Chronic daily headache represents a range of disorders characterized by the occurrence of long-duration headache 15 or more days per month. The classification of these disorders continues to undergo revision to make them more clinically relevant, such as that which has been most controversial, the classification of chronic migraine. The role of medication overuse in what has commonly been known as rebound headache can have a significant influence on these disorders. The diagnosis of the chronic daily headaches, including chronic migraine and chronic tension-type headache, truly cannot be made if patients are having medication-overuse headache. This article reviews the criteria for medication-overuse headache and the subset of headaches making up chronic daily headache, as well as the epidemiologic and therapeutic aspects of these disorders.

The term chronic daily headache (CDH) refers to a group of disorders characterized by very frequent headaches (>15 days a month), including those headaches associated with medication overuse. The CDH group can be categorized into primary and secondary varieties. Secondary CDH has an identifiable underlying cause such as acute headache medication overuse, head trauma, cervical spine disorders, vascular disorders, and disorders of intracranial pressure. Primary CDH is not related to a structural or systemic illness, and is often subdivided into long- or short-duration disorders, based on whether the individual headache episodes last more or less than 4 hours on average.

When headache duration is less than 4 hours, the differential diagnosis includes cluster headache, paroxysmal hemicrania, idiopathic stabbing headache, hynic headache, and short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT).

When headache duration is greater than 4 hours, the major primary disorders for which there are operational diagnostic criteria as defined by the second edition of the International Classification of Headache Disorders (ICHD-2) are chronic migraine, hemicrania continua, chronic tension-type headache (CTTH), and new daily persistent headache (NDPH). Chronic migraine is used by the ICHD-2 in place of transformed migraine (defined by the Silberstein and Lipton criteria). Chronic tension-type headache was included in the first International Headache Society (IHS) classification and inappropriately equated to CDH. Chronic migraine, NDPH, and hemicrania continua are new to the ICHD-2.

Long-duration CDH is a significant public health concern. Approximately 5% to 5% of the population worldwide have daily or near-daily headaches. Patients with long-duration primary CDH, most of which is transformed migraine, account for the majority of headache subspecialty practice consultations in the United States. The disability associated with this disorder is substantial, as patients have a significantly diminished quality of life and mental health, as well as impaired physical, social, and occupational functioning.

Transformed and Chronic Migraine
Many studies have described the process and associated features of transformed migraine. This headache has been variously called transformed or evolutive migraine or mixed headache. Patients with transformed migraine often have a past history of episodic migraine that began in their teens or twenties. Most patients with this disorder are women, 90% of whom have a history of migraine without aura.

Patients often report a process of transformation characterized by headaches that become more frequent
over months to years, with the associated symptoms of photophobia, phonophobia, and nausea becoming less severe and less frequent.\textsuperscript{5,6,11,13,15} Patients often develop (or transform into) a pattern of daily or nearly daily headaches that phenomenologically resembles a mixture of tension-type headache (TTH) and migraine. That is, the pain is often mild to moderate and is not always associated with photophobia, phonophobia, or gastrointestinal features.

Other features of migraine, including aggravation by menstruation and other trigger factors, as well as unilateral and gastrointestinal symptoms, may persist. Attacks of full-blown migraine superimposed on a background of less severe headaches occur in many patients. The term \textit{transformed migraine} has been used to refer to this process. The term \textit{chronic migraine} is now being used by the IHS, in part because a history of transformation is often missing.

Silberstein and Lipton’s revised criteria for transformed migraine (Table 1) provide three alternative diagnostic links to migraine\textsuperscript{14}:

- \(A\) a prior history of IHS migraine;
- \(B\) a clear period of escalating headache frequency with decreasing severity of migrainous features; or
- \(C\) current superimposed attacks of headaches that meet all the IHS criteria for migraine except duration.

Migraine transformation most often develops when there is medication overuse, but transformation may occur without overuse.\textsuperscript{5,16} About 80\% of patients with CDH seen in subspecialty clinics overuse symptomatic medication.\textsuperscript{5,6,13,15} Headache frequency often increases when medication use increases. Stopping the overused medication frequently results in distinct headache improvement, although it may take days to weeks. Many patients have significant long-term improvement after detoxification. When the original IHS (ICHD-1) criteria\textsuperscript{9} were used, a diagnosis of headache induced by substance use or exposure required that the headaches remit after the overused medication is discontinued. This criterion was difficult to apply reliably, and diagnosis was impossible until the overused medication was discontinued.\textsuperscript{4} The IHS now attempts to get around this issue by using the term \textit{probable chronic migraine}.

The IHS, in its newest classification (ICHD-2),\textsuperscript{2} classifies chronic migraine as a complication of migraine. Its diagnosis requires migraine headache occurring on 15 or more days a month for more than 3 months without medication overuse (Table 2). When medication overuse is present, the diagnosis is unclear until 2 months after medication has been withdrawn without improvement. Medication overuse, if present (ie, medication-overuse headache [MOH]), is the most likely cause of chronic symptoms. Therefore, the default rule is to code such patients according to the antecedent migraine subtype (usually migraine without aura) plus probable chronic migraine plus probable MOH. When these criteria are still fulfilled 2 months after medication overuse has ceased, chronic migraine plus the antecedent migraine subtype should be diagnosed and probable MOH discarded. If at any time sooner these criteria are no longer fulfilled because improvement has occurred, code for MOH plus the antecedent migraine subtype and discard probable chronic migraine.\textsuperscript{2}

The requirement that the daily headache must meet criteria for migraine without aura each day is a significant problem with the ICHD-2 criteria and one of the major reasons for its lack of generalizability in clinical practice. While up to 80\% of headaches experienced by episodic migraine sufferers will fulfill criteria for migraine or probable migraine (1.1 or 1.6), migraineurs do experience a spectrum of headaches that may phenotypically resemble or fulfill criteria for TTH.

As headache frequency increases, the phenotypic spectrum of individual headache episodes broadens, and the clinical distinction between migraine and TTH may become less obvious. Many clinicians and epidemiologists now believe that most headaches experienced by migraine sufferers that phenotypically resemble TTH are biologically similar to migraine and responsive to migraine-specific modes of therapy.\textsuperscript{3} Furthermore, attacks are often treated early, before severity increases and associated symptoms develop.

Based on the clinical trial and clinic-based data reviewed, the criteria for ICHD-2 chronic migraine do not accurately reflect the headache phenotype of those patients with a history of migraine that evolves into a pattern of frequent or daily headache (\(\geq 15\) days per month). Alternate diagnostic criteria are being developed for this entity. To eliminate confusion with the current IHS-defined \textit{chronic migraine}, this entity will be called \textit{transformed migraine}. By definition, of course, all patients meeting the IHS cri-

<table>
<thead>
<tr>
<th>Table 1</th>
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<tbody>
<tr>
<td><strong>1.8 Chronic Migraine</strong></td>
</tr>
<tr>
<td><strong>A.</strong> Daily or almost daily (&gt;15 days/month) head pain for &gt;1 month</td>
</tr>
<tr>
<td><strong>B.</strong> Average headache duration of &gt;4 hours/day (if untreated)</td>
</tr>
<tr>
<td><strong>C.</strong> At least one of the following:</td>
</tr>
<tr>
<td>- <strong>1)</strong> History of episodic migraine meeting any International Headache Society (IHS) criteria 1.1 to 1.6</td>
</tr>
<tr>
<td>- <strong>2)</strong> History of increasing headache frequency with decreasing severity of migrainous features over at least 3 months</td>
</tr>
<tr>
<td>- <strong>3)</strong> Headache at some time meets IHS criteria for migraine 1.1 to 1.6 other than duration</td>
</tr>
<tr>
<td><strong>D.</strong> Does not meet criteria for new daily persistent headache (4.7) or hemicrania continua (4.8)</td>
</tr>
<tr>
<td><strong>E.</strong> Not attributed to another disorder</td>
</tr>
</tbody>
</table>

Table 2
New International Headache Society Criteria for Chronic Migraine

<table>
<thead>
<tr>
<th>Diagnostic criteria:</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Headache fulfilling criteria C and D for 1.1 <em>Migraine without aura</em> on ≥15 days/month for ≥3 months</td>
</tr>
<tr>
<td>B. Not attributed to another disorder</td>
</tr>
</tbody>
</table>


Table 3
New International Headache Society Criteria for Chronic Tension-Type Headache

2.2 Diagnostic criteria:

<table>
<thead>
<tr>
<th>Diagnostic criteria:</th>
</tr>
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<tbody>
<tr>
<td>A. Headache occurring on ≥15 days per month on average for ≥3 months (≥180 days per year) and fulfilling criteria B–D</td>
</tr>
<tr>
<td>B. Headache lasts hours or may be continuous</td>
</tr>
<tr>
<td>C. Headache has at least two of the following characteristics:</td>
</tr>
<tr>
<td>1. bilateral location</td>
</tr>
<tr>
<td>2. pressing/tightening (nonpulsating) quality</td>
</tr>
<tr>
<td>3. mild or moderate intensity</td>
</tr>
<tr>
<td>4. not aggravated by routine physical activity such as walking or climbing stairs</td>
</tr>
<tr>
<td>D. Both of the following:</td>
</tr>
<tr>
<td>1. no more than one of photophobia, phonophobia, or mild nausea</td>
</tr>
<tr>
<td>2. neither moderate or severe nausea nor vomiting</td>
</tr>
<tr>
<td>E. Not attributed to another disorder</td>
</tr>
</tbody>
</table>


Chronic Tension-Type Headache

The IHS describes CTTH17 (Table 3) as:

A disorder evolving from episodic tension-type headache, with daily or very frequent episodes of headache lasting minutes to days. The pain is typically bilateral, pressing or tightening in quality and of mild to moderate intensity, and does not worsen with routine physical activity. There may be mild nausea, photophobia or phonophobia.

The headaches frequently involve the posterior aspect of the head and neck. **In contrast to patients with chronic migraine, prior or coexistent episodic migraine is absent in patients with CTTH, as are most features of migraine. Diagnosis of CCHT requires headache on at least 15 days a month for at least 3 months (previously 6 months). Although the pain criteria are identical to those for episodic tension-type headache (ETTH), the IHS classification allows nausea but not vomiting.17** This inclusion of nausea assumes that mild nausea or photophobia or phonophobia are compatible with the diagnosis of CTTH.5,17 However, the need to include any of these migrainous features in the IHS definition of CTTH may be a result of the practice of including chronic migraine under the rubric of CTTH.

The ICHD-2 continues to permit only one of the symptom criteria (mild nausea, photophobia, and phonophobia), but excludes moderate or severe nausea or vomiting. The ICHD-2 has an appendix that provides alternate criteria for CTTH. The alternate criteria do not allow for nausea, photophobia, or phonophobia.) The ICHD-2 still does not require a minimum duration of headache; therefore, a headache that lasts 5 minutes a day for 15 days a month could still be CTTH. Chronic tension-type headache is still subclassified based on the occurrence or absence of pericranial tenderness.

Coexistent migraine and CTTH could coexist with the proviso that the nonmigrainous headaches have no migrainous features. Guitera et al18 suggest, based on population-based epidemiologic data, that CTTH and migraine can coexist if, and only if, the current headache has no migrainous features and there is a remote history of migraine.

Chronic tension-type headache may evolve from ETTH. Just as with chronic migraine, when medication overuse is present, the diagnosis is uncertain until 2 months after the overused medication has been withdrawn without improvement. The introduction of *chronic migraine* into the ICHD-2 creates a problem in relation to the differential diagnosis between chronic migraine and CTTH. Both diagnoses require headache (meeting the criteria for migraine or TTH, respectively) on at least 15 days a month. Therefore, it is theoretically possible for a patient to have both these diagnoses.

Silberstein and Lipton19 developed criteria in which the diagnosis of one disorder took precedence over the diagnosis of another. They suggest that a putative diagnosis of CTTH has not met criteria for hemicrania continua, NDPH, or chronic migraine. This diagnosis would handle the difficulty of a small group of patients who fulfill the IHS diagnostic criteria for both chronic migraine and CTTH. This solution would be possible when two (and only two) of the four pain characteristics are present and headaches are associated with mild nausea. These cases are most likely chronic migraine and have been shown to be associated with elevated calcitonin gene-related pep-
tide (CGRP) levels (a marker for migraine). The headaches should be
coded as CTHH and episodic migraine
only if the daily baseline headache has no
migrainous features. If the daily baseline
headache is migrainous, the headaches
should be coded as chronic migraine,
despite what the new criteria state.

Chronic tension-type headache is
often associated with medication overuse.
Similar diagnostic classification rules per-
tain here as they do for chronic migraine.

New Daily Persistent Headache
New daily persistent headache (Table 4)
is characterized by the relatively abrupt
onset of an unremitting primary
CDH.\textsuperscript{19,20} The IHS now includes NDPH
in the classification. (Previously used
terms included \textit{de novo chronic headache}
and \textit{chronic headache with acute onset}). The
daily headache develops abruptly, over
less than 3 days. The IHS states that the
pain is typically bilateral, pressing or
tightening in quality, and mild to mod-
erate in intensity. Photophobia, phono-
phobia, or mild nausea may be present.
Silberstein and Lipton\textsuperscript{14} elected not to
classify NDPH as a type of de novo
CTTH, for it is not clear whether this con-
dition is etiologically related to TTH.
The absence or presence of a past history of
headache distinguishes NDPH from
CTTH and chronic migraine. New daily
persistent headache is likely to be a het-
erogeneous disorder. Some cases may
reflect a postviral syndrome.\textsuperscript{19} Patients
with NDPH are generally younger than
those with transformed migraine.\textsuperscript{19,20}

New daily persistent headache
requires the absence of a history of evo-
lution from migraine or ETTH. In the
absence of rapid development, it is coded
as CTHH or chronic migraine. Excluding
all patients with a history of ETTH is
problematic, as almost 70\% of men and
90\% of women have had a TTH in the
past. Silberstein and Lipton\textsuperscript{14} allowed a
diagnosis of NDPH in patients with
migraine or ETTH if these disorders do
not increase in frequency to give rise to
NDPH. New daily persistent headache
may or may not be associated with med-
ication overuse. A diagnosis of NDPH
takes precedence over chronic migraine
and CTTH.

The ICHD-2\textsuperscript{2} recognizes NDPH as
distinct from CTHH. New daily persistent
headache is unique in that headache is
daily and unremitting almost from the
moment of onset, typically in individ-
uals without a prior headache history.

New daily persistent headache can
have features suggestive of either
migraine or TTH. I believe that the pro-
posed IHS criteria inappropriately
exclude headaches that are phenomeno-
logically migraine with sudden onset.

Secondary headaches, such as low cere-
brospinal fluid (CSF) volume headache,
raised-CSF pressure headache, post-
traumatic headache, and headache
attributed to infection (particularly viral
infection) should be ruled out by appro-
priate investigations.\textsuperscript{1}

Table 4
New International Headache Society Criteria for New Daily Persistent Headache*\textsuperscript{} \textsuperscript{}

<table>
<thead>
<tr>
<th>Diagnostic criteria:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A.</strong> Headache that, within 3 days of onset, fulfills criteria B–D</td>
</tr>
<tr>
<td><strong>B.</strong> Headache is present daily, and is unremitting, for \textgreater{}3 months</td>
</tr>
<tr>
<td><strong>C.</strong> At least two of the following pain characteristics:</td>
</tr>
</tbody>
</table>
| \begin{itemize}
| \item bilateral location |
| \item pressing/tightening (nonpulsating) quality |
| \item mild or moderate intensity |
| \item not aggravated by routine physical activity such as walking |
| \item or climbing |
| \end{itemize} |
| **D.** Both of the following: |
| \begin{itemize}
| \item no more than one of photophobia, phonophobia, or mild nausea |
| \item neither moderate or severe nausea nor vomiting |
| \end{itemize} |
| **E.** Not attributed to another disorder |


Hemicrania Continua
Hemicrania continua is a rare, indomethacin-responsive headache dis-
order characterized by a continuous, moderately severe, unilateral headache
that varies in intensity, waxing and
wanning without disappearing com-
pletely.\textsuperscript{21,22} It may rarely alternate sides.\textsuperscript{23}

Hemicrania continua is frequently asso-
ciated with jabs and jolts (idiopathic stab-
bing headache). Exacerbations of pain
are often associated with autonomic dis-
turbances, such as ptosis, miosis, tearing,
and sweating.

Hemicrania continua is not triggered
by neck movements, but tender spots in
the neck may be present (Table 5). Some
patients may have photophobia, phono-
phobia, and nausea. The IHS now
includes hemicrania continua in the clas-
sification. It is described as a “persistent
strictly unilateral headache responsive
to indomethacin.”\textsuperscript{23}

Although the disorder almost invari-
ably has a prompt and enduring
response to indomethacin, the require-
ment of a therapeutic response as a diag-
nostic criterion is problematic. It effec-
tively excludes the diagnosis of
hemicrania continua in patients who
were never treated with indomethacin
(perhaps because another agent helped),
and patients who failed to respond to
indomethacin. Treatment response is
generally not part of IHS case definitions
of headache disorders. Cases have been
described that did not respond to
indomethacin but meet the phenotype;
for this reason, Goadsby and Lipton\textsuperscript{24}
Table 5  
New International Headache Society Criteria for Hemicrania Continua* 

4.7 Hemicrania continua  

Diagnostic criteria:

A. Headache for >3 months fulfilling criteria B–D  
B. All of the following characteristics:
   1. unilateral pain without side-shift  
   2. daily and continuous, without pain-free periods  
   3. moderate intensity, but with exacerbations of severe pain  
C. At least one of the following autonomic features occurs during exacerbations and ipsilateral to the side of pain:
   1. conjunctival injection and/or lacrimation  
   2. nasal congestion and/or rhinorrhea  
   3. ptosis and/or miosis  
D. Complete response to therapeutic doses of indomethacin  
E. Not attributed to another disorder  


have provided an alternate means of diagnosis. A case that responded to piroxicam-β-cyclodextrin further suggests that though the nonsteroidal anti-inflammatory drug response is of great interest, it points to, rather than expresses, the pathophysiology.

Although there are no reports of secondary hemicrania continua, it can be aggravated by a C7 root irritation due to a disc herniation.25 A case of a mesenchymal tumor in the sphenoid bone in which the response to indomethacin faded after 2 months has also been reported.26 These cases suggest that physicians should be suspicious of escalating doses or loss of indomethacin’s efficacy and reevaluate the patient. Hemicrania continua is also seen in non-Caucasian populations.27

Drug Overuse and Rebound Headache

Medication overuse headache, previously called rebound headache, drug-induced headache, and medication-misuse headache (Table 6), is an interaction between a therapeutic agent used excessively and a susceptible patient. Patients with frequent headaches often overuse analgesics, opioids, ergotamine, and triptans.28-31 When a new headache occurs for the first time in close temporal relation to substance exposure, it is coded as a secondary headache attributed to the substance. This is also true if the headache has the characteristics of migraine, TTH, or cluster headache. When a preexisting primary headache is made worse in close temporal relation to substance exposure, two possibilities exist: Patients can either be given only the diagnosis of the preexisting primary headache, or they can be given both this diagnosis and the diagnosis of headache attributed to the substance. Factors that support adding the latter diagnosis are:

- a very close temporal relation to the substance exposure;  
- a marked worsening of the preexisting headache;  
- very good evidence that the substance can aggravate the primary headache; and, finally,  
- improvement or resolution of the headache after the substance’s effects are terminated.

A diagnosis of headache attributed to a substance usually becomes definite only when the headache resolves or greatly improves after exposure to the substance is terminated. In the case of MOH, an arbitrary period of 2 months after overuse cessation is stipulated by the IHS; if the diagnosis is to be definite, improvement must occur in that time frame. Prior to cessation, or pending improvement within 2 months after cessation, the diagnosis of probable MOH should be applied. If improvement does not then occur within the 2-month period, this diagnosis must be discarded.

The most common cause of migraine-like headaches or mixed-migraine-like and TTH-like headaches that occur on 15 or more days per month is overuse of acute headache drugs. Overuse is now defined in terms of treatment days per month. What is crucial is that treatment occurs both frequently and regularly (ie, several days each week). For example, the diagnostic criterion of use on 10 days or more per month translates into 2 to 3 treatment days every week. Bunching treatment days and going for long periods without medication intake, as practiced by some patients, is much less likely to cause medication-overuse headache.

The amount of use that constitutes overuse depends on the drug. Ergotamine-overuse headache requires intake on 10 or more days per month on a regular basis for 3 or more months. (Bioavailability of ergots is so variable that a minimum dose cannot be defined.) The headache is often daily and constant. Triptan-overuse headache is usually frequent, intermittent, and migrainous. Triptan intake (any formulation) on 10 or more days per month may increase migraine frequency to that of chronic migraine. Evidence suggests that this occurs sooner with triptan-overuse than with ergotamine-overuse.29,30

Analgesic-overuse headache requires the intake of simple analgesics on 15 or days per month for more than 3 months.29,31-34 This criterion is based on expert opinion rather than formal evidence. Opioid-overuse headache requires opioid use on 10 or more days per month. Prospective studies indicate that patients who overuse opioids have the highest relapse rate after withdrawal treatment.

Combination-medication–overuse headache requires the intake of combination medications1 on 10 or more days per month for more than 3 months.31 Combination medications typically implicated are those that contain simple analgesics combined with one or more of the following: opioids, butalbital, or caffeine.
Epidemiology
In population-based surveys using the Silberstein and Lipton criteria, primary CDH occurred in 4.1% of Americans, 4.35% of Greeks, 3.9% of elderly Chinese, and 4.7% of Spaniards. Scher et al ascertained the prevalence of primary CDH in 13,343 individuals aged 18 to 65 years in Baltimore County, Maryland. The overall prevalence of primary CDH was 4.1% (5.0% women, 2.8% men; 1.8:1 ratio of women to men). In both men and women, prevalence was highest in the lowest educational category. More than half (52% women, 56% men) met criteria for CTTH (2.2%), almost one third (33% women, 25% men) met criteria for transformed migraine (1.3%), and the remainder (15% women, 19% men) were unclassified (0.6%). Overall, 30% of women and 25% of men who were frequent headache sufferers met IHS criteria for migraine (with or without aura). On the basis of chance, migraine and CTTH would co-occur in 0.22% of the population; the fact that transformed migraine occurred in 1.3% of this population would suggest that the co-occurrence of migraine and CTTH is more than random.

Prognosis
The “natural history” of primary CDH, and MOH in particular, has never been studied and probably never will be for ethical and technical reasons. Recognition of medication overuse is probably therapeutic in and of itself and could affect the patient’s behavior or the physician’s approach. Retrospective analysis suggests that there may be periods of stable drug consumption and periods of accelerated medication use. Patients treated aggressively generally improve.

The medical literature contains reports of spontaneous improvement of CDH headache in population-based studies. Silberstein and Silberstein conducted follow-up evaluations on 50 hospitalized patients with primary CDH and medication overuse who were treated with repetitive intravenous administration of dihydroergotamine mesylate and became headache-free.

Once detoxified, treated, and discharged, most patients did not resume daily analgesic or ergotamine use. Seventy-two percent continued to show significant improvement at 3 months, and 87% continued to show significant improvement after 2 years. This rate would suggest at least a 70% improvement at 2 years in the initial group (35 of 50), allowing for patients lost to follow-up.

Comment
Chronic daily headache is common. Most patients have transformed migraine often associated with medication overuse. Therefore, physicians should be alert to the possibility of medication overuse by their patients and the role it plays as an underlying cause of headache disorders.

Table 6
New International Headache Society Criteria for Medication Overuse

| Diagnostic criteria: |
| A. Headache present on >15 days/month fulfilling criteria C and D Characteristics depend on drug |
| B. Regular overuse for >3 months of a medication |
| Amount depends on drug |
| Ergotamine, triptans, opioids, and combination analgesics ≥10 days/month |
| Simple analgesics ≥15 days/month |
| C. Headache has developed or markedly worsened during medication overuse |
| D. Headache resolves or reverts to its previous pattern within 2 months after discontinuation of overused medication |

References


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Answer sheet to Supplement 2 JAOA April 2005 CME quiz

1. a b c d e
2. a b c d e f g
3. a b c d e
4. a b c d
5. a b c d e f g
6. a b c d e f g
7. a b
8. a b
9. a b
10. a b
d
11. a b c d
d
12. a b c d
d
13. a b c d
d

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