Progress report

Psychological factors in the irritable bowel syndrome

SUMMARY This paper reviews recent psychological studies of patients with the irritable bowel syndrome (IBS) or ‘functional abdominal pain’. Many studies have used unreliable or invalid methods of assessment and some have confused personality with treatable psychiatric illness. Reliable and valid measures have indicated that 40–50% of patients with recently diagnosed functional abdominal pain have demonstrable psychiatric illness; these patients have a worse prognosis than those who are psychologically normal. When psychiatric disorder is diagnosed in a patient with IBS there are three possibilities: (1) The patient may have developed abdominal and psychiatric symptoms simultaneously in which case treatment of the latter may relieve the bowel symptoms. (2) Psychiatric disorder may precipitate increased concern about bowel symptoms, and consequent attendance at the gastroenterology clinic, of those with chronic mild symptoms. In this case it is illness behaviour, rather than abdominal symptoms, that is caused by the anxiety/depression. (3) Those with chronic neurotic symptoms as part of their personality must be screened for organic disease if they have a fresh onset of bowel symptoms; but they are at high risk of becoming persistent clinic attenders. Further research is needed to clarify when psychological abnormalities play a role in the aetiology of IBS and when they are coincidental, but lead to illness behaviour. The role of psychological factors in the aetiology of the irritable bowel syndrome (IBS) is far from clear, but a review of the literature suggests that some consistent patterns are emerging in spite of methodological problems.

There have been three major defects with studies that have linked IBS with neurotic symptomatology. First, the measurement of psychological factors has generally been imprecise. Second, most studies have considered IBS patients as a single group, without making allowance for differing symptom patterns. Third, conclusions have been drawn about hospital samples and extrapolated to all IBS subjects, without taking account of factors which affect consulting behaviour. Most studies have been concerned with psychological factors so these will be considered in most detail.

Psychological factors

In their classic study Chaudhury and Truelove identified psychological factors which appeared to influence the onset or exacerbation of IBS in over 80% of their 130 cases. These were equally common in the spastic colon and painless diarrhoea types of the disorder, but were more common in women. The list of psychological factors considered by Chaudhury and Truelove includes three separate categories of factors which would now be measured individually: (a) diagnosable psychiatric illness – for example, obviously
dressed; (b) personality types – for example, life long worrier; (c) environmental stress – for example business or family problems.

In psychiatric research today, reliable instruments are available to measure each of these factors, yet studies continue to be published in which they have not been assessed accurately. Some studies have used an unreliable measure, others have used a reliable instrument inappropriately, and some have drawn the wrong conclusions from the data collected. Problems with selection of subjects and the absence of control groups have often been ignored.

We shall use some of the studies of psychiatric illness in IBS to illustrate the above points, showing how the choice of measure may affect the results obtained. Those studies with good methodology will then be discussed, as important conclusions can be drawn from these papers. The section concerning personality and social factors in IBS is brief reflecting the small number of satisfactory studies.

**Diagnosable Psychiatric Illness**

This section concerns psychiatric illness that is clear enough to warrant a diagnosis and therefore would merit specific psychiatric treatment.

*Use of an unreliable measure*

All patients presenting to a gastroenterology clinic, who did not have an organic cause for their pain were regarded by Gomez and Dally as having psychiatric illness. They were classified as follows: 12 drank excessively, 31 were diagnosed as suffering from depression, 21 from chronic tension, and 17 manifested ‘hysterical symptoms and used their abdominal pain as communication or to obtain necessary narcissitic satisfaction’.

This classification is based on ‘clinical judgment’. It is idiosyncratic, bears no relationship to research criteria and suggests that 100% of IBS sufferers are psychologically abnormal. The psychiatrists may have had a preconceived idea that patients with non-organic abdominal pain had an underlying psychological cause and diagnosed ‘tension’ and ‘hysterical states’ purely on the basis of the abdominal pain. Evidence of psychological disturbance apart from the abdominal pain must be shown, and be more common than in a control group, if psychological disturbance is to be reliably associated with IBS. We shall see below that reliable measures of psychiatric illness yield a prevalence of approximately 50%.

*Inappropriate use of a reliable measure*

The use of a reliable psychiatric measure alone does not necessarily overcome all the difficulties of assessment. The often quoted studies of Liss, and Young illustrate further problems even when a reliable measure is used. These studies used Feighner’s diagnostic criteria of hysteria, which require that 25 or more ‘medically unexplained symptoms’ should have developed in nine different bodily systems before the age of 30 years.

It has long been recognised, and recently confirmed, that those who attend clinics with IBS may complain of many bodily symptoms, but this does not necessarily imply psychiatric disorder. The unsatisfactory nature of the Feighner criteria in this setting accounts for the fact that only two of 25 patients were regarded as psychologically normal. Clearly the diagnosis of hysteria is fraught with difficulty in these patients and is best avoided.
More recently, another standardised instrument, the Di-Beck inventory, has been used to detect depression in a group of surgical out patients with abdominal disorder. The cutoff point for depression used in this study, however, was too low: 5 instead of 14. This gave the prevalence of depression among IBS subjects as 68%, when the more usual cutoff point of 14 would have provided a lower and more realistic figure.

Interpretation of findings
The increased prevalence of psychiatric illness among IBS patients, compared with a control group allows no firm conclusion about causality; the timing of onset of symptoms is important. Young et al. used the Feighner criteria, which diagnose hysteria on the basis of many symptoms before the age of 30, whereas the average age of their sample was 44 years. Closer examination of the results indicates that of the 23 patients with ‘psychiatric illness’, 17 had psychiatric symptoms before the onset of gastrointestinal symptoms, (often many years before) and in only four subjects did the psychiatric illness and IBS occur simultaneously. So there may be no direct relationship between the psychiatric and gastrointestinal symptoms. The high prevalence of psychiatric symptoms in this study has often been wrongly quoted as evidence that psychological factors are important in the aetiology of IBS. This could only reasonably be claimed for four of the 23 patients in Young’s study.

Selection of subjects
One strength of Young’s study was the selection of IBS subjects. These were consecutive attenders at an outpatient clinic. By contrast Latimer et al. used patients specially referred for a motility study. These IBS patients turned out to be even more psychologically disturbed than a control group of psychiatric outpatients, which strongly suggests that a selected group of patients were being referred.

Kingham and Dawson used a systematic measure of depression (Hamilton rating scale) in 22 patients with functional bowel disorder, whose pain was reproduced by balloon distension in the gut. These patients had severe symptoms; they had been seen by a total of 79 consultants and undergone 38 abdominal operations, which had been unsuccessful in relieving the pain. Four were rated as severe cases of depression, six moderate and four mild, an overall prevalence of depression of 64%. This figure is higher than other studies that used a sound methodology, probably reflecting the chronic and severe bowel complaints (Table).

The clear description of the method of selection in this study contrasts with that of most other studies; it indicates that these patients were mostly secondary or tertiary referrals and the prevalence of psychiatric illness might reflect this fact. It is necessary to emphasise that the results of studies involving selected patients, cannot be generalised to IBS patients as a whole.

Use of a control sample
The study by Kingham and Dawson would have been strengthened by the use of a comparison group of patients with chronic bowel symptoms of organic aetiology. In fact, many of the studies purporting to demonstrate the relationship between psychological disorder and IBS have not used a control group. Of those using a control group, Hislop used attenders at a
Table  Prevalence of psychiatric illness in patients with functional abdominal pain

<table>
<thead>
<tr>
<th>Study</th>
<th>Subjects (n)</th>
<th>Psychological measure</th>
<th>Functional abdominal disorder (%)</th>
<th>Organic GI disorder (%)</th>
<th>Community sample (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macdonald and Bouchier (1980)</td>
<td>32</td>
<td>Clinical Interview Schedule</td>
<td>53</td>
<td>20</td>
<td>-</td>
</tr>
<tr>
<td>Craig and Brown (1984)</td>
<td>179</td>
<td>Present State Examination</td>
<td>40</td>
<td>18</td>
<td>8</td>
</tr>
<tr>
<td>Kingham and Dawson (1985)</td>
<td>22</td>
<td>Modified Hamilton Dep Scale</td>
<td>64</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Fava (1985)</td>
<td>14</td>
<td>DSM III Diagnostic Crit.</td>
<td>28</td>
<td>43</td>
<td>-</td>
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</table>

Appendix A

Instruments used to measure psychiatric disorder in IBS patients

<table>
<thead>
<tr>
<th>Name</th>
<th>Self administered or interview</th>
<th>Measure of:</th>
<th>Studies using measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Middlesex Hospital Questionnaire (now known as CCEI)</td>
<td>s/a</td>
<td>mental state</td>
<td>17</td>
</tr>
<tr>
<td>SCL-90 Hopkins Check list</td>
<td>s/a</td>
<td>neurotic symptoms</td>
<td>29, 32</td>
</tr>
<tr>
<td>Eysenck Personality Inventory</td>
<td>s/a</td>
<td>personality</td>
<td>17, 18</td>
</tr>
<tr>
<td>General Hospital Questionnaire</td>
<td>s/a</td>
<td>mental state</td>
<td>30</td>
</tr>
<tr>
<td>Clinical Interview Schedule (CIS)</td>
<td>i/view</td>
<td>diagnose psychiatric illness</td>
<td>4</td>
</tr>
<tr>
<td>Present State Interview (PSE)</td>
<td>i/view</td>
<td>diagnose psychiatric illness</td>
<td>15, 24</td>
</tr>
<tr>
<td>Hamilton Rating Scale</td>
<td>i/view</td>
<td>severity of depression</td>
<td>10</td>
</tr>
<tr>
<td>Di-Beck</td>
<td>s/a</td>
<td>severity of depression</td>
<td>7</td>
</tr>
<tr>
<td>Feighner criteria</td>
<td></td>
<td>American diagnostic criteria applied to data collected at interview.</td>
<td>4, 5</td>
</tr>
</tbody>
</table>

Appendix B

Questions that indicate possible psychiatric disorder in IBS patients:

Anxiety:
* Do you ever find that you get anxious or frightened for no good reason?
* Do you worry a lot about things?

Depression:
* Have you had difficulty sleeping recently?
* Have you had spells of feeling sad or miserable?
* Do you sometimes feel hopeless?

If patient answers 'yes' to any question they should be asked in more detail about other symptoms of anxiety or depression, the date of onset of these symptoms and whether the bowel symptoms changed at that time.

casualty department, and Young used general medical outpatients. It is important, however, to control for the severity and duration of bowel symptoms and in practice this means patients with organic GI disorder, which was the control group used in the studies considered next.
Psychological factors in the irritable bowel syndrome

Studies with adequate methodology

Two studies have used reliable instruments for measuring psychiatric disorder, used appropriate control groups, recruited consecutive patients and drawn appropriate conclusions from their findings.

McDonald and Bouchier independently assessed, physical and psychological aspects of 67 patients with abdominal symptoms. The physician’s assessment led to 32 patients being classified as having organic gastrointestinal disease and 35 patients as non-organic gastrointestinal disease. The psychiatrist used a standardised research interview (CIS), to assess whether the patient experienced a sufficient number of symptoms severe enough to indicate psychiatric illness. There were seven (20%) cases of psychiatric illness in the organic group compared to 17 (53%) in the non-organic group. This is a statistically significant difference, so there is a definite association between functional abdominal pain and psychiatric illness.

The study of McDonald and Bouchier enables us to establish two points in contrast with the earlier study of Gomez and Dally. Firstly, it allows some patients with IBS to be categorised as not having psychiatric illness. Secondly, some patients with organic disease do have treatable anxiety or depression. This surely accords with clinical practice.

By indicating a prevalence of psychiatric disorder of 100%, the study of Dally and Gomez falsely supported the idea that the term ‘functional’ – that is, no organic illness demonstrated, always indicates underlying psychopathology. McDonald and Bouchier’s study showed that half of those patients with functional gastrointestinal symptoms have diagnosable psychiatric illness, but the remaining patients have symptoms for which no pathology (psychiatric or physical), has been demonstrated.

Craig and Brown managed to study 79 subjects with functional bowel disorder which had occurred for the first time within the previous year, or recurred after a symptom free period (21 were specified as having the irritable bowel syndrome). Forty two per cent of those with functional bowel disorder had definite psychiatric illness, compared with 18% of a matched comparison group with organic gastrointestinal illness, and 8% of those in a community comparison group. These figures are strikingly similar to those of MacDonald and Bouchier and clearly indicate that anxiety and depressive illnesses are more common in IBS than organic gastrointestinal illness.

There has been one additional study with sound methodology that reached the opposite conclusion, namely that psychiatric disorder was more common in patients with organic gastrointestinal illness, than those with functional gastrointestinal illness. The numbers were very small in this study and the results are in conflict with the others which have used reliable measures (Table).

We can conclude that the prevalence of psychiatric disorder in most clinic populations of IBS patients is 40–50%. The questions that most readily identify these patients are listed in Appendix B, which also indicates the different types of instrument available for detecting psychiatric disorder (Appendix A).

Personality measures

Very few studies have adequately considered the role personality may play in the development of bowel symptoms, but there are two studies, which
used samples of adequate size, and where the method of selection is quoted. Both used the Eysenck Personality Inventory (EPI).

Palmer and colleagues\textsuperscript{17} assessed 41 IBS patients. The groups means showed that the IBS subjects were significantly more neurotic and less extroverted than the established normative data but significantly less neurotic and more extroverted than psychiatric outpatients. Esler and Goulston\textsuperscript{18} found that only diarrhoea predominant IBS subjects had neuroticism scores on the EPI significantly higher than control subjects with ulcerative colitis and general medical patients.

The scores quoted in these two studies are group means, however, and if the standard deviations are examined, there is much overlap between the IBS population, the organic groups and healthy controls. (Fig. 1).

In addition to measuring personality, both sets of authors also used a measure of anxiety. Esler and Goulston specifically remarked that even some of the diarrhoea predominant IBS subjects had anxiety scores well within the normal range. This suggests that IBS patients are not a homogeneous group, but include some people who are as neurotic as psychiatric patients, and others who are as free of neurosis as healthy controls.

Raised neuroticism scores on the EPI may result from prolonged physical or psychiatric illness, so the results of studies using personality measures alone are ambiguous. In fact the results of these two studies may be interpreted as indicating that a proportion of IBS subjects have frank anxiety states, while others are not at all anxious.

For this reason, research in psychosomatics has moved away from reliance on personality measures as a sole source of information. The two studies

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already quoted did use physiological measures in addition. Palmer et al found that forearm blood flow was increased in a small number of IBS subjects whose anxiety scores were raised on the MHQ. Esler and Goulston found raised catecholamines in the diarrhoea predominant subjects who had raised anxiety and neuroticism scores. But on these measures of anxiety there was also a considerable overlap between the IBS patients and normal controls.

ENVIRONMENTAL STRESS
In their original list of psychological factors associated with irritable bowel syndrome, Chaudhary and True love found that the following environmental stresses were common: marital difficulties, problems with children or parents, and worries related to business or career. Two studies provide anecdotal evidence that a majority of patients with IBS report stress factors precipitating their bowel symptoms.

The accurate measurement of environmental stress has recently been achieved but cannot readily be applied to patients with the irritable bowel syndrome because of the lack of a clear datable onset shortly before presentation to the doctors. Of the following studies only the last two provide a reliable measure of life events as defined by Bass.

Mendeloff et al compiled their own ‘life stress score’ for 102 irritable bowel syndrome patients and found that precipitating stress events were more common than among patients with ulcerative colitis and healthy comparison subjects. On the other hand, Hislop found that neither recent economic or occupational difficulties nor problems in childhood were more common in IBS patients than control subjects (casualty attenders). Hislop did record that dysharmony in close relationships and divorce/separation were more common in the IBS patients.

If life events are to be regarded as playing a part in the aetiology of IBS they must have occurred before the onset of bowel symptoms. This requires accurate dating of the onset of symptoms.

Because there is often difficulty dating onset in IBS, Creed studied life events before appendicectomy. Those with an appendix classified as ‘not acutely inflamed’ had a pattern of recent life events significantly different from those with appendicitis and almost identical to that of patients with depressive illness. One third of this group had definite psychiatric symptoms and these patients with depression were most likely to continue to have abdominal pain, during the post operative year. Although they have correctly been regarded as cases of undiagnosed abdominal pain at the time of the appendicectomy many of these patients are later found to have the irritable bowel syndrome.

A similar study of life events was done by Craig and Brown on patients with functional and organic bowel disease whose onset of symptoms could be accurately dated. A very similar pattern emerged with 67% of the functional bowel disorder group having experienced a severely threatening life event or chronic difficulty before the onset of bowel symptoms, compared with 23% of both patients with organic gastrointestinal illness and healthy community comparison subjects.

These studies of appendicectomy subjects and gastroenterology clinic attenders have produced remarkably similar results and indicate that severely threatening life events, most commonly marital separation or the
breakup of a similar close relationship, frequently precede the onset of functional bowel disorder, when this can be dated.

**Different groups of IBS patients**

**SYMPTOM PATTERN**
The usual definition of the irritable bowel syndrome requires negative investigations for physical illness as a central criterion, but this leads to a heterogeneous group of patients with abdominal symptoms being included. Some progress has been made, however, towards making a positive diagnosis on the basis of the symptom pattern.\textsuperscript{28} It is not known whether such a method of making the diagnosis would affect the prevalence of psychiatric disorder.

Thompson has suggested that psychiatric disorder should be measured separately in those with the different types of the disorder, namely constipation predominant and diarrhoea predominant.\textsuperscript{1} One study already mentioned\textsuperscript{18} showed that it was only those patients with the diarrhoea predominant type of disorder who showed a rise in catecholamines and were more neurotic in personality than general medical controls but this study used small numbers of subjects.

Whitehead et al\textsuperscript{29} also used a small number of subjects but found no difference on psychological testing, (using the self-administered Hopkins symptom check list), between the diarrhoea and constipation predominant IBS patients.

The 48 patients studied by Lancaster-Smith et al\textsuperscript{30} showed no significant difference in symptom pattern at the start of a treatment study between those with high scores on the GHQ, (probable psychiatric cases), and the remainder. But at the end of the study those with psychiatric symptoms showed significantly more diarrhoea and abdominal pain but no difference in constipation.

It is possible that those IBS patients with diarrhoea have more anxiety than those with predominant constipation, but this requires further study with larger numbers of patients, especially as diarrhoea is a well recognised symptom of anxiety states and constipation of depressive illness.

**RECENT VERSUS CHRONIC SYMPTOMS**
Most studies poorly describe the duration of bowel symptoms, but it is likely that the majority of IBS patients attending hospital clinics have long standing disturbance of bowel function.\textsuperscript{12,15} It has been repeatedly suggested that when neurotic symptoms occur, they do so as a consequence of chronic bowel disturbance. Three pieces of evidence suggest this cannot always be the case, however. First, patients with longstanding bowel disturbance of organic cause show less neuroticism than those with functional bowel disorder. Second, some patients have developed psychiatric symptoms before the onset of bowel symptoms.\textsuperscript{15,29} Third, the majority of studies show no correlation between severity or duration of bowel symptoms and neurotic symptomatology.\textsuperscript{10,29,30}

Thus there may be three groups of IBS subjects; those who are neurotic from the outset, those who become increasingly neurotic with years of disturbed bowel function, and those who have never been neurotic. Longitudinal studies of patients with early IBS are needed to clarify the
Factors that affect consulting behaviour

Most studies of IBS subjects have been carried out on patients attending medical outpatient clinics. There are, however, many patients with IBS who are only treated by general practitioners or who never consult a doctor at all. The typical syndrome pattern of IBS has been recorded in about 13% of apparently healthy British individuals most of whom have not sought treatment for it. One study has found no difference in anxiety levels (according to a self report scale) between such people in the community and clinic attenders with IBS, but this result must be treated with caution because the clinic attenders of this study had lower anxiety scores than those of most other studies.

It has been assumed that patients with more severe forms of IBS are seen in hospital outpatient clinics whereas patients with relatively mild symptoms remain untreated in the community. But there is only one study which has shown that this is the case and this aspect requires confirmation. In addition to assessment of symptom severity this study did attempt to measure the tendency for people in the community to complain about, and seek treatment for, symptoms in general. They found that compared with non-consulters, those patients with bowel dysfunction who consulted a doctor were also more likely to consult for non-GI symptoms. The increased rate of consultation remained even, however, when the number of symptoms was controlled, indicating a separate dimension of consulting behaviour.

A telephone study, whose results should be treated with caution, suggested that those who complained of the symptoms of IBS were more likely than those who had a peptic ulcer to report many colds and other minor illneses, to regard these as worse than those suffered by other people and to seek treatment more frequently from doctors. Such ‘illness behaviour’ is increasingly being recognised among persistent hospital clinic attenders, notably those at a pain clinic.

Among IBS patients illness behaviour is likely to be least apparent among those who consult a GP only, and greatest among persistent hospital attenders, such as those studied by Kingham and Dawson. There are two aspects of abnormal illness behaviour; one is the reporting of many symptoms when asked (even over the telephone), the other is the frequent attendance at a doctor for treatment. It is easy to see how persistent requests for help with the symptoms of IBS might lead, (a) to referral to a hospital clinic, and (b) to chronic attendance at that clinic.

Although it is desirable to measure symptom severity separately from illness behaviour, this is very difficult as the doctor has to rely on the patient’s self report of severity of bowel symptoms. Two recent studies have shown that patients with functional abdominal pain record high scores on an illness behaviour questionnaire. High scores on this questionnaire are also recorded by those with depression, however, and it may be that the
excessive demands made upon doctors by certain patients with IBS reflects underlying depressive illness.

In summary there may be several factors that distinguish attenders from non-attenders: (i) more severe bowel symptoms; (ii) presence of anxiety/depression; (iii) illness behaviour.

Because severity of bowel symptoms relies on self report by the patient this may be influenced by the patient’s mental state (increased anxiety leading to report of worse symptoms). Similarly other aspects of illness behaviour, as measured by the illness behaviour questionnaire, are increased by the presence of depression. So it is a logical next step to consider those with and without anxiety/depression separately. When this was done among clinic attenders it was found that the tendency to report certain symptoms was as great among those with psychiatric disorder as the remainder, but the former had more complaints of pain. It is necessary now to establish whether the prevalence of anxiety/depression is greater among clinic attenders than non-attenders and whether this is true even when bowel symptom severity is controlled.

Conclusion

There are few studies of psychological factors and IBS which satisfy the criteria outlined in this review. Those studies which have done so indicate that psychiatric illness, as defined by research criteria, occurs in approximately 50% of clinic attenders. The importance of detection of such psychiatric illness has both theoretical and practical implications.

Theories regarding the relationship between IBS and psychological disturbance can only be properly tested once an attempt is made to standardise the abdominal symptomatology of IBS in the same way as psychiatric symptoms have been individually rated in research interview schedules. Patients can then be subdivided into less heterogeneous groups, first in terms of the predominant bowel symptoms and second according to the presence or absence of psychiatric illness. These would then need to be studied independent of clinic attendance.

Greater attention also needs to be paid to the time relationship between abdominal and psychiatric symptoms. If they occurred simultaneously it may be that psychiatric illness plays a major part in the aetiology of the bowel symptoms and treatment of the psychiatric illness would lead to resolution of the bowel symptoms. If the bowel symptoms have been present for many years and the psychiatric disorder is recent, the latter may be responsible for the clinic attendance – that is, illness behaviour, rather than the bowel symptoms themselves. If the psychiatric disorder was present first and the bowel symptoms occurred much later, there may be two independent disorders and the bowel symptoms require thorough investigation to avoid missing physical disease, even though the patient appears ‘neurotic’.

The practical importance of detection and treatment of psychiatric illness among IBS patients by the gastroenterologist is therefore threefold: (a) Untreated anxiety/depression impairs the response to conventional treatment, whereas in some patients psychiatric treatment might improve the symptoms; (b) Persistent clinic attendance may be perpetuated by the presence of psychiatric disorder rather than severe bowel disorder – such
patients ‘never get better’. Treatment aimed at the illness behaviour rather than the bowel symptomatology, should be tried; (c) It cannot be assumed that the ‘neurotic’ patient does not have organic disease, but many papers suggest that the gastroenterologist should not overinvestigate patients with IBS. The only way out of this apparent dilemma is to elucidate the date of onset of psychiatric and bowel symptoms separately.

Greater recognition of definite psychiatric disorder among patients with IBS will be the first step in clarifying its role in the aetiology of the syndrome.

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References

Creed and Guthrie

27 Reference deleted.
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