The Tired Patient

Don A. Rockwell, M.D. and Bill D. Burr, M.D.

Davis, California

One of the most challenging diagnostic problems that comes into the physician's office is the patient who complains of "being tired." It can prove to be a frustrating experience for the physician (especially if the physician is also tired) and to the patient.

This article will propose and describe a two-pronged systematic approach to the patient that can increase the probability of a satisfying outcome for both physician and patient. Our approach assumes the "complaint" of every patient has both *informational value* ("I think there's something wrong.") and *transactional meaning* ("Please take care of me."). Tiredness, fatigue, "exhaustion" need to be seen simultaneously as information and need. Both aspects require simultaneous workup.

Differential Diagnosis of Fatigue

The vagueness of the nonspecific complaint of tiredness covers a host of possibilities from brain tumor through incipient diabetes to being up all night with a sick child. However, most tired patients fall into one of three major subgroups of fatigue.

I. *Physiologic Fatigue*

Patients and physicians are prone to ignore the fact that fatigue is reasonable to expect in the following circumstances:

1. Prolonged physical exertion without adequate rest.
2. Inadequate amount or restless sleep.
   Drugs may interfere with REM sleep, such as many of the hypnotics and some tranquilizers. Drugs which have little effect on REM sleep are flurazepam (Dalmane) and doxepin (Sinequan).
3. Acute severe dieting or chronic moderate dieting.
   Ketosis, negative nitrogen balance.
4. Sedentary life style.
   Poor cardiopulmonary reserve.
5. Pregnancy.
   Prenatal and postpartum.
6. Prolonged mental stress.
7. Advancing age.
   Decreased physiologic reserve.

II. *Acute Fatigue*

Lassitude or tiredness of recent or sudden onset should direct the physician's attention towards:

1. Prodrome or sequelae of acute infection.
   Among the worst offenders are the meningitides, cerebral abscess, mononucleosis and most viral infection.
2. Metabolic disturbance.
   Any fluid or electrolyte imbalance, especially with extracellular fluid deficiency, whether naturally occurring or iatrogenic, is associated with fatigue. Hyponatremia and hypo and hypermagnesiumemia are most notable although hypokalemia is most common.
3. Circulatory failure and/or digitalis toxicity.
4. Hemolytic anemia and acute leukemia.

III. *Chronic Fatigue*

Longer, more insidious causes are found here and the differential diagnosis includes:

1. Chronic infection.
   These possibilities include subacute bacterial endocarditis, tuberculosis, brucellosis, parasitic infestations, and chronic pyelonephritis or osteomyelitis.
2. Anemias.
   Megaloblastic and iron deficiency anemias are most common but consider also polycythemia and hemoglobinopathies.
3. Nutritional dysfunction.
   Any deficiency in diet, such as calories, protein, or vitamins, may induce fatigue. A careful nutritional history is important since a "normal" diet may mean that the patient is a vegetarian or macrobiotic "freak." Pellagra and cerebral beri-beri have not disappeared. Exogenous obesity is exhausting in itself.
4. Chronic exogenous intoxication.
   Careful attention should be directed to common chronic intoxicants such as alcohol, barbiturates, and minor tranquilizers as well as less common ones, such as heavy metal, gasoline, carbon monoxide and insecticide/pesticide poisoning.
5. Chronic endogenous intoxication.
   Most commonly uremia and hepatic insufficiency.

From the Departments of Psychiatry and Family Practice, School of Medicine, University of California, Davis, California. Requests for reprints should be addressed to Dr. Don Rockwell, Department of Psychiatry, School of Medicine, University of California, Davis, California, 95616.

TABLE I

Discriminators of Depression by Socioeconomic Class*

Low	Middle	High
Affective		
Hopelessness	Loneliness	Decreased Social Life
Self-accusation	Helplessness	Pessimism
Crying	Guilt	Dissatisfaction
Dissatisfaction	Crying	Anxiety-Tension
Guilt	Anxiety-Tension	
Depressed Mood	Depressed Mood	
Somatic		
Palpitation	Decreased sex drive	Fatigue
Headache	Urinary complaints	Insomnia
Anorexia	Trouble falling asleep	
Waking early	Headache	
	Anorexia	
	Waking early	

Adapted from Schwab[7]

6. Endocrine disorders.
   The following are associated with fatigue: diabetes mellitus, hyper and hypopituitarism, hyper and hypoadrenal function, hyper and hypothyroid function and hyperparathyroidism.
7. Malignancies.
   Fatigue may be an early sign and is a common accompaniment of middle and end stage malignancy.
8. Iatrogenic fatigue.
   The following drugs are frequently associated with fatigue as a significant side effect:
   - All sedatives and hypnotics
   - All tranquilizers
   - All antihistamines
   - Most anti-convulsants
   - Most analgesics and salicylates
   - Nicotine
   - Tetracyclines
   - Colchicine
   - Cycloserine
   - Adrenocorticosteroids
   - Progesterones (i.e., many birth control pills)
   - Ergot alkaloids
   - Insulin
   - Mild digitalis toxicity
   - Mild Vitamin A toxicity
   - Mild Vitamin D toxicity
9. Neuropsychiatric dysfunction.
   Including intracranial neoplasia, subdural and extradural hematomas, amyotrophic lateral sclerosis, narcolepsy, myasthenia gravis, Sydenhams chorea, depression and hysterical characters.

Making the Diagnosis

Crucial to the differential diagnosis of fatigue is a careful history. We suggest detailed information on the following items:

1. Onset of symptom; relationship to known factors such as starting medication, increased activity, decreased sleep, important life changes such as job and new family member; duration; periodicity; intensity; and associated symptoms.
2. Careful family history of diabetes, anemia, endocrine disturbances, depression, alcoholism.
3. Full review of systems — perhaps using a self report or automated history taking.
4. Oral intake history — *anything* the patient puts into his mouth both in terms of nutrition and in terms of drugs. Careful inquiry concerning daily use of some over-the-counter or prescribed medication, as well as alcohol intake, may be especially rewarding.

Having elicited the above history, we consider which subgroup of fatigue the patient falls into — physiologic, acute or chronic fatigue. Taking cognizance of the differential diagnosis suggested by the particular subgroup of fatigue, we next move to a complete physical exam and related appropriate laboratory and x-ray examinations. Special exams are done when indicated by history or by age of the patient. In the physical examination, special attention is focused on evidence of muscle wasting, organomegaly, lymphoadenopathy and skin changes. Laboratory examination routinely includes a CBC with differential, urinalysis and a chemistry panel with blood sugar and liver function studies. Other studies are done as indicated by clinical status and age.

In spite of its lack of scientific status we rely heavily on the clinician's intuitive sense that "something's up" and will pursue this. Trust in intuitive skills is important in the work-up of the "tired patient" since chronic fatigue may precede positive physical and laboratory findings. In our experience a careful history and physical examination will uncover 80-85 percent of causes, the screening laboratory studies an additional 5 percent and the remainder will require more time and repeated evaluation.

We often use a threshold model to explain chronic fatigue to ourselves and to our patients since in many cases the causes are multiple and additive. For example, chronic fatigue may be precipitated by a minimal anemia in a patient already at threshold as a result of chronic minimal sleep loss (baby in the house) and minimal increase in usual physical activity (toddler in the house). For many patients such a reality orientation is both reassuring (i.e., there's nothing seriously wrong) and educational (i.e., maybe I can alter one aspect of the pattern and feel better).

Through this approach we are often able to avoid a fruitless search for esoteric explanations. At the same time, we are particularly wary of snap "psychiatric" or "organic" ex-

TABLE II

Classification and Treatment of Depression

Retarded Depression	Anxious Depression	Hostile Depression	Hypochondriacal
Deeply depressed	Much "unworthiness" and guilt	Paranoid and projective	Little guilt
Psychomotor retardation evident	Agitated	Hostile belligerency	Moderate depression
Lacks environmental reactivity	Reactive to environment		Agitated
Loss of interest in life		Hopelessness	Feel "abandoned and unloved"
Visceral symptoms	Reports anxiety	Angry	Multiple somatic complaints
No self pity	Self pity		
No sense of humor	May have sense of humor — teasing in character	Sense of humor is often sadomasochistic in character	
No precipitating stress (it came over like a black cloud)	Precipitating stress		
Tend to be older	Prior history of neurotic or behavioral problems common	Prior history of neurotic or behavior problems common	Lifelong history of disturbances
Weight loss common			
Early morning or middle of the night awakening	Trouble falling to sleep		
Suicidal	Tend to cling to M.D.	Provocative	Demanding
Best psychopharmacologic agents —Imipramine (Tofranil) —AM 1 Triptyline (Evavil) plus supportive psychotherapy — if no response after adequate dosage over three weeks consider electroconvulsive treatment	Best psychopharmacologic agents—Phenothiazines like Perphenazine (Trilafon) plus psychotherapy may use Doxepin (Sinequan) as alternative agent	No best psychopharmacologic agent—often need a combination of Tricyclic and Phenothiazine	Psychopharmacologic agents likely to associate with many "troublesome side effects."

planations of fatigue. Invariably the "organically" caused fatigue has an emotional reaction associated with it that requires attention. The patient who becomes depressed as a result of being on reserpine is no less a suicide risk! Thus while running down the "organic" causes (i.e., the informational aspect of the complaint) we also attend to the transactional or need side of the complaint. A psychiatric "explanation" of fatigue is never a diagnosis of exclusion. If we find no positive evidence of psychiatric disease using conservative diagnosis then we conclude that the etiology is still unknown and necessarily continue to explore with the patient sources of fatigue. Just as a diagnosis of anemia requires significant change in red cell indices, so a diagnosis of depression or hysterical character requires significant positive evidence. The skilled clinician never diagnoses purely by exclusion.

Common Patterns of Tired Patients

In everyday practice, there are several major patterns for the tired patient which merit further discussion.

1. *Depression*

The first major group of tired patients are the depressive patients and patients with depressive equivalents. A developmental appreciation of depression is important for us since depression is manifested in quite different ways according to age, sex and socio-economic status. Infants and children rarely manifest depression by the typical "lowered mood." Infants and children may be manifesting depression when they are hyperactive, running away, withdrawing, having school, eating or sleeping problems and when having vague physical complaints. Adolescents likewise may frequently "act out" depressive conflicts with the result that depression manifests in boys as antisocial behavior or poor school performance, in girls in sexual misconduct or running away, and in both by "doing drugs," drinking and through psychosomatic problems. Young adults more frequently somatize or act out depression then evidence a classic picture. By middle age we see more typical "textbook" depressive pictures, but also be aware that depression continues to manifest often via acting out behaviors — particularly sexual and drug — and in somatic problems. At all stages "accidents" may be depressive unconscious self-destructive equivalents. A close look at the antecedents of "accidents" is worthwhile.

Somatization is a theme that also pervades the life cycle of depressive equivalents. Gastrointestinal symptoms lead the way as an arena for the expression of depression. The irritable colon syndrome is the most common equivalent, but remember that other functional or organic syndromes, such as peptic ulcer and ulcerative colitis, can be "symptoms" of depression and are commonly accompanied by depression. While any organ system may be involved, skin disorders and pain syndromes (headache, backache, residual pain) lead the list after the GI tract.

Tiredness is a very common symptom of depression. It is important to recognize that the signs and symptoms of depression vary not only by age but also by sex and socio-economic status. Males more commonly manifest depres-

sion by lowered mood, pessimism, guilt and a sense of helplessness. Comparable early signs in women are insomnia, headache and social withdrawal. Table I points out the variation in the presentation of depression according to the patient's background.

Once depression has been recognized, we must then attempt to decide whether it is normal (as in grief), typical, or atypical. We classify depression following Grinker and Hollister.[1] A brief summary of their work is shown in Table II.

On the treatment side of the equation we rely heavily on both the relationship with the patient (frequent brief visits) and an aggressive psychopharmacological approach. Once having selected an appropriate psychoactive agent, one should persist with that agent for from three to six weeks and push the total daily dosage to near "toxic" levels. If the patient is not having side effects their "treatment" is not likely to be effective. We often attempt to involve the family in the treatment program, having found as Cammer did that the family can greatly facilitate progress.[2] Once we have even merely entertained the possibility of the patient having a depression, whether as a primary source of tiredness or secondary to other "organic" illness, we believe a direct inquiry into the patient's potential for suicide is mandatory. Continued attention to this risk is necessary throughout the treatment course of the depressed patient.

2. *Hysteria*

A second group of tired patients are the so-called hysterics. Woodruff and Guze[3] have developed a diagnostic pattern characteristic of the hysteric. This includes:

a. A complicated or dramatic medical history.
b. A minimum of 25 symptoms in 9 of 10 systems in the review of symptoms ("a positive review of systems").
c. A minimum of 25 symptoms without a medical explanation of etiology.

If a patient meets Guze's criteria, there is a 90 percent chance that the clinical condition will remain stable and that other *serious* medical and psychiatric illnesses will *not* develop. This can be explained to the patient and also has an effect on our management of these patients.

These patients represent a very small proportion of medical practice. It is crucial that the diagnosis be limited to those patients meeting Guze's criteria since we otherwise get into a sophisticated kind of name calling. No one denies the existence of these patients but the etiology has often been hotly debated. It seems important to us that we not deny the presence of this life style but rather maximize the possibility of a positive outcome. For us this includes:

a. Not putting the patient through the pain and expense of a nonproductive workup.
b. Recognizing the transactional nature of the complaint.
c. Recommending appropriate "treatment" which for a female patient can include suggesting that she reexamine her current role in view of changing women's roles.
d. Allowing the physician to recognize the common counter-transference problem of frustration, anger, undue interest and therapeutic impotence in dealing with these patients.

3. *Situational Exhaustion*

A third important group of tired patients is "situational exhaustion." We see this as a form of physiologic tiredness but common enough to merit special comment. These are situations where being tired is an appropriate response and symptomatic purely of lack of rest, relaxation and sleep. This common sense diagnosis needs only two caveats. Be aware that in spite of all labor-saving devices many people continue to have too much to do. And also be aware that many "workaholics" are appropriately tired as a result of their being driven internally.

The "workaholic" needs to be advised of the diagnosis and sometimes given prognosis of his condition. "Hard work" or "overwork" often is a symptom of underlying personal or family problems. The person must be educated to appreciate that chronic overwork:

a. is a symptom
b. may well be detrimental to long range physical and emotional health and happiness
c. is treatable using "reality"[4] and family therapy techniques.

The physician's role in treatment may be to involve the patient's family, and together with the patient and family realign health priorities and responsibility.

4. *Stress and Exhaustion*

A fourth group of tired patients relates to stress and exhaustion. Be attentive to chronic stress or a recent increase in stress on a patient. We are well aware that life changes are additive and can lead to increased illness and accidents.[5] There is evidence to indicate that chronic overwork plus a sudden recent work increase is a cardiac "drain" and often antecedes an acute myocardial infarct.[6] An "enforced" vacation may be in order for these patients and certainly a "prescribed" change of pace is in order. The examples of this are innumerable but keep in mind several practice-related situations:

a. Families with chronically ill or dying members (especially if the patient is a child).
b. Families in considerable emotional conflict often manifested by sexual problems.
c. Upwardly mobile young men and women.

Concluding Remarks

The tired patient presents the physician with an informational problem ("Tell me what is wrong with me.") and a transactional problem ("I'm scared about . . . and need you to take care of me."). Careful attention to both issues is crucial. Elucidation of the specific cause or causes of fatigue is sometimes difficult, but effective management requires an active diagnosis rather than a passive diagnosis by exclusion. If the causation is unclear we continue the search until a positive explanation is evident. At the same time, attention to the "need" side of the equation is effective treatment for some patients in and of itself. Utilization of the basic skills of the physician and his or her team will result in effective successful intervention in most cases.

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