Unfortunately, textbooks don’t smell as their contents rot, so readers will need to develop alternative crap detectors to avoid poisoning their minds and robbing their patients of current best care [1].

Until recently, psychiatry was dominated more by clinical than by scientific views. Treatments, while respecting or dominated by the sectarian Zeitgeist of the period, were generally driven by the individual clinician’s judgment. Such an approach could, and still can, be strongly defended. In his essay ‘The Music of Psychiatry’, Ellard [2] provided such a defence. He observed that although ‘science is an essential part of psychiatry, it is not its essence’, and was particularly critical of the ‘tone deaf’ who
neither hear nor have the music and ‘who do psychiatry by numbers’.

The clinical psychiatrist can argue reasonably against reducing psychiatry to a ‘painting by numbers’ exercise, pointing to the heterogeneity of psychiatric illness (i.e. not merely disease, but illness and psychosocial predicaments as well), the multimodal nature of the problems presented by patients, the need to respect the ‘biopsychosocial model’, the individual needs of the particular patient, and thus the need for pluralistic and multimodal approaches: issues detailed by Ellard [2] and which reduce the utility of prescriptive approaches to any particular psychiatric condition.

Andrews’ initiative, in introducing [3] the Quality Assurance Project in Australia, heightened and then assisted in overcoming professional apprehension about guidelines being used as ‘inflexible rules of practice’. He argued that information derived from three sources (i.e. literature meta-analysis, opinions of a sample of psychiatrists and views of a panel of nominated experts) would have benefits in that psychiatrists ‘would know what the results of current research indicate, what therapies his colleagues practise and what a group of experts would recommend as good practice’. Thus, guidelines can provide a firmer template for consideration and modification of clinical practice than anecdotal clinical opinion or ex cathedra statements.

The practising psychiatrist is now flooded with (generally consensually driven) ‘treatment’, ‘practice’ and ‘expert consensus’ guidelines, in addition to ‘diagnostic’ and ‘management’ algorithms, as well as several contrasting approaches (i.e. meta-analyses, evidence-based psychiatry), where conclusions and recommendations are variably based on controlled trials and on expert opinion. There is an implicit assumption to generated guidelines, that they not only assist but that they also change practice. While Continuing Medical Education (CME) has been closely examined, and effective and ineffective components identified [4], the capacity of treatment guidelines to change practice has never been formally evaluated.

As members of an advisory board for a pharmaceutical company, we were recently presented with a company-commissioned report examining Australian psychiatrists’ prescribing habits and attitudes in relation to relapse prevention in schizophrenia. We suggested to the company that the report contained information worthy of wider dissemination as it has the potential to inform us of psychiatrists’ views about contemporary drug management of schizophrenia in Australia, and to assess whether more recent guidelines about its management have ‘filtered through’ to clinicians. We, therefore, summarise its more important findings, with co-authors (i.e. commentators) providing their own views and considering the extent to which the data might variably indicate practice in step or in disjunction with current expert views about the management of schizophrenia.

Method

Emjay Research Consultants were commissioned by Lundbeck, a pharmaceutical company, to undertake a quantitative survey of a sample of psychiatrists based in three capital cities and who were ‘qualified as regularly treating schizophrenic patients’. Psychiatrists were approached and invited to participate in a 10-minute phone interview and, for those who accepted, a copy of the questionnaire was faxed just prior to the interview in late 1996. Regrettably, no record was kept of the number of psychiatrists approached, preventing any estimate of the response rate. The questionnaire sought to assess aspects of their general management of patients with schizophrenia, both directly and in response to several vignettes.

Of the final sample of 139 psychiatrists, 55 were from Sydney, 53 from Melbourne and 31 from Brisbane (and with 65% predominantly in public practice). While there were some regional differences, we focus on reports by the whole sample. Of the participating psychiatrists, 23% had been in practice for 1–5 years, 26% for 6–10 years, 27% for 11–20 years, and 24% for more than 20 years.

Results

Predicting the chance of relapse

First, clinicians’ general views about neuroleptic relapse medication were sought. Nearly two-thirds (i.e. 61%) of the psychiatrists believed, on the basis of their own clinical experience, that at least one in two schizophrenic patients will relapse within 12 months after initial episode if neuroleptic medication is not maintained. In patients who had had multiple episodes, 50% of the psychiatrists believed that three-quarters of such patients would relapse if neuroleptic medication was withdrawn, even if the patient had been relapse-free for 3–5 years.
Our comment

We first note a review by Gilbert et al. [5] of 66 controlled studies, and which quantified aggregate relapse rates as 51% in the neuroleptic-withdrawn group and 16% in the matched maintenance group. Those data were further analyzed by the same group [6] who quantified the relapse rates in the neuroleptic-withdrawn groups as 44% in the first 3 months, 49% (i.e. an extra 5%) by 6 months, 54% by 12 months and 59% by 24 months, as compared to rates of 6%, 11%, 17% and 27%, respectively, in the neuroleptic-maintained patients. Such a data set indicates that: (i) there is a persisting advantage to neuroleptic maintenance; (ii) after 3 months the chance of relapse is relatively low and stable over subsequent 6-month periods for those who cease medication; and (iii) some 40% had not relapsed.

By contrast, Davis et al. [7] undertook a meta-analysis of 35 random controlled trials and concluded that virtually all people not in receipt of neuroleptic medication will relapse within 3 years. Such contrasting reviews (i.e. a significant minority of non-relapses versus the rarity of non-relapse after 2–3 years) make a definitive statement difficult and presumably reflect characteristics of the contrasting databases, and in particular, the percentages with first-admission and recurrent episodes. We suggest then that the psychiatrists’ estimates in the local study were in broad agreement with the literature, which suggests that maintenance therapy does not eliminate relapse but instead acts more to reduce the relapse rate and gives the patient longer periods between relapse. While this might suggest that continuous therapy appears warranted, there is a less substantial data bank for those with first episodes, and extrapolation here must remain cautious. We suggest that, after a period, a percentage of subjects may safely have medication withdrawn and a greater percentage have the total dose reduced but, as yet, our indicator sets fail to allow us to predict membership of each of the groups.

We also take the opportunity to note that relapse rates are strongly influenced by the duration of time the patient is off neuroleptic drugs, with relapse being uncommon in the immediate post-discontinuation phase because of the long half-life of most neuroleptic drugs, contributing to a mean relapse interval of about 4 months [8–10], and with the relapse rate dropping considerably if the patient has been without relapse for 6 months post-withdrawal.

Satisfaction with neuroleptic medications’ capacity to prevent relapse

Asked to state their level of satisfaction with the current state of relapse prevention for schizophrenia, 59% of the psychiatrists held it to be unsatisfactory, and principally for two reasons. Specifically, four-fifths of those holding the situation as unsatisfactory nominated medication non-compliance, while 66% nominated side effects (such as tardive dyskinesia, extrapyramidal symptoms, fatigue, lethargy and sedation, muscular rigidity and stiffness, cognitive impairment and dulling of thinking). Thus, treatment inefficacy was not viewed as a major problem (being noted by only 26%).

Our comment

We suggest that 100% of psychiatrists should be dissatisfied. The facts that (i) at least one-quarter of subjects relapse on medication over 2 years [6], and (ii) so many patients become non-compliant because of side effects are issues of concern. We argue that available neuroleptic medications are less than optimal, and that as a percentage of the psychiatrists surveyed appear satisfied with suboptimal treatments, psychiatrist nihilism about the management of schizophrenia is suggested. There is a substantial minority of patients with schizophrenia who derive little or no benefit from current neuroleptic medication, including many with ‘positive’ symptoms as well as subgroups with ‘negative’ symptoms and neurocognitive features [11]. That one-quarter of the surveyed respondents did not view treatment inefficacy as a major problem suggests a touching faith in the efficacy of neuroleptic medications, particularly when most studies show that they induce (at best) only a slight to modest percentage reduction in schizophrenic symptoms and generally fall well short of what could be regarded as a ‘remission’ (although their residual status is often the consequence of being ‘marooned’ on high maintenance doses).

Tardive dyskinesia

Respondents were requested to estimate rates of tardive dyskinesia or TD (as a side effect of neuroleptic medication prescribed over a 5-year period to prevent relapse). A ‘mild reversible’ form was thought likely to have a prevalence of 20% by one-quarter of respondents while a prevalence of 5% was expected by at least 80% of respondents.
Our comment

Such responses suggest that most of the surveyed psychiatrists underestimated the prevalence of TD. There are data [12] to suggest that TD occurs in approximately 4% of patients per year of treatment. Thus, for patients who have been on neuroleptic drugs for 5 years, 20% would be expected to have TD. The prevalence over the same intervals is higher in older patients.

Drug treatment for an acute episode

Several vignettes were presented to provide standardised clinical scenarios for respondents.

Vignette A focused on management of an acute episode, and involved ‘a 24-year-old unmarried student with first episode-paranoid hallucinatory schizophrenia. The patient is not tense, poses no danger to himself or others and there is no insomnia. Oral therapy is indicated. What drug and what average daily dosage would you recommend after the first week of treatment if the patient exhibits no serious side-effects?’

The four options (and confirmed priority) provided to sample members were haloperidol (33%), risperidone (33%), trifluoperazine (29%) and ‘other’ (5%), with trifluoperazine being distinctly more likely to be recommended by those psychiatrists with 20 years or more experience. The most common daily dosages, after the first week of therapy, were 5 mg and 10 mg for haloperidol; 4 mg and 6 mg for risperidone; and 10 mg for trifluoperazine.

Of those recommending haloperidol, the lowest recommended dose was less than 5 mg/day (by 12% of the respondents) while the highest dose was 15 mg (by 15%). For risperidone, the lowest recommended dose was 2 mg/day (21%) and highest dose 8 mg (3%). For trifluoperazine, the lowest recommended dose was 5 mg/day (26%) and the highest 15 mg (22%).

Our comment

Survey responses indicate a move from prescribing traditional neuroleptic drugs to prescribing the newer atypical agents, such as risperidone, which have fewer adverse events and are more likely to be continued with by patients. Such views are consistent with the shift by most ‘experts’: that the atypical drugs should be the first line of treatment. Second, it is clear that a percentage of psychiatrists prescribe neuroleptic medication at excessively high doses (e.g. 15 mg of haloperidol). At such a dose, there are increased possibilities of extrapyramidal symptoms, worsening of negative symptoms and the dose having passed the maximum responsiveness, so compromising compliance. Survey responses may reflect the influence of the cultural-specific tendency of North American psychiatrists to overprescribe high potency neuroleptics. For those of us involved in first-episode research and treatment, we argue strongly, and have evidence to support it, that very low doses of atypical neuroleptics are efficacious and lead to long-term improvements in compliance. Low dose traditional antipsychotics (such as haloperidol) are equally effective on positive symptoms, but compliance is less owing to the side-effect profile.

Handling resistance to the drug of first choice

If the patient was resistant to the psychiatrist’s first choice, 32% of the respondents would wait no more than 2 weeks before changing medication, an additional 17% would wait until the end of the third week, and an additional 20% would wait until the end of the fourth week, leaving 31% who would persist beyond 4 weeks. The most commonly nominated second-line treatments were risperidone (39%), haloperidol (34%) and trifluoperazine (10%), with each being prescribed at a similar dose to first-line dose nominations, and other (17%). The most common linkage was between haloperidol and risperidone in the sense that if one failed, the other was likely to be nominated. High dosages were nominated by only a small percentage of respondents (i.e. haloperidol 20 mg by 17% and 40 mg by 2%; more than 10 mg of risperidone by only 2%; and with 21% nominating 20–100 mg trifluoperazine).

Our comment

Responses indicate that many clinicians have an inaccurate view about the time required for neuroleptic medications to work. From our collective experience, we suggest that the ‘core’ symptoms of psychosis (i.e. positive symptoms) take many weeks to ‘improve’, let alone resolve. Again from our experience, we suggest that it may take an even longer period (i.e. months) for negative symptoms and neuropsychological deficits to respond to medications such as clozapine. Thus, unless there are significant adverse effects or a lack of necessary sedation, recourse to a second-line treatment should not occur
as early as 2 weeks. Instead, the initial drug and dose should be maintained for at least 3–4 weeks, and perhaps even longer in those who have had a lengthy untreated period, as time to remission and degree of remission is associated with duration of untreated psychotic symptoms [13]. The percentage of survey respondents prepared to increase doses to high levels (e.g. 19% prescribing more than 10 mg of haloperidol) is of concern when there is strong evidence to show that prescribing more than 10 mg of haloperidol is no more effective but is associated with a higher adverse event rate [14]. Some of our commentators even argued for an optimal dose of 5 mg for haloperidol, both from clinical experience and positron emission tomography (PET) studies of D2 occupancy, with some PET studies indicating 2 mg to be adequate.

Neuroleptic maintenance

The psychiatrists considered Vignette B, focussing on maintenance and prophylaxis following an initial episode: ‘A 24-year-old unmarried student suffers a first schizophrenic episode with paranoid and hallucinatory symptoms 2 months ago. The patient was treated with 15 mg of haloperidol (or an equivalent dose of a similar neuroleptic) daily, and his symptoms have now stably remitted. With no further knowledge about the patient, what would you recommend?’

In response, 3% of the surveyed psychiatrists recommended neuroleptic discontinuation after 2–3 months, 14% recommended tapered discontinuation after 2–3 months, while 81% favoured ongoing neuroleptic medication for 3 months or longer (i.e. 35% for 3–6 months, 35% for 6–12 months; 9% for up to 2 years; and 2% indefinitely). Those with 20 or more years of experience were the most likely subgroup to recommend preventive therapy extending for more than 12 months.

Our comment

First, we note that the probe question itself involved a dose of haloperidol much higher than the appropriate dose (i.e. 5 mg) for a first episode [15]. Second, our commentators varied in considering treatment duration. One noted that the differing responses of the psychiatrists illustrated the benefit of extensive clinical experience and wondered why the concept of extended relapse prevention had not been taken up by ‘younger psychiatrists’. Two commentators judged that, as the patient’s illness trajectory was not yet established or clear, they recommended treatment for 12 months, and if a good remission occurred, to taper medication slowly and observe closely for another 12 months, akin to the American Psychiatric Association [16] guidelines. In practice, however, this is often difficult especially if there is a rapid and complete remission of an initial episode.

Depot medication as prophylaxis

Respondents were requested to nominate the minimum prescribed dose of three depot medications (i.e. haloperidol decanoate, flupenthixol decanoate, fluphenazine decanoate) after 6 months ‘without significantly increasing the risk of relapse’. For those (i.e. 96% of the sample) who recommended continuing medication at that stage, the modal dose of haloperidol was 50 mg/month (and range 20–300 mg), with 31% judging less than 50 mg/month as being sufficient, as against 24% who nominated 100 mg or more as the monthly minimum dose. For flupenthixol, the minimum recommended monthly dose ranged from 10 to 150 mg (with 23% nominating 20 mg and 26% nominating 40 mg/month). For fluphenazine, 58% of the psychiatrists nominated either 12.5 mg or 25 mg/month.

Our comment

Our commentators noted the generally high average doses favoured (e.g. when a dose of 6.25 mg fluphenazine is often effective, while the optimal dosage is considered to be 12.5–25 mg), and expressed concern about the percentages nominating excessively high levels of medication. One commentator noted the importance of understanding the kinetics of depot medications, as their effective half life is quite different from their oral counterparts in that, while drugs with nominal 2-week cycle lengths (e.g. flupenthixol, fluphenazine) have reduced equivalent monthly doses, this phenomenon does not hold for haloperidol.

Relapse management

Vignette C focussed on management of a relapse: ‘A 30-year-old married attorney suffered a first paranoid-hallucinatory schizophrenic episode a year ago. Full remission was achieved with neuroleptic treatment which was then discontinued. Two months after discontinuation, the patient suffered a second schizo-
phrenic episode which has just remitted fully under neuroleptic treatment. Which would you recommend?'

Three options were provided: (i) tapered or (ii) non-tapered discontinuation of neuroleptic medication after 2–3 months, or (iii) neuroleptic medication prevention for...months.

The vast majority of respondents (88%) voted for neuroleptic relapse prevention medication for at least 12 months (with 49% of that group voting for 2 years or more, and 10% for 5 years or more), and with a clear majority (i.e. 68%) offering a duration of 12–24 months. Only 3% recommended discontinuation after 2–3 months. Psychiatrists having less than 5 years of experience were more likely (at 19%) compared to other groups (6–9%) to vote for extended therapy (i.e. 5 years or more).

Our comment

Responses suggest that current practice is likely to be broadly congruent with modern guidelines. The finding that psychiatrists with fewer years of experience (and presumably comprising those who have undergone training more recently) voted for longer treatment periods suggests that education (be it from treatment guideline or otherwise), as against clinical experience, may have had a significant impact on clinical practice.

Discussion

While neuroleptic medication has long been held as the cornerstone of the management of schizophrenia, both for acute episodes and as maintenance to reduce new episodes, a number of important themes have emerged in the last decade (e.g. the introduction of the ‘new’ and ‘atypical’ antipsychotic drugs; reduction in recommended dosage levels; and the need to distinguish the management of patients with a first episode versus those with treatment-resistant multi-episodes, particularly in terms of neuroleptic drug doses). The present survey has some potential to inform us as to what extent such information has been assimilated into the clinical practice of Australian psychiatrists. It has, nevertheless, a number of limitations. For instance, the probe questions focus on schizophrenia with positive symptoms, running an attendant risk of reifying older views about the target areas for neuroleptic drugs (i.e. being weighted to ‘positive’ symptoms), and minimising several realities of their actions (e.g. that they may benefit negative symptoms and neurocognitive deficits, and that for the latter, especially if a lengthy duration, evidence of improvement may be quite slow). Survey responses may or may not indicate actual clinical practice. While the survey was limited to assessing issues in relation to neuroleptic medication, the management of schizophrenia involves a much wider range of interventions (e.g. psychosocial, cognitive behavioural strategies) to reduce symptoms and address disability.

The Quality Assurance Project (QAP) published treatment guidelines for the management of schizophrenia in the College journal in 1984 [17], and these serve as an early set of local recommendations against which to determine if the survey views respect the earlier guidelines or more recent ones. Key QAP recommendations were for antipsychotic drugs during the active phase of the disorder and, subsequently, the ‘consistent but conservative use of antipsychotic drugs’ complemented by social interventions and a family management program. The QAP team obtained responses from 173 psychiatrists to a detailed questionnaire which, in part, sought their management recommendations in response to several vignettes. Vignette A was a 19-year-old male having a first episode of paranoid schizophrenia. Their initial treatment regime nearly always involved a phenothiazine (99%), usually trifluoperazine or chlorpromazine, with phenothiazines being ‘regarded as the most critical treatment element by almost all (93%)’. In response to the several vignettes, phenothiazines were the predominant first treatment option, both for maintenance and to address non-compliance, and fluphenazine decanoate was the most common medication regime endorsed by respondents.

Our comment

One of our commentators suggested that the QAP recommendation of chlorpromazine might have reflected: (i) a lack of other neuroleptic medications in Australia at that time; (ii) ignorance of the photoconversion of chlorpromazine in sunlight; and that (iii) the QAP respondents must have been dominated by psychiatrists from Melbourne, as there ‘sunlight is more a curiosity than a problem with photosensitivity’. Another comment was that Australia is reputed to have the highest per capita rate of patients on depot medications, and that it may be interesting to establish determinants of that custom. Clearly, and as a reality rather than a criticism, the QAP guidelines are
now outmoded in that there are substantive arguments (i) to use atypical neuroleptics first and (ii) not proceed to depot medication so rapidly as in the past, as non-compliance is a common response which needs to be addressed at the personal and education level, with depot medication being a ‘fall-back’ option in certain restricted situations.

The QAP recommendations noted: (i) standard doses of 400 mg/day for chlorpromazine and thioridazine, and 20 mg/day for trifluoperazine and fluphenazine; (ii) a need to get the ‘dose as low as possible’; and (iii) after 6–12 months, giving consideration ‘to ceasing drug therapy in patients who have remained symptom-free and are functioning well’, or when side effects are difficult to control and ‘the remission appears adequate’. For those resistant to antipsychotic drugs, the suggestion was put of ‘the possible benefits of a trial of high-dose fluphenazine decanoate 75–100 mg twice weekly for 3–6 months’.

**Our comment**

The QAP recommended dosage levels are twice as high as currently favoured, while the maintenance period of neuroleptic medications recommended by QAP has been extended. The QAP suggestion for a high-dose fluphenazine trial is now strongly rejected by our commentators as an option, both on clinical grounds and as it has no empirical evidence to support it. Thus, we can see support for the view that guidelines do evolve, and appear to have salient effects on clinical practice.

Recently, the *Journal of Clinical Psychiatry* published, within its Expert Consensus Guideline Series (ECGS), recommendations for the treatment of schizophrenia [18]. Their panel of 87 North American psychiatrists was derived on the basis of a number of credentialling components. Our commentators view their recommendations as generally sound, but suggest that they provide insufficient information about effective doses of typical high potency neuroleptic drugs. As first-line therapy for an acute schizophrenic episode, the ECGS panel recommended high potency conventional antipsychotics (e.g. haloperidol) or the newer antipsychotic risperidone as first-line treatments and as being more appropriate than low potency conventional antipsychotics (e.g. chlorpromazine) or clozapine (mean scores, respectively, of 8.1, 7.6, 6.2 and 3.3, and with higher scores reflecting a more favourable weighting), whether the episode was dominated by ‘positive’ or ‘negative’ symptoms. Allow potency conventional antipsychotic was recommended as a second-line treatment. For a patient who had had a first episode respond favourably to pharmacological treatment, the recommended duration of ongoing medication (prior to either tapering or discontinuation) was 12 months (mean score = 6.4) or 24 months (6.0) versus lifetime (4.2) or briefer periods such as 6 months (3.9) or 3 months (2.3).

In addition, the ECGS panel recommended risperidone and high potency agents (almost equally) as first-line selections for those with relapsing multiple episodes, minimum and maximum waiting periods of 3–8 weeks before switching to another preparation if there was no therapeutic response to first-line medication during a first episode, but longer (i.e. 5–12 weeks) if there was a partial response. If, at the end of an adequate trial of a conventional antipsychotic for those having an acute exacerbation of schizophrenia there were prominent positive symptoms, the panel favoured switching to risperidone (7.4), clozapine (6.3) or another conventional antipsychotic (6.1), and demonstrated a ‘shifting away’ from the use of previously common augmentation strategies such as lithium (5.0), electroconvulsive therapy (3.3) and adding reserpine (2.5).

Turning to non-drug therapies, the QAP recommendations [17] noted that, while there was no evidence that dynamically orientated psychotherapy was helpful, a range of social interventions appeared of benefit, including developing a relationship with a primary therapist or case manager, family intervention and psychoeducation, as well as day centre and related attachments. The ECGS panel prioritised psychoeducation (8.0), cognitive–behaviour therapies (6.4), social skills training (5.8), with supportive psychodynamic therapies being viewed as of little benefit (3.7), in fact, rating lower than no psychotherapeutic approach (4.2).

Additionally, the American Psychiatric Association has recently published [16] guidelines for the management of schizophrenia, and we suggest that these warrant close reading. Here we note one overall conclusion from that report: ‘Review of the need for maintenance antipsychotic medication and the required dose should be done at least annually. Patients with only one episode of positive symptoms who have had no symptoms during the following year of maintenance therapy may be considered for a trial period without medication. For patients who have experienced multiple episodes, maintenance antipsychotic medication treatment should be continued in most cases for at least 5 years and possibly indefinitely’.

Finally, as noted earlier, management of schizophrenia...
Conclusions

It is clear that evidence for the optimal management of schizophrenia will continue to change over time, and guidelines will go out of date faster than ever. Where data are available to show that treatments are ineffective or dangerous, we must change our practices urgently. Unfortunately, there are many areas of modern psychiatry that are not addressed by high quality evidence (e.g. randomised controlled trials, systematic reviews and meta-analyses, etc.). In these instances, expert guidelines and surveys of practice are weak tools to help guide the way. Clinicians should then view guidelines derived by such strategies with some scepticism. The authors of this article do not wish to suggest that recommendations that received the most ‘votes’ by the survey participants should be accorded great weight. It is, however, of interest to see how responsive the participants have been to recent evidence, however presented to them. Overall, the results suggest that Australian management practices are reasonably congruent with recent practice recommendations (in having strongly accepted duration guidelines, but have been less responsive to dosage guidelines) and have almost certainly changed in the last decade. That is important information for a profession. However, most recommendations are a product of the pre-1990s, with weightings to the management of positive symptoms, so that our comments refer only to that restricted domain in the management of schizophrenia.

The task for education is to reduce the lag between evidence and practice. Information systems such as those published electronically by the Cochrane Collaboration, and as detailed by White [19], may be of great assistance in this respect. Equally, education must involve a broader approach prior to generating guidelines, and ensure that broader questions are asked about outcome.

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