The prevalence of Addison’s disease in Coventry, UK

Andrew C Willis, Frank P Vince

Summary
The prevalence of Addison’s disease (chronic adrenal failure) has not been widely investigated and is usually given as 39 in a million. We conducted a prevalence study using a postal survey of general practitioners in Coventry. Three quarters (139/188) replied, representing 79,850 (93%) of the practices. Thirty cases of Addison’s disease were found from a total patient list of 323,852, of which a third were tuberculous in origin and two-thirds non-tuberculous (12/30 autoimmune, 8/30 unclassified). We conclude that Addison’s disease is 2.4 times more common than previously reported. The tuberculous group was older, 65 vs 52 years (p < 0.05), and had had the disease for longer than the non-tuberculous group, 20 vs 12 years (p < 0.05). There was no significant difference in the age at diagnosis.

Keywords: Addison’s disease, adrenal hypofunction, epidemiology, tuberculosis

Since Thomas Addison first described the condition of chronic adrenal failure, its prevalence has rarely been defined. In 1968, a hospital-based survey found a prevalence of 39 in a million. This seemed likely to be an underestimate and we performed a prevalence study in a West Midlands industrial city in the UK.

Methods
In 1992 general practitioners (GPs) on the Coventry Family Health Services Authority (FHSA) list were asked by post if they had any patients with Addison’s disease (chronic adrenal failure) on their practice lists. Non-responders were telephoned. We sought at least one reply per practice. Cases were also sought in a hospital endocrine clinic. The population size was taken from the FHSA patient list for July 1992. Medical records were examined for evidence of primary adrenal failure. These patients were divided into a tuberculous and an autoimmune group. Those cases that could not be placed in either group were added to the autoimmune group to form a non-tuberculous group. The statistics were performed using a Student’s t-test.

Results
The survey was sent to 188 GPs in 85 practices, looking after 323,852 patients. Replies were received from 139 (74%) of the GPs in 79 (93%) of the practices. Of the six practices that did not reply, four were single-handed and two double-handed. A total of 30 patients with Addison’s disease were identified, of whom 26 were found in general practice, two in the hospital endocrine clinic and two from other sources. All patients were registered with Coventry GPs. Ten patients were not being followed up in a hospital clinic. In 25 patients there was a description of their clinical state at presentation and 24 had recorded biochemical evidence of hypocortisolaemia. Of the six that did not have a record of their cortisol state at presentation, all were being treated for Addison’s disease. One had bilateral adrenal calcification on X-ray, one had a tuberculous kidney removed, one presented in an Addisonian crisis and with pulmonary tuberculosis, two were diagnosed elsewhere and for one no other information was available.

Of the 30 patients, 10 (five men, five women) were classified as tuberculous (table 1), 12 (two men, 10 women) were classified as autoimmune (table 2) and eight (five men, three women) had no evidence of tuberculous, autoimmune or other infiltrative disease, making 20 (seven men, 13 women) non-tuberculous cases. The prevalence was calculated as 93 in a million, 33% of whom were tuberculous. The majority (26/30) had one or more of the following features of primary adrenal failure: increased pigmentation at presentation, adrenal calcification on X-ray, no response to a
The prevalence of Addison's disease

Table 2 Patients classified as having autoimmune Addison's disease

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Autoantibodies</th>
<th>Thyroid</th>
<th>Gastric</th>
<th>Thyroid disease</th>
<th>Diabetes mellitus</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Adrenal</td>
<td></td>
<td></td>
<td>pos</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>F</td>
<td>pos</td>
<td>pos</td>
<td>N/A</td>
<td>pos</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>pos</td>
<td>pos</td>
<td>neg</td>
<td>neg</td>
<td>neg</td>
<td>vitiligo</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>pos</td>
<td>neg</td>
<td>neg</td>
<td>neg</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>pos</td>
<td>neg</td>
<td>pos</td>
<td>neg</td>
<td>neg</td>
<td>menopause at 30</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>pos</td>
<td>pos</td>
<td>neg</td>
<td>pos</td>
<td>pos</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>N/A</td>
<td>pos</td>
<td>pos</td>
<td>pos</td>
<td>pos</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>N/A</td>
<td>neg</td>
<td>neg</td>
<td>pos</td>
<td>pos</td>
<td>vitiligo</td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>N/A</td>
<td>neg</td>
<td>neg</td>
<td>pos</td>
<td>pos</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>pos</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>neg</td>
<td>neg</td>
<td>N/A</td>
<td>pos</td>
<td>neg</td>
<td>PA</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>pos</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>pos</td>
<td>TB</td>
</tr>
<tr>
<td>12</td>
<td>M</td>
<td>pos</td>
<td>neg</td>
<td>neg</td>
<td>neg</td>
<td>neg</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: F=female; M= male; pos=test positive; neg=test negative; N/A=test not recorded; PA=pernicious anaemia; TB=tuberculosis; thyroid autoantibodies=thyroid microsomal + thyroglobulin autoantibodies

Table 3 The mean ages of tuberculous and idiopathic Addisonian patients (ranges in parentheses)

<table>
<thead>
<tr>
<th>Tuberculous cases</th>
<th>Idiopathic cases</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>65 (43-80)</td>
<td>52 (39-62)</td>
</tr>
<tr>
<td>Age at diagnosis</td>
<td>43 (16-56)</td>
<td>34 (10-47)</td>
</tr>
<tr>
<td>Length of disease</td>
<td>20 (8-37)</td>
<td>12 (1-24)</td>
</tr>
</tbody>
</table>

NS: not significant

Addison's disease: causes

Common
- autoimmune
- tuberculosis

Uncommon
- bilateral adrenalectomy
- infiltration: metastatic carcinoma, amyloidosis, fungal infection (eg, histoplasmosis), haemochromatosis
- meningococcal septicaemia
- haemorrhage/infarction
- adrenal vein thrombosis
- congenital: adrenoleucodystrophy (Schilder's disease), congenital adrenal hyperplasia, X-linked congenital adrenal hypoplasia
- drugs: rifampicin, ketoconazole
- AIDS

Box 1

Clinical features

Symptoms
- common: lethargy, dizziness, weight loss, nausea and vomiting
- less common: loss of appetite, abdominal pain, cramps, salt craving

Signs
- increased pigmentation
- postural hypotension

Associated conditions
- vitiligo
- hypothyroidism
- diabetes mellitus
- premature ovarian failure
- hypoparathyroidism

Box 2

Discussion

The causes and clinical features of Addison's disease are given in boxes 1 and 2. In the current study, we found Addison's disease to be 2.4 times more common than previously reported. This study had a high response rate (74% of GPs, 93% of practices) and a high detection rate by GPs (26/30, 89% of cases), who reported 10 cases not attending a hospital clinic. We cannot say if the prevalence of Addison's disease has changed but believe that the previous figure of 39 in a million was an underestimate because cases were not sought outside hospitals.¹

This was a retrospective study and full details of the diagnosis were not always available. Of the 30 cases, 27 were diagnosed locally but in three cases the diagnosis was made elsewhere and has been taken on trust. These are limitations of the data.

Our evidence for classifying patients as tuberculous or autoimmune is summarised in tables 1 and 2. One-third of our cases were tuberculous, consistent with other series.²³ Of these, six had been treated for tuberculosis, three others had radiological evidence of old tuberculosis and one had had a strongly positive Mantoux test but had not been treated for tuberculosis. There was virtually no evidence of autoantibodies or associated autoimmune disease in these patients, which is consistent with findings of Kasperlik-Zaluska et al.² Patient 2 (table 1) became hypothyroid seven years after diagnosis and patient 8
inconsistently positive antithyroglobulin auto-
antibodies (negative at the time of diagnosis). 
Only 30% of tuberculous cases had radiologi-
cal adrenal calcification, similar to the 26% of 
Kasperlik-Zaluska et al. Tuberculosis was 
previously a common disease and evidence of 
old tuberculosis does not exclude the possi-
ilitv of autoimmune Addison’s disease, as 
adrenal antibodies are only found within the 
first eight years of the disease. In a series 
involving computed tomography and autopsy, 
adrenal calcification was seen in 55% of 
tuberculous cases and 76% had evidence of 
extra-adrenal tuberculosis, but pulmonary tu-

berculosis was seen in 46% of cases considered 
to have idiopathic disease. Six of our tubercu-


lous cases had evidence of extra-adrenal 
tuberculosis, in three there was only evidence 
of pulmonary tuberculosis and in one the site 
of the infection was not known. Of the 12 
patients with autoimmune disease, eight had 
adrenal autoantibodies and the remaining four 
had evidence of other autoantibodies or auto-
imune disease. These figures compare with a sex 
ratio of 1.7/1 and 31% with thyroid disease in 
Kasperlik-Zaluska et al and it is likely that 
our cases have been correctly classified. 

The finding that two quite different disease 
processes produce adrenal failure at a similar 
age and that the tuberculous patients are older 
and have had Addison’s disease for longer is 
interesting. We cannot tell from this work 
whether this is due to a change in the relative 
incidence of tuberculous and autoimmune 
adrenal disease or whether the latter has a 
higher mortality risk, perhaps due to an 
associated disease such as diabetes mellitus.

We would like to thank all the general practitioners 
in Coventry who helped us with this study.

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