<th>FEV1</th>
<th>FEF25.75%</th>
<th>PEFR</th>
<th>FEF25</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of resting value</td>
<td>87.73</td>
<td>72.93</td>
<td>54.46</td>
<td>72.87</td>
<td>52.79</td>
</tr>
<tr>
<td>(mean and SD)</td>
<td>(14.04)</td>
<td>(16.26)</td>
<td>(19.69)</td>
<td>(18.84)</td>
<td>(22.55)</td>
</tr>
<tr>
<td>% of responders</td>
<td>42.86</td>
<td>88.57</td>
<td>85.71</td>
<td>70.00</td>
<td>68.57</td>
</tr>
</tbody>
</table>

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our opinion, it is essential first to establish the mode of response in the normal population in a specified protocol and to use this as a standard for the estimation of EIB. Our experience of a group of 48 normal children suggests that a reduction in FEV\(_1\) of 15 percent is too great and that 10 percent would be more appropriate for the detection of EIB.

We recently have studied the response to exercise in 70 atopic asthmatic children (Table 1). The MEFV curves were obtained before and then 2, 5, and 10 min after 6 min of free-running exercise. The FVC, FEV\(_1\), PEFR, FEF\(_25-75\) and FEF\(_25\) were recorded, and responders were defined as having a fall greater than normal group mean, 2 SD, in any of the parameters used (ie, >10 percent fall in FEV\(_1\) and FVC; >17.5 percent in PEFR; >26 percent in FEF\(_25-75\)); and >40 percent in FEF\(_25\). There was a marked reduction in all pulmonary function tests (Table 1) with the greatest drop being at 5 min post exercise. The pattern of response indicated that changes occurred both in the large and in the small airways. Sixty-three patients had a positive response to exercise in at least one of the five tests used, and the combination of FEV\(_1\) and FEF\(_25-75\) enabled detection of all responders.

Our results strongly suggest that by using more than one MEFV curve parameter, additional valuable information is provided. We would, therefore, support the approach proposed by Haas et al\(^1\) that integrates changes in all MEFV curve parameters to clinical symptoms, history, and other important factors.

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To the Editor:

We appreciate the comment of Dr. Čustović et al regarding our article. We all agree that the best approach to assessing exercise-induced bronchospasm (EIB) integrates changes in all MEFV curve parameters with clinical symptoms, history, and any other relevant factors.

The difference between their criteria and ours in judging a subject as a responder or not reinforces the difficulty in setting arbitrary criteria based on only one parameter. Dr. Čustovic et al's FEV\(_1\) criterion, for example, was more inclusive than ours was, ie, >10 percent compared to our 15 percent. This difference may explain why, if based on a single criterion, only 74 percent of our group as compared with 89 percent of their group were judged as responders.

We would also like to comment on yet another pattern of response, one seen primarily in patients who exhibit an obstructive flow-volume curve pattern before exercise. The PFTs shown in Table 1 were obtained from a 33-year-old fire fighter with EIB symptoms, before and after a 12-min cold air and exercise provocation test. The patient pedalled a bicycle ergometer at 60 revolutions per minute. The load was progressively increased over 3 min until his heart rate reached a steady state between 150 to 160 beats per minute. He breathed room air for the first 6 min and—5°C for the last 6 min. By conventional criteria, this subject does not have EIB (column 3). If, however, a top-to-bottom index (ie, maximum reduction in parameters after exercise compared with maximum increases during or immediately after exercise) is used, as was suggested by Godfrey,\(^1\) this subject would clearly be highly responsive (column 4). Should the magnitude of the dilatory component, therefore, be taken into consideration when evaluating EIB? Our contention is that it should be taken into account; therefore, this patient qualifies as being EIB susceptible.

It is evident from the brief discussion in our article, Dr. Čustović's letter and this individual case that there are still many nuances needing elucidation before we can successfully devise a foolproof diagnostic algorithm for the assessment hyperactive airways.

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REFERENCE


Amylase Concentrations in Pleural Effusions

To the Editor:

We read with interest the article by Joseph et al,\(^1\) in which a prospective study of amylase-rich pleural effusions was reported. The authors found 25 cases of amylase-rich effusions by analysis

| Table 1—Comparison of Parameters Obtained From Flow-Volume Curves Before and After an Exercise/ Cold Air Provocation Test |
|-----------------|----------------|----------------|-------------------|
|                  | Baseline %     | 30-s post %    | 6-min post %      | Top/Bottom Index* |
|                  | Actual Pred    | Actual Pred    | Actual Change    | % Change          |
| FVC (1)          | 3.61 86        | 4.06 12        | 3.35 -7          | -17.5             |
| FEV\(_1\) (1)    | 2.47 72        | 3.02 23        | 2.19 -11         | -27.5             |
| PEF\(_R\) (1/s)  | 7.77 93        | 8.10 4         | 6.68 -14         | -17.5             |
| FEF\(_25-75\) (l/a) | 1.48 42     | 2.34 38        | 1.39 -6          | -40.6             |

*[(30 s post-6 min post)/30 s post]-100.