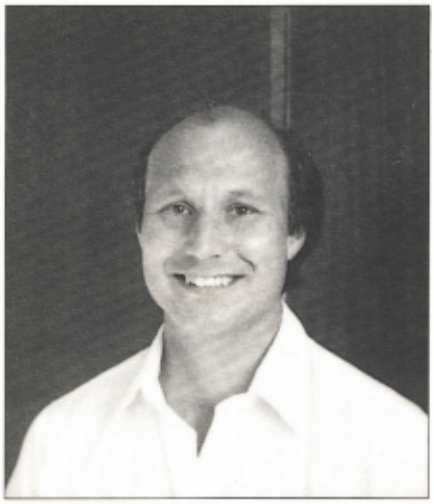
The Mystique of Migraine
Part 1: Its Nature and Diagnosis— Ron Henbest



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Curriculum vitae

Ronald J Henbest was born in Edmonton, Alberta (Canada) where he qualified in 1974 with a BSc in Maths and Psychology and in 1978 with an MD from the University of Alberta. He then completed two years postgraduate study (residency) in Family Medicine with the Department of Family Medicine at the University of Western Ontario (Canada) and obtained his CCFP from the College of Family Physicians of Canada. Ron joined the Department of Family Medicine at Medunsa in 1980. He has a particular interest in the doctor-patient interaction and its importance for healing. He returned to the University of Western Ontario in 1984 to take their Master of Clinical Science Degree in Family Medicine (MClSc), which emphasizes patient care, teaching and learning, and research. His thesis on Patient-Centred Care involved the development of a method for measuring patient-centredness and testing it against patient outcomes. In 1989, Ron returned to his home city, Edmonton, for a period of 21 months where he was engaged as an associate professor in the Department of Family Medicine at the University of Alberta. During this time, he also completed further training in systemic family therapy. In October 1990, Ron returned, with his wife Judy and four year old son Benji, this time as associate professor and deputy head of the Department of Family Medicine at Medunsa.

Summary

This is the first of a two part publication on the mystique of migraine. This paper discusses a number of important aspects of migraine in the light of current research findings; its incidence and prevalence, its nature, its classification and diagnostic criteria. Part II will review the available evidence concerning the pathogenesis, and discuss the meaning of migraine.

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Terrifying as well as fascinating, migraine has probably plagued mankind since mankind began. Aretaeus of Cappadocia is credited with having identified a distinctive, severe, paroxysmal, unilateral headache associated with nausea, at the end of the first century.[1] Not long thereafter, Galen introduced the term 'hemicrania' which was later modified to 'hemigranea', 'epigranea', 'migranea', 'megrim', and finally to 'migraine', a French derivative of the Greek word for hemicrania meaning 'half a head'.

In spite of having attracted an enormous amount of study, perhaps more than all other headache entities combined, migraine still remains a mystery.

This paper discusses a number of important aspects of migraine in the light of current research findings, including its incidence and prevalence, its nature and its classification and diagnostic criteria. A second paper will review the evidence concerning its pathogenesis and conclude with a discussion of the meaning of migraine.

Incidence and Prevalence

Incidence and prevalence are important determinants of diagnostic probability. Common things are common. How common is migraine? Even more important, how common is migraine in the patient population that you serve?

Unfortunately, but understandably, an accurate estimate of the incidence and prevalence of migraine is hard to determine for a number of reasons. First, migraine is a syndrome rather than a specific entity. Second, at least until recently, universally agreed upon specific diagnostic criteria have been absent. Third, many studies have researched select populations, such as patients attending headache clinics which are not representative of the general population, nor of patients attending family practice or primary care facilities. Consequently their results are not generalizable and may even be misleading. Keeping these things in mind, what estimates are there?

General population estimates quoted in previous reviews of migraine have ranged from 2 to 20%[2,3] with a female predominance of 3:1.[1] More recent studies give similar or lower estimates but reveal less of a difference between the sexes with a female:male ratio closer to 2:1. Spierings gives American figures of 9% of males, 16% of females, and 3 to 4% of children suffering from migraine.[4] A nationwide survey of 1590 adults Finns found that "migraine or other severe headache"

occurred in 14% of the population, 8% of men and 19,7% of women, aged 15 to 74 years.[5] A large study of over 10,000 adolescents and young adults in the United States (aged 12 to 29 years) revealed a lifetime history of one or more headaches among 90,8% of the men and 95,3% of the women with a prevalence (having suffered from at least one headache during the month prior to the study interview) of 62,4% (57,1% for males and 76,5% for females).[6] The prevalence for migraine was 3,0% and 7,4% for males and females respectively. Even lower prevalences were found in a rural population of almost 5000 people in northern Spain, using the specific diagnostic criteria recently agreed upon by the International Headache Society.[7] The prevalence of all chronic headaches combined, was 106/1000; the prevalence of migraine was only 22/1000 (2,2%).[8]

In contrast, family practice (patient-based) estimates are lower, in keeping with the observation that only a small minority, perhaps 10 to 20%, of persons experiencing headaches present to doctors. For example, statistics in the United Kingdom suggest an incidence of new headaches presented to general practitioners of 5 to 10/1000 (0,5 to 1%)[9] and it has been estimated that 1% of patients in North America present to family doctors with headache.[10] What proportion of these headaches are migraine? In other words, faced with a patient, who presents with headache, what are the chances that the headache will be migraine? Family practice/primary care studies would seem to show a disproportionately high percentage of migraine headaches when compared to figures for the general population, indicating that patients with migraine more likely to seek medical help than patients with tension headache. For example, the Headache Study Group of the University of Western Ontario conducted a one year prospective study of two hundred and sixty-five patients who presented to family physicians with a new complaint of headache.[11] Organic headaches were

Migraine is a symptom

diagnosed in 21,2% of patients, nonorganic headaches in 78,9%. Migraine accounted for 37,3% of the nonorganic headaches (6,2% were classic migraine, 31,1% were common migraine). Similar results were obtained in the general outpatient department of a large black hospital in South Africa. Of 100 patients whose main presenting complaint was headache, 27% were diagnosed as having organic headache and 73% as nonorganic. Migraine was responsible for 27,4% of the nonorganic headaches.[12]

The Nature of Migraine

Migraine headache is but part of a widespread disturbance that can be observed with varying manifestations throughout the lifespan, starting with colic and cyclic vomiting attacks in infancy and early childhood, followed by motion sickness in older children and finally by headache in adolescence and adulthood.[13,14] In addition, migraine has been linked to a number of other conditions including hypertension, vascular disease, diabetes, Raynaud's phenomenon, systemic lupus erythematosis, endocrine disorders, mitral valve prolapse, Prinzmetal's angina, renal disease and stroke.[3,14] A positive family history has been identified in approximately two-thirds of patients suffering from migraine,[13,14,15] and it has been suggested that a predisposition to migraine may be inherited as an autosomal dominant trait with incomplete penetrance.[3]

The classic description of migraine for the past three decades has been the one provided by the Ad Hoc Committee of the National Institute of Neurological Diseases and Blindness.[16] They defined 'Vascular headaches of the migraine type' as: "Recurrent attacks of headache, widely varied in intensity, frequency, and duration. The attacks are commonly unilateral in onset; are usually associated with anorexia and, sometimes with nausea and vomiting; in some are preceded by, or associated with conspicuous sensory, motor, and mood disturbances; and are often familial."[17]

Migraine has a number of striking features including its periodicity, intensity, quality, site, duration, associated symptoms, associated mood disorders, aggravating and relieving factors, association with hormonal changes, aura and post headache recovery period, but most striking of all, perhaps, is its variability - variability with respect to all of the foregoing characteristics.

Periodicity/Frequency/ Occurrence/Onset

Periodicity has long been recognized as the outstanding feature of migraine.[1] The periodicity varies a great deal with some people having attacks predictably once or twice per week, others once or twice a month and others once or twice in a lifetime.

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Attacks may also occur frequently (once or twice per week) for a number of months and then disappear for several years, or they may occur daily for a week every three to four months for years on end.

Migraine most commonly commences during adolescence[13] and tends to decrease in frequency with the passage of years.[3] However, migraine can begin at any age and occasionally starts in late middle life.[1] Although the frequency of migraine attacks varies tremendously from daily to once in a lifetime, most patients have one to four headaches per month.[3,18] Roux found a significant difference between migraine and tension headaches in this regard. Tension headaches tended to occur daily (when they occurred), in contrast to migraine which tended to occur less often than once per week, but more frequently than once per month.[12] Another feature of migraine is its occurrence during 'let down' periods such as weekends (after a hard week at the office), and the first few days of a holiday, or after specific stressful events such as exams, or the prolonged illness of a loved one.[1,14] The commonest time of onset of a migraine headache is during the night or early morning[14] in contrast to tension headaches which usually develop during the day.

Intensity/Severity

Migraine headaches range from relatively mild to severe, from low to high intensity, from barely perceptible 'background' headaches to headaches that not only completely dominate the person during the time of the headache, but the rest of his or her life as well.

Although the intensity of migraine varies, studies consistently show that migraine headaches are most often severe and are considerably more severe than tension headaches. Iversen et al found that the majority of patients with migraine classify the intensity of their headache as moderate or severe, in contrast to patients with tension headache who classify the intensity as mild or moderate.[18] In fact, 53% of the migraine only group reported that their headaches were always or usually severe and an additional 40% reported that their headaches were usually a moderate intensity. Not a single patient with tension headache

Prevalence of migraine in the population; 2% to 7%

reported the headache as usually or always severe. The Headache Study Group found that 70 to 80% of patients with migraine reported severe pain in contrast to 20 to 55% of patients with muscle contraction headaches.[11] Further, Roux found that patients with migraine are more likely to interrupt their work (80%) than patients with tension headache (less than 50%).[12]

Quality/Character of the Pain

The classic characteristic of the pain of migraine is its throbbing or pulsating quality.[1,3,15] The pain may however start as a dull ache that progessively worsens into a throbbing, pulsating pain that later becomes constant and nonthrobbing.[1,3] Although it is true that some migraine headaches never throb, most do. A recent study done in Denmark, found that only 10% of patients with migraine never have a pulsating headache and that 70% of migraine patients reported that their headaches always or usually pulsated.[18] This was in marked constrast to their finding that 86% of patients with tension headache stated that their headaches never or seldom pulsated.

Site/Location

Another distinguishing feature of migraine is its unilaterality – notably temporal, supraorbital, retrobulbar, parietal, postauricular, and occipital.[1] Although usually unilateral in onset, migraine often becomes generalized and may be generalized even from the onset. "Side-shift" (varying from side to side) in successive attacks is diagnostic of migraine and at least some switching provides reassurance that the headache is not caused by a fixed organic lesion. Diamond and Dalessio[3] give a figure of 70% of migraine headaches being unilateral in adults in contrast to migraine usually being bilateral in children. Recent studies have found unilaterality at some time, occurring in 84% of patients diagnosed as having classic migraine in Norway[19] and in 95% of patients having migraine with aura in the United States.[20] Sideshift has been found to occur in every patient with unilateral migraine and thus acts as an important discriminant against other types of unilateral headache including cluster, chronic paroxysmal hemicrania, and cervicogenic headache, where the pain is always on the same side.[19,21]

Duration

Migraine headaches may last anywhere from a few minutes to a few weeks and may include short

duration high-intensity attacks, long duration low-intensity attacks or anything in-between. Most commonly however, migraine headaches last from 'sun-up' to 'sun-down' with onset in the early morning and resolution in the early evening.[1] Fortunately, the intensity of the headache seems to be in inverse proportion to its duration. Cluster headaches last 30 to 90 minutes, classic migraine from 1 to 6 hours and common migraine takes all day or even longer.[14]

In terms of time taken to reach a peak, subarachnoid haemorrhage is usually described as a hammer blow, cluster takes five minutes, classic takes thirty to sixty minutes and common migraine may take three to four hours. One recent study that examined the duration of headaches in some detail, classified headaches as 'migraine only' for headaches in patients suffering exclusively from migraine, as 'migraine mix' for migraine headaches occurring in patients who experienced both migraine and tension headaches, as 'tension mix' for tension headaches in patients having both migraine and

A positive family history has been identified in 60% + of patients suffering from migraine

tension headaches and as 'tension only' for headaches in patients suffering exclusively from tension headaches.[18] The duration of untreated or unsuccessfully treated headache episodes were significantly longer for both migraine groups than the tension headache groups. The migraine only and migraine mix groups had median durations of nineteen and twenty-four hours in contrast to a median duration of twelve hours for both the tension only and tension mix groups. In addition, the median durations of the shortest and longest attacks ever experienced, were significantly longer in the migraine groups than in the tension headache groups.

Associated Symptoms

Yet another hallmark of migraine is the association of acute headache with gastrointestinal complaints, including anorexia, nausea, vomiting, abdominal bloating and diarrhoea. In-between attacks, constipation may be a problem.

Anorexia would seem to be an accompaniment of most migraine headaches and nausea is common. Vomiting is more common the more severe the headache and may be the most important aspect of the attack, causing prostration during the attack and delay in recovery after its termination.[1] Ziegler et al found that 88% of patients presenting with unilateral headaches had nausea and/or vomiting during at least some attacks.[20] They also found that nausea accompanied unilateral attacks of headache either with great frequency or with comparative rarity: 33% of patients had nausea in more than 90% of attacks; 27% in 10% or fewer of attacks. Roux found that migraine headaches were much more frequently associated with nausea (70%) than were tension headaches (10%) and more frequently associated with vomiting (30%) than tension headaches (0%).[12]

It has also been shown that the nausea experienced with migraine headaches is much more frequently rated as severe than the nausea experienced with tension headaches. For example, Inversen et al, found that only 33% of the patients who

Periodicity has been identified as the outstanding feature of migraine for many years

suffered exclusively from migraine rated their nausea as mild in contrast to the 91,7% of tension headache patients who rated their nausea as mild.[18] In addition, patients who suffered from both migraine and tension headache much more frequently identified the nausea associated with their migraine headaches as more severe than the nausea associated with their tension headaches.

Other, less common symptoms which may precede or accompany the headache include photophobia, phonophobia, polyuria, diarrhoea and mood disorders. I think that the irritability, irascibility hostility, decreased memory, attention and concentration, and poor judgement that have been observed to accompany migraine attacks[1] can be accounted for by the severity of the pain of the headache and the unpleasantness of the associated nausea, rather than being a unique feature of migraine.

Aura/Preheadache Symptoms

Perhaps nowhere is the variability of migraine better exemplified than with respect to aura. Most migraine sufferers never experience a clearly defined prodome or aura (classic

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migraine makes up only 15 to 20% of all migraine headaches[3]). However, some people experience a sense of euphoria before and/or after a migraine attack. As Wolff has so beautifully articulated, "The evening before the onset of an attack is often characterized by a feeling of especial well-being with excessive talkativeness and high spirits, unwillingness to retire, and increased appetite for food. After an attack, again patients often experience a period of buoyancy and well-being."[22] Others may be aware only of a mounting tension, hunger, or wakefulness or alternatively a declining energy and drive.

At the other end of the spectrum, there are some who predictably have a clearly defined aura immediately preceding the onset of the headache, but this is probably a very small number indeed. Ziegler et al found that even among those who felt it necessary to attend a headache clinic, only one-third had ever had an aura and that such attacks accounted for only a small percentage of their total

Migraine has a *throbbing*, pulsating quality

number of headaches.[20] Visual auras were by far and away the most commonly identified prodrome, being identified by 97% of patients having auras. Paresthesias, as auras, occurred in 31% of those having visual auras, but rarely (1%) on their own. Of those having visual auras, 44% had such an aura at some time without subsequent headache.

The classic visual disturbance is that of a "... fortification spectra of scintillating lights expanding laterally in one or both visual fields with homonymous hemianopsia and blindness temporarily following in its wake."[23] The two key features of the visual aura are flashing lights and blind spots, both of which may interfere with vision. The flashing lights may take on almost any pattern including wavy lines, golden balls, stars, geometric designs, serrations and tessellations as well as the so-called fortification spectra.[1] The blind spots (scotomata) may be isolated or arranged in visual field quadrants resulting in homonymous, quadrantic, or hemianopic field defects usually contralateral to the side of the headeache.[1] Flashing lights and blind spots are not to be confused with other visual difficulties such as photophobia, blurred vision, and tearing that may accompany the headache itself.

The classic aura precedes the headache, lasts twenty to thirty minutes and ends before the onset of the headache. However, the aura may last longer, rarely persisting for hours and may overlap the headache.

Postheadache/Recovery

As mentioned in the previous section, migraine headache may be followed by a period of relaxation, a sense of well-being, and even by a feeling of energy, drive, and enthusiasm. Less often, a person may feel drained or depleted, especially if there has been severe vomiting. Also well recognized, especially after severe or prolonged headaches, is the occurrence of edema of the head and sometimes the face, such that the patient notices the scalp being tender to touch when combing the hair. Vasomotor phenomena such as blushing or blanching, as well as rhinorrhoea, nasal stuffiness and tearing may also occur.

Hormones/Pregnancy

Approximately 70% of women have migraine attacks associated with their menstrual periods and up to 80% of women experience relief with the onset of pregnancy.[14] Menopause also brings relief approximately three-quarters of the time.[3]

It is mainly common migraine that is prevented by pregnancy, especially during the last two trimesters. Classic

Menopause often brings relief

migraine is sometimes accentuated by pregnancy, sometimes with frightening prodomes.[24] Both oral contraception and estrogen therapy may worsen the migraine syndrome. Migraine patients also have an increased incidence of toxemia and hyperemesis gravidarum.[14]

Aggravating Factors

The intensity of migraine headaches may be increased by anything which increases the blood pressure. This includes any form of exertion, a sudden change in position, jarring the head, coughing, bending, bright lights, loud sounds, and mental effort.[1,15]

Classification and Diagnostic Criteria

As far as classification goes, migraine is number one. The conventional classification, based on the recommendations by the Ad Hoc

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Committee, called its first category, 'Vascular Headaches of the Migraine Type'[16]. This category contained five subgroups, namely: classic migraine, common migraine, cluster headaches, hemiplegic and ophthalmoplegic migraine, and lower-half headache. This classification was based primarily on the mechanisms of head pain derived from the comprehensive research of Wolff and his colleagues dating from the late 1930s.[1,25,26] The classification provided descriptions based on clinical experience rather than specific diagnostic criteria validated by prospective studies of patients with headache. One result has been that individual investigators and clinicians have defined their own diagnostic criteria which have often included 'definite' and 'probable' or 'possible' categories.[11,27] In addition, previously held certainties about the pathophysiology of both migraine and tension headaches[28] has been questioned and there has been a growing recognition that the nonorganic headaches represent a functional continuum, from muscle-contraction or tension headache at one end of the spectrum, through common migraine to classic migraine to cluster headache at the other end of the spectrum.[29,32] Some have even questioned the usefulness of differentiating between common migraine and tension headaches and argue for a single category such as "recurrent nonspecific headache (RNSH), for functional headaches that cannot be classified as classic migraine or cluster headache.[11,33]

In response to these increasingly recognized difficulties with the conventional classification of headache, the International Headache Society appointed a committee to revise the classification to reflect the changing understanding of the pathogenesis of a number of types of headache and to recommend specific diagnostic criteria.[7] The revised classification has two main categories: primary and secondary. Headaches are classified as primary unless they occur de novo in close temporal relation to an organic disorder in which case they are classified as secondary and coded according to the organic disorder. Four main categories of primary headaches are identified:

1. Migraine
2. Tension-type headaches,
3. Cluster headaches, and
4. Miscellaneous headaches unassociated with structural lesions.

Prevalence in women - 2x that in men

Migraine remains number one and is now simply called 'migraine', no longer assuming an underlying primarily vascular pathogenesis. The terms classic and common have been dropped and migraine is now subclassified as:

1. migraine without aura,
2. migraine with aura,
3. ophthalmoplegic migraine,
4. retinal migraine,
5. childhood periodic syndrome,
6. complications of migraine, and
7. migrainous disorders not fulfilling the above criteria.

Migraine with aura is further subdivided into migraine with typical aura, migraine with prolonged aura, familial hemiplegic migraine, basilar migraine, migraine aura without headache, and migraine with acute onset aura. The complications of migraine are classified as status migrainous and migranous infarction. Cluster headache is now a separate category altogether. The term 'combined headaches' has been dropped and if more than one type of headache occurs, each receives a diagnosis. As well, such terms as acephalgic migraine[34] (or migraine equivalants) are no longer used.

The diagnostic criteria for the first two subcategories of migraine are as follows. The diagnosis of 'migraine without aura' requires at least five attacks of headache lasting 4 to 72 hours (untreated or unsuccessfully treated) with at least two of the following four characteristics: unilateral location, pulsating quality, moderate or severe intensity and aggravation by walking stairs or similar routine physical activity, and at least one of the two following associations during headache: nausea and/or vomiting or photophobia and phonophobia. The diagnosis of 'migraine with aura' requires the above criteria and at least two attacks with three of the following four characteristics: 1. one or more fully reversible aura symptoms indicating focal cerebral, cortical and/or brain stem dysfunction, 2. at least one aura symptom develops gradually over more than four minutes or two or more symptoms occur in succession, 3. no single aura symptom lasts more than sixty minutes, and 4. headache follows the aura with a free interval of less than sixty minutes (although it may begin before or simultaneously with the aura). A 'typical aura' must fulfil all four of the above criteria.

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The revised classification has stimulated a renewed interest in nosographic studies of headache. Two recent studies have specifically set out to test the recommended diagnostic criteria. Iversen et al[18] interviewed eighty-one patients that had been diagnosed as having migraine, tension headaches or both according to the previously used criteria of the Ad Hoc Committee. Although the original diagnosis also fulfilled the IHS criteria in every patient, the criteria were only fulfilled in half or less of the attacks in 9 patients and by applying the IHS criteria, an additional diagnosis was achieved. This study demonstrated that IHS criteria did not radically change the diagnoses and that overall, the new critera were both sensitive and specific. The study findings also suggest that the criteria might be improved by grading the accompanying symptoms (of nausea and photophobia) rather than merely ascertaining their presence or absence. Of particular note, was the finding that aggravation of pain by routine physical activity was the best pain criteria for differentiating between migraine and tension-type headaches – better than unilaterality or pulsating quality.

Martinez-Lage et al's survey of almost five thousand people in a rural Spanish county also found the IHS classification system to be suitable overall, but identified a problem with the interpretation of some of the diagnostic criteria.[8] The criteria demonstrating the greatest sensitivity were: (1) at least five attacks, (2) lasting 4 to 72 hours, (3) pulsating quality, (4) moderate or severe intensity, and (5) associated with nausea and/or vomiting. The criteria having the greatest specificity were (1) at least five attacks (2) lasting 4 to 72 hours, (3) unilateral location, (4) aggravation by walking stairs or similar routine physical activity, and (5) associated with nausea and/or vomiting. The criterion found to be the most difficult to interpret was aggravation by walking. Equivocal responses were reported if this criterion was asked as stated, but unequivocal responses were obtained by asking, "Is your pain aggravated by head movements?" As might have been anticipated, the criteria of at least five attacks depended on the duration of headache and age of onset, and the time period of 4 to 72 hours did not differentiate migraine from episodic tension-type headaches. They also found the term 'pulsating' to be somewhat confusing and that a scale of 0 to 10 was a more useful way of rating intensity of head pain than simply as moderate or severe.

Conclusion

Migraine retains its mystique in spite of a long history and a great deal of research. Even its incidence and prevalence remain somewhat of a mystery. However, based on the evidence reviewed in this paper, it would seem that the overall prevalence of migraine ranges from 5 to 15% in large population surveys in a number of different countries and that the prevalence in women is about twice that in men. Although migraine makes up only some 10% of all headaches in the general population, it is over-represented in the doctor's office accounting for 20-30% of all headaches and perhaps even one third or more of the 'functional' or nonorganic headaches.

The nature of migraine consists of a number of striking features including periodicity, unilaterality, the quality and intensity of the pain, and an association with nausea and/or vomiting. Each of them is an enigma in itself, but perhaps the most striking and mysterious thing of all is its extreme variability.

Recently, a revised headache classification has been proposed and specific operational diagnostic criteria recommended. Initial studies have found it to be an improvement on the previous one. Migraine is now classified simply as migraine, reflecting an appropriate loss of certainty about its pathogenesis – the subject of: The Mystique of Migraine: Part 2.

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