Correspondence

Incidence of gastric side effects in controlled trials with unbranded aspirin and with various long-acting aspirin preparations

Sir,
Huskisson and Scott (1978) record an amazingly high incidence of gastric side-effects with 'aspirin' in osteoarthritis, but offer no comment on this nor on the form of aspirin used.

<table>
<thead>
<tr>
<th>Reference</th>
<th>'Aspirin'</th>
<th>Named aspirin preparations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Gastric side effects</td>
<td>Daily dose (g)</td>
</tr>
<tr>
<td>Huskisson and Scott (1978)</td>
<td>10/16 (63%)</td>
<td>3-6</td>
</tr>
<tr>
<td>Sperryn et al. (1973)</td>
<td>10/21 (48%)</td>
<td>4-0</td>
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<tr>
<td>Hill et al. (1974)</td>
<td>8/50 (16%)</td>
<td>4-0</td>
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<tr>
<td>Billings et al. (1975)</td>
<td>3/20 (15%)</td>
<td>4-0</td>
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<tr>
<td>Fosdick and Shepard (1969)</td>
<td>48/513*</td>
<td>Variable</td>
</tr>
<tr>
<td>Dippy et al. (1976)</td>
<td>48/513*</td>
<td>Variable</td>
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</table>

*Patient weeks in a long-term trial.

Few rheumatologists would expect such a high level of gastric side-effects, and most use quality aspirin of known brand rather than 'aspirin' (any old ... and unspecified). A review of a few controlled studies, in which 'aspirin' (any old ... and unspecified) was used, shows a variable incidence of gastric side-effects but none as high as those recorded by Huskisson and Scott.

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References

Thoracolumbar spine abnormalities in rheumatoid arthritis

Sir,
Sims-Williams et al. (1977) recently described 6 patients with rheumatoid arthritis and lumbar spinal abnormalities. All patients demonstrated osseous erosion about

![Fig 1](http://ard.bmj.com/) *Intervertebral disc degeneration (intervertebral osteochondrosis). Note herniation of a portion of the nucleus pulposus into the vertebral body with surrounding bone sclerosis (arrows).*

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apophyseal joints and 2 had alterations at the discove vertebral junction. The authors speculated that these discove vertebral changes might be related to apophyseal joint involvement in one of two ways: (1) apophyseal joint instability might lead to abnormal motion at the discove vertebral junction or (2) inflammatory synovial tissue might extend from the apophyseal joints directly into the discs. These investigators also noted 2 other possible mechanisms for discove vertebral changes in rheumatoid arthritis: synovial infiltration into fissures within the degenerating nucleus pulposus of the intervertebral disc or neuropathic alterations secondary to analgesic or steroid therapy.

It has previously been attractive to suggest that inflam matory tissue in rheumatoid arthritis might extend from a synovial joint to an adjacent intervertebral disc. In this manner, one could account for cervical disc lesions related to inflammation in the neighbouring 'synovial lined' joints of Luschka, and thoracic and lumbar disc lesions related to synovial inflammation in the apophyseal or, in the case of the thoracic spine, costovertebral joints.

Recently, Martel (1977) has suggested that cervical discove vertebral destruction in rheumatoid arthritis is a consequence of cervical instability caused by apophyseal arthritis and ligament laxity. Supporting evidence for this concept are the appearance of apophyseal joint destruction at the same level as the involved discove vertebral junction, the close apposition of vertebral bodies in the area of vertebral change, the absence of inflammatory change on microscopic evaluation of the disc, and the absence of similar lesions in juvenile-onset rheumatoid arthritis in which bony ankylosis of the apophyseal joints may protect the adjacent discove vertebral junction.

Our radiological and pathological observations in patients with rheumatoid arthritis (and related disorders) support the concept that vertebral lesions in this arthritic disease may relate to occult trauma at the discove vertebral
Serum copper levels in rheumatoid arthritis

Sir,

Recent correspondence concerning the level and distribution of copper in the serum of patients undergoing therapy for rheumatoid arthritis (Bajpayee, 1975; Sorensen, 1976a) and observations that copper complexes of anti-inflammatory drugs are more active in animal models than the drugs themselves (Sorensen, 1976b) suggest that copper may possibly play an important, if little understood, role in the inflammatory process. Accordingly, the serum copper levels of a group of patients with rheumatoid arthritis who were undergoing therapy with different drug regimes were measured (Table). All subjects in the group had been treated with the drug indicated in the Table for at least 1 month before analysis of a sample of serum for copper by atomic absorption spectrometry using carbon furnace atomisation (Kamel et al., 1978). The results suggest that there is a correlation between serum copper level and drug therapy and, in particular, the levels found with aspirin and indomethacin are significantly different from non-rheumatoid controls at the 0.1% level.

We attempted to assess the effect of the duration of therapy over a period of 6 months by following the serum copper levels of selected patients who remained for that length of time on each drug listed except gold. Penicillamine produced a definite reduction in the average serum value during this period and, indeed, in some patients a level close to that of the controls was achieved. With aspirin, indomethacin, and levamisole there were some variations but no obvious trends were observed with these drugs in the time scale of this investigation. Previous studies have referred to groups of 'untreated' rheumatoid patients (Bajpayee, 1975; Sorensen, 1976a) but in our case all patients had been treated in some manner previously. Their copper levels before hospital treatment varied from 2.15 to 1.11 mg/ml.

The correlation between drug therapy and copper level was somewhat unexpected. Serum copper variations have been noted for quite a wide range of physiological conditions such as sex, pregnancy and contraception, stress and diurnal rhythms and these effects might have been expected to obscure any drug-related changes. However,

| Table Serum copper levels of patients with rheumatoid arthritis undergoing therapy with different drugs |
|-------------------------------------------------|-----------------|--------------|--------------|--------------|-----------------|--------------|
| Controls | Indomethacin | Aspirin | Levamisole | Penicillamine | Gold |
| Number   | 17            | 21        | 15          | 49           | 14              | 7            |
| Mean copper level (µg/ml) | 1.03          | 1.65      | 1.61        | 1.37         | 1.32             | 1.65         |
| Standard deviation | 0.15          | 0.20      | 0.18        | 0.28         | 0.18             | 0.42         |
Thoracolumbar spine abnormalities in rheumatoid arthritis.
D Resnick

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