Fever of Unknown Origin: 
The Naming of Uncertainty

So many medical stories begin when the patient arrives at the doctor’s office or the hospital. The doctor enters the room, and the patient begins the narrative that will determine a diagnosis and treatment. But as hospitalists, we see patients with their stories already unfolding. Someone already made a diagnosis, or at least obtained preliminary information to get us to that point. That affords hospitalists a degree of certainty that can be reassuring to some, frustrating to others. But what happens when the patient arrives and no one knows the answers? What do we do in the face of uncertainty?

The Nameless Patient

Our nameless patient arrived carrying a folder full of diagnostic statements, pathology reports, and a couple of compact discs with radiologic images. She was 14 years old, thin, and had dark circles under her eyes. “She has not been sleeping well,” her mother said, “the fevers keep her up at all times of the night.” The mother also looked exhausted, sharing her daughter’s dark circles of sleeplessness.

Our patient had fevers for almost 3 weeks, sometimes with temperatures as high as 106°F, intermittently feeling sick and acting normally, with symptoms appearing and disappearing almost as quickly: leg aches, a rash, lethargy, and swollen lymph nodes.

She stayed in the hospital for about 10 days. During the hospitalization, her blood counts, electrolytes, endocrine studies, plain x-rays, computed tomography scans, and magnetic resonance imaging scans were all normal. A bone marrow aspiration revealed no malignancy. A lymph node biopsy showed normal lymphatic tissue. When one of the specialists recommended a full body positive emitron tomography scan, the mom requested we discharge them so she could obtain a second opinion.

By then, our patient had completed several treatments, including antibiotics, for potential diagnosis. Clinicians use such abductive thinking, in which a “backward flow” of directly related hypotheses helps identify the origin of a problem, when the diagnostic process is not clear. While saying “we’ll use this, which usually works for X condition, and, if it works, then the patient probably has X” may help narrow down the differential list, it is not as reassuring to the patient or the family. To them, it feels like we are experimenting, that in lieu of a definitive diagnosis, we are fumbling in the dark for a possible explanation.

Inevitably, the unknowing begets dissatisfaction. They left the same way they came, with their folder of medical information a little heavier this time. We kept...
pointing out to the mother that the
girl’s fever curve was coming down,
that something we did might be help-
ing. But that was not an answer, only
an observation couched with more un-
certainty. The origin of the fever was
still unknown. “They were not mad at
us,” the nurses said, “they were just
tired and frustrated.”

**Fever of Unknown Origin**
A diagnosis is a baptism, a naming of
the signs and symptoms into a single
entity that leads to appropriate treat-
ment. Fever of unknown origin (FUO)
is an un-naming, a fancy placeholder in
our ever-present search for evidence-
based precepts to guide our daily
medical lives. To diagnose an FUO is
to name the unknown, and by default,
acknowledging the existence of the
unknown. There are many recom-

The diagnosis was originally called
“fever of unexplained origin” by the
authors of the seminal modern article
on the subject² Robert Pedersdorf and
Paul Beeson, who pointed out that
“(F.U.O.)…is likely to be a source of
perplexity and frustration to the physi-
cians, and for the patient the discom-
forts of illness are compounded by the
anxiety of uncertainty.” By calling
its origin “unexplained,” Pedersdorf
and Beeson acknowledged that the
cause of the fever was still out there
ready to be discovered with a bit of
effort. By calling it “unknown,” the
possibility exists of never finding out
the source.

One of the criteria established by
Petersdorf and Beeson for the diag-
nosis of FUO included “diagnosis
uncertain after 1 week of study in
hospital.” In other words, when the
patient arrives, she has no diagnosis;
when she leaves, she has one, albeit
one that does not confer the prognos-
tic near certainties of others, what has
been called “the palpable outcomes”³
of our field. While the patient leaves
searching for more explanations,
“wander[ing] from hospital to hos-
pital, repeatedly enduring the same
questions, the same examinations, the
same laboratory tests,”³ we are left
with uncertain feelings ourselves. Did
we fail? Could we have done better?
So many stories end when the doctor
smiles in triumph over illness, or with
tears at a perceived failure because
of human limitations. When a patient
with an FUO leaves, what do we feel?

**Uncertainty**
Uncertainty causes anxiety. Patients
come to us with the expectation that
our education and experience provide
us with a glimpse of things to come.
Our training puts us through a rigor-
ous boot camp of intellectual rigor
during which we deal with the com-
mon and the obscure, with simple ill-
nesses and their complications, with
rare diseases and their common mani-
festations. We come out at the other
end thinking we have mastered worlds
of scientific knowledge in the span
of a few years. But one of the cer-
tainties of medicine is that it always
changes, and that the truths that you
hold so dearly at one point become the
outmoded, outdated, and arcane way
doing things in the future. Nothing
in medicine is 100%, I tell my patients
when they ask me about certainties,
just as nothing in life is.

So what our patients want is not cer-
tainty, because they know it does not
exist in medicine. After all, they watch
the medical dramas on television, and
search the Internet for information
about mysterious illnesses. Patients
know we are human, and they know
that being human means having limits

to our knowledge.

Then what do they want? They want
certainty to the best of our knowledge,
as close to certainty as we can give.⁴
They want someone who sits down
and acknowledges that there are
gaps in our knowledge, that there are
no absolutes in medicine, that things
change from one day to the next
and that the diseases we learn about
from books and case studies some-
times do not behave the same way in
real life.

They want to know when we do not
have all the answers; and they want
to know that we will try to look for
them.

**The End is the Naming**
At the end of their study, Petersdorf
and Beeson make a series of “tena-
vative conclusions,” as if to conclude
anything about such a nebulous diag-
nosis was in itself folly. They point out
that most cases of FUO are uncom-
mon manifestations of common con-
ditions and not unusual diseases; that
delays in diagnosis can happen with
the inappropriate use of already avail-
able information; and that attempts to
obtain tissue samples for pathologic
studies were sometimes unnecessarily
delayed, particularly in the presence of enlarged organs and masses. They also advocate the use of therapeutic trials, but only after “rational methods of diagnosis have been tried.” In other words, they find that the potential for establishing the known about a patient with FUO is pretty high, if only we apply ourselves in our search.

The diagnosis comes at the end, but it is not the end. Rather, the naming of a diagnosis, just like a baptism, is the beginning of something else. The naming of FUO, with its inevitable unknowingness, leads to further searches, until the fever, either by treatment or by tincture of time, eventually goes away. Or the actual malady manifests itself, and the diagnosis changes, from something of near uncertainty, to something for which we can offer as much certainty as we can.

If that happens, we sigh in relief that we may have an answer. Maybe. The uncertainty continues until “only time will tell.” Sometimes the newly uncovered answer, the no-longer-unknown origin of the fever, causes more anxiety for the patient than the terrible uncertainty of an FUO. Sometimes, uncertainty is a blessed relief.

References
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