A New Way of Thinking About Fatigue: A Reconceptualization

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This article has been chosen as particularly suitable for reading and discussion in a Journal Club format. The following questions are posed to stimulate thoughtful critique and exchange of opinions, possibly leading to changes on your unit. Formulate your answers as you read the article. Photocopying of this article for group discussion purposes is permitted.

1. Is this article research based? Can we assess the level of evidence being presented?
2. To what extent do our patients complain of fatigue? Where on the continuum detailed in this article do many of them fall?
3. What therapies do we administer that are associated with the side effect of fatigue?
4. How do we assess fatigue? How can we improve?
5. What sorts of patient teaching do we provide about fatigue? Should we consider adjusting our teaching based on this article?

At the end of the session, take time to recap the discussion and make plans to follow through with suggested strategies.

Purpose/Objectives: To present a reconceptualization of fatigue.

Data Sources: Studies indexed in CINAHL®, MEDLINE®, PubMed, PsycINFO, SPORTDiscus, and CancerLit from 1995–2004; studies included in the bibliographies of indexed articles; and five qualitative studies conducted by the author.

Data Synthesis: Tiredness and exhaustion are conceptually distinct from fatigue. All three concepts are located along an adaptational continuum in a manner consistent with stress theory.

Conclusions: Interventions should focus on the elimination or reduction of stressors and the increase of patients' resistance to stressors.

Implications for Nursing: Interventions that prevent or delay progression from tiredness to fatigue will be different from those that prevent or delay progression from fatigue to exhaustion.

Key Points . . .

- ➤ Tiredness, fatigue, and exhaustion are hypothesized to be behavioral markers for degrees of adaptation to stressors.
- ➤ Interventions should focus on reducing stressors and increasing patients' abilities to resist stressors.
- ➤ The nursing interventions for the prevention or at least the delay of fatigue are likely to be different from those for the prevention or at least the delay of exhaustion.
- ➤ Recovery from exhaustion to fatigue and from fatigue to tiredness is possible but very difficult in the context of advanced cancer. Nevertheless, interventions that may achieve these objectives should be included in cancer rehabilitation programs.

Nursing colleagues initially identified the lack of fit between clinical observations and existing conceptualizations of fatigue in an outpatient oncology setting. In response to queries about how they were feeling, patients told nurses that they were "so tired." Some withdrew from potentially curative treatment, saying that they were "too tired." The author conducted a review of the conceptualizations of cancer-related fatigue, summarized in this article, in an attempt to identify factors that might distinguish individuals who withdrew from treatment because of fatigue from those who did not report fatigue and were able to continue treatment as planned.

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Historical Overview

The earliest reference to fatigue is attributed to Galvani in 1786, who described the existence of electrical potentials in nerves and muscles (Rasch & Burke, 1967). Nearly 100 years later, Beard (1869) hypothesized that fatigue in neurasthenia was caused by chemical changes in the central nervous system that stemmed from the body's inability to excrete byproducts of overused muscles. He noted that, at its worst, fatigue included the inability to feel some or all of its own effects, because the act of feeling requires energy. Cowles (1893) distinguished between normal fatigue resulting from daily activities and pathologic fatigue. He stated that pathologic fatigue resulted from impoverishment of nervous tissue and the body's inability to repair itself. Cowles recommended a period of rest followed by mild exercise for those experiencing pathologic fatigue because exercise was hypothesized to promote appetite and excretion of waste products.

During the 1900s, the fatigue literature expanded to include work-related fatigue. The publication of Bartley and Chute's (1947) monograph provided the first detailed analysis of fatigue as a concept. The analysis, based on published work in psychology, physiology, and exercise, described fatigue as a subjective feeling comprised of lassitude and reduced activity because of an accumulated oxygen debt in muscle tissues. Bartley and Chute believed that fatigue was an "early warning" signal that personal resources were overtaxed. That line of reasoning, pursued later by Grandjean (1968), formed the foundation for the "fatigue as a marker for alertness or functional status" approach to the study of cancer-related fatigue.

Fatigue as a Marker for Alertness or Functional Status

Grandjean (1968) stated that fatigue was part of a feedback system composed of the mechanisms responsible for activation and inhibition, which include the thalamus; the reticular activating system; neural pathways linking regions in the cerebral cortex responsible for consciousness, perception, and thinking; and humoral factors. If a person's inhibitory mechanisms predominate, he or she experiences fatigue. Using this model, Grandjean conceptualized fatigue as a continuum, ranging from sleepy and tired to fresh and alert.

Grandjean's (1968) work underpinned conceptualizations developed by five cancer nursing researchers and research groups. Ryden (1977) argued that, because the body must transform energy into a useable form, any interference with the transformation might affect the availability of energy. Other studies (Piper, 1986; Piper et al., 1989; Piper, Lindsey, & Dodd, 1987) hypothesized that four contributors to the development of fatigue existed: accumulation of metabolites, depletion of energy-yielding substances, changes in the transmission or regulation of energy, and humoral factors. According to Winningham's psychobiologic-entropy hypothesis (Nail & Winningham, 1993; Winningham & Barton-Burke, 2000; Winningham et al., 1994), fatigue results from an energy deficit caused by disease, treatment, decreased activity or rest, symptom perception, and functional status. Irvine, Vincent, Graydon, Bubela, and Thompson (1994) attempted to show a relationship between a number of physiologic factors and the onset of fatigue but identified no significant predictors. Aaronson et al. (1999) hypothesized that energy could be made available through the combined effect of internal physiologic and psychological resources.

Fatigue as a Stress Response

Bartlett (1953) led the development of an alternative conceptualization of fatigue, reporting that fatigue can develop over short periods of time, provided that the energy demand is sufficiently excessive. He also disagreed with the idea of fatigue as an "early warning" signal and argued instead that because the sensations associated with fatigue were the result of excessive expenditure of energy, they arrived too late to be of any practical value. This assessment is consistent with the stress response as developed by Selye (1952, 1956, 1971).

Selye (1952) described stress as the nonspecific response to any demand, whether pleasant or unpleasant. If present over time, he argued, stressors trigger the general adaptation syndrome (GAS), a physiologic response that comprises an alarm reaction, resistance, and exhaustion. He noted that the resistance stage of the GAS had profound energy requirements and that over time, capacity for resistance became depleted, triggering the third stage of the GAS, exhaustion. Exhaustion, if unchecked, led to death.

The "fatigue as a stress response" approach has given rise to conceptualizations of fatigue by four authors. Cameron (1973) labeled factors that lead to fatigue as stressors and noted that if a person was subjected to stressors over time, the GAS would be triggered. Rhoten (1982) conceptualized fatigue as part of a stress response triggered in the context of surgery and outlined stressors related to an individual's preoperative state, surgery and anesthesia, pain, and pain medication. Aistars (1987) stated that fatigue in the context of cancer is a function of the source of stress, perception of stress, coping mechanisms, and duration of stress and that prolonged or intense exposure to stressors could lead to energy depletion. Glaus (1993, 1998) viewed fatigue as a stress response that is modified by the population in which it is experienced because of linguistic and cultural factors.

Two important differences should be noted between the "fatigue as marker of alertness or functional status" and "fatigue as a stress response" approaches. First, Selye (1956, 1971) proposed the stress response as a purely biologic model that can proceed without being perceived. Thus, an individual might experience physiologic stressors of sufficient magnitude to trigger the GAS but not be aware of this fact. In the "fatigue as a marker of alertness or functional status" approach, on the other hand, perception of fatigue is a hallmark of all of the conceptualizations. Second, although Piper (1986) noted that objective and subjective correlates of fatigue exist, researchers working in the "fatigue as a marker of alertness or functional status" model have not demonstrated links between the correlates. In the "fatigue as a stress response" model, however, Mason (1971) showed that psychosocial interventions can modulate the biologic stress response. Lazarus (1977) and Mason viewed the cognitive appraisal of a threat and the coping strategies that follow to be primary mediators of the stress response, a perspective that others (Cassel, 1975; Cobb, 1974; Kiritz & Moos, 1974; Maddison & Walker, 1967) have supported.

Although studies testing the "fatigue as a stress response" model were not identified, it has several features that make

it more useful than the "fatigue as a marker of alertness or functional status" model. First, it provides an explanation (i.e., appraisal of threat and coping ability) for the reasons that some individuals experience a stress response under certain conditions but others do not. Second, adaptation, a key construct in stress theory, provides a theoretical mechanism for movement between tiredness (establishment of an alarm response), fatigue (maintenance of resistance), and exhaustion (depletion of capacity to resist).

The Problem of "Close Enough"

The problem in all of the conceptualizations mentioned is that the researchers assumed, mistakenly, that the definition of the scientific concept of cancer-related fatigue was "close enough" to the unspoken and implied definition of the lay concept of tiredness that they could treat fatigue as a synonym for tiredness experienced by patients. Piper (1986) and Rhoten (1982) understood that tiredness and exhaustion differ from fatigue, but their models demonstrate that the difference was understood to be one of intensity rather than substance. A lack of attention to the differences between the lay concept of tiredness and the scientific concept of fatigue has resulted in a conceptual gap, which might explain why the nurses discussed at the beginning of the article were unable to obtain a satisfactory explanation for their clinical observations.

By assuming that fatigue was "close enough" to tiredness, researchers missed opportunities to answer key clinical questions. Tiredness is a word that exists in everyday conversations in English. When people tell each other they are tired, they have a general sense that they understand what this means. The everyday meaning is broad and blurry, however, and does not require the specificity of a scientific concept, because no one intends to build frameworks or develop interventions based on it. In the clinical setting, however, "too tired" takes on an additional scientific meaning. To intervene, clinicians must know whether patients are experiencing a more severe or distressing form of the tiredness found in everyday life, whether "too tired" is the same as "more tired," and whether patients who are "too tired" are experiencing a more extreme form of tiredness or something subtly but significantly different. When questioned, patients said that "so tired" and "too tired" were very different from anything they had experienced before, despite leading busy lives. Patients used "so tired" and "too tired" differently than "tired." The difference in use indicated that "tired," "so tired," and "too tired" might be different concepts that had inadvertently been brought together within the scientific concept of fatigue and that a reconceptualization of fatigue was warranted (Morse, Hupcey, Mitcham, & Lenz, 1996).

Revisiting the Concept of Fatigue

Method

Design: The author's team undertook a review of fatigue as a concept using the pragmatic utility approach to concept analysis (Morse, 2000, 2004). Conceptual definitions are drawn initially from a critical appraisal of the way in which the concept is used in published literature across contexts. Model cases or exemplars are not constructed. Rather, the researcher undertakes qualitative studies to further refine the features of the concept.

Data collection: Key words (malaise, discomfort, weariness, lassitude, boredom, depression, irritation, exhaustion, weakness, impatience, anxiety, and fatigue) were identified from classic studies of cancer-related fatigue and used in various combinations to search CINAHL®, MEDLINE®, PubMed, PsycINFO, SPORTDiscus, and CancerLit for research published from 1995–2004. Published peer-reviewed studies across the populations of interest (cancer, depression, chronic fatigue syndrome, shift workers, and athletes) that provided information about the antecedents, definitions, attributes, boundaries, and outcomes of fatigue were identified, critically appraised, and entered into a ProCite® (Thomson ResearchSoft, Carlsbad, CA) database. Additional relevant studies, particularly those published before 1995, were identified from the bibliographies of the selected articles. This process, published elsewhere (Olson & Morse, 2005), yielded definitions of fatigue and two new concepts: tiredness and exhaustion. Table 1 shows the six key domains of tiredness, fatigue, and exhaustion.

Next, qualitative studies were conducted in each of the populations from which the research literature was drawn. Following receipt of ethical clearance, patients with cancer were recruited from a cancer center in western Canada, whereas participants diagnosed with depression were recruited through advertisements in newspapers and magazines. Individuals with chronic fatigue syndrome were recruited through a support group, and shift workers were recruited from an industrial setting with help from a union and management. Recreational distance runners were recruited through a fitness training program based at a university in western Canada (see Table 2 for a summary of the samples).

Participants from each population were interviewed one to three times. Interviews were recorded and transcribed to facilitate analysis. Initial interviews were unstructured, and data were analyzed as they were collected. Thus, interview questions in each study became more structured as the study progressed. In the studies of fatigue in cancer, shift work, and chronic fatigue syndrome, the researcher focused explicitly on the antecedents, characteristics, and consequences of fatigue using ethnoscience (a research method used to order the knowledge participants have about their culture based on the language they use to talk about it [Evaneshko & Kay, 1982; Leininger, 1985]). In the studies of fatigue in depression and recreational distance runners, ethnoscience and grounded theory were used to explore the strategies used to manage fatigue as well.

Findings

Based on the fit between the findings of the qualitative studies and the conceptual definitions developed from the literature, participants were labeled as tired, fatigued, or exhausted. Articles outlining the detailed findings of each qualitative study currently are being finalized. The information presented in the current article is intended to provide some examples to illustrate the conceptual definitions drawn from the literature and the findings of the qualitative studies.

Sleep Quality

Tired individuals were able to respond to sleepiness and experience restful sleep, whereas fatigued individuals had difficulty sleeping. One woman with cancer who reported fatigue

Table 1. Key Domains of Adaptation in Relation to Tiredness, Fatigue, and Exhaustion

Term	Sleep Quality	Cognition	Stamina	Emotional Reactivity	Control Over Body Processes	Social Interaction
Tiredness	Normal sleep pattern, feel rested	Forgetful	Gradual loss of energy in proportion to energy expended	Impatient	Body and mind work together.	Engages in normal social activities
Fatigue	Chronic disrupted sleep pattern, do not feel rested	Inability to concentrate	Gradual loss of energy out of proportion to energy expended	Anxious	Mind over body	Saves energy for participation in enjoyable activities
Exhaustion	Erratic sleep pattern, including periods of insomnia and periods of hypersomnolence	Confusion	Sudden loss of energy out of proportion to energy expended	Emotionally numb	Body over mind	Withdraws from all social activities

noted that she was unable to sleep without sleeping pills. Exhausted individuals reported an erratic sleeping pattern that included trouble staying awake and difficulty sleeping.

Stamina

Individuals with tiredness experienced loss of energy in proportion to the amount of energy expended, whereas individuals with fatigue experienced loss of energy sooner than expected (not increased weakness) and out of proportion to the amount of energy expended. Individuals with exhaustion experienced a sudden and unpredictable loss of energy, often without any identifiable energy expenditure. One woman with advanced cancer said, "all of a sudden [exhaustion] came on to me, and I knew that I was going to fall."

Cognition

Changes in cognition showed the same subtle discontinuous shifts as individuals moved among tiredness, fatigue, and exhaustion. Tired individuals reported forgetfulness, whereas fatigued individuals reported difficulty concentrating (not more forgetfulness), and exhausted individuals reported that they became confused. One individual stated that she "couldn't find my way home from the grocery store where I had shopped for 20 years."

Emotional Reactivity

Emotional reactivity ranged from impatience in tired individuals to emotional numbness in exhausted individuals. Those who experienced fatigue reported uncharacteristic anxiety but not increased impatience.

Body Process

Changes in body processes and social networks only occurred among individuals who were fatigued or exhausted.

Table 2. Summary of Sample Sizes for Phase II

Population	Men	Women
Cancer or palliative care	14	13
Depression	5	9
Chronic fatigue syndrome	1	13
Shift workers	12	7
Recreational distance runners	8	5

Body process changes associated with fatigue included increased sensitivity to light, noise, touch, and taste, as well as feeling cold, being off balance, and having increased nausea and diarrhea. Individuals "forced" themselves to continue with at least some activities of daily living, hence the notation listed in Table 1 of "mind over body." During exhaustion, however, the body took over. Participants reported an overwhelming need to lie down, experienced numbness in some body parts, and said that their bodies felt unfamiliar to them.

Social Interaction

Changes in social interaction associated with fatigue included saving energy for events one enjoyed and pushing oneself to interact. Individuals with exhaustion, in contrast to fatigue, found themselves unable to tolerate the stimulation associated with social interactions. One woman said, "[I] don't want to talk to anybody. I don't want to listen to anybody."

Figure 1 displays the basic model developed based on the current research. According to the model, tiredness, fatigue, and exhaustion exist along an underlying continuum labeled "adaptation." The concept of adaptation was chosen because the changes in behavioral patterns from tiredness to fatigue and from fatigue to exhaustion seemed consistent with the decreased ability to adapt outlined by Selye (1952, 1956). The behavioral patterns associated with tiredness are hypothesized to be markers for the alarm phase; those associated with fatigue are hypothesized to be markers for the resistance phase; and those associated with exhaustion are hypothesized to be markers for the exhaustion phase. These relationships will be tested with studies to examine the correlations among the behavioral patterns of tiredness, fatigue, and exhaustion and the standard physiologic indicators of stress adjusted for circadian and other rhythmic variations.

Creating New Conceptual Definitions

In the qualitative studies conducted for this project, charts were constructed to show the ways in which the six key domains were manifested in each study population as participants moved among tiredness, fatigue, and exhaustion. Consistent with the definition of tiredness, participants in all five study populations reported that changes in the domains of sleep quality, stamina, cognition, and emotional reactivity occurred first. This state was labeled tiredness. Participants noted that

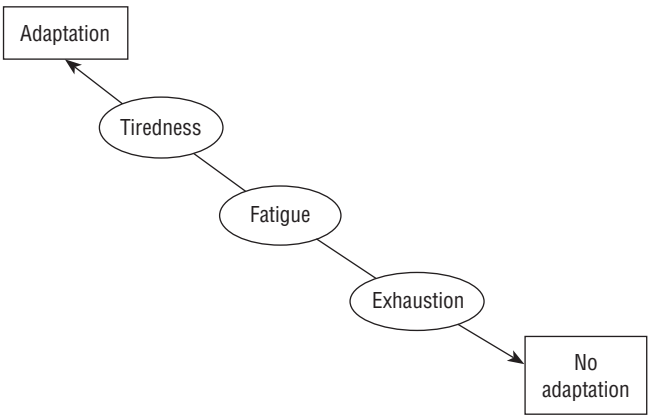

Figure 1. The Fatigue Adaptation Model

decreased control over body processes and reduced social interaction were associated with further qualitative declines in the first four domains. This state was labeled fatigue. Many, but not all, participants in each of the populations reported a third qualitative decline, labeled exhaustion.

Tiredness

Tiredness is characterized by forgetfulness, impatience, a gradual heaviness or weakness in muscles following work, and sleepiness alleviated by rest, but it is not characterized by any changes in social interaction or decreased control over body processes. Tiredness is hypothesized to be an adaptive response to stressors that occur during the alarm phase of the GAS, outlined by Selye (1952, 1956). The antecedents of tiredness are factors that challenge homeostasis. If adaptation is effective, tiredness is relieved. If adaptation is not effective, individuals eventually progress to fatigue.

Fatigue

Fatigue is characterized by difficulty concentrating; anxiety; a gradual decrease in stamina that is out of proportion to energy expended; difficulty sleeping; increased sensitivity to light, noise, taste, and touch; a feeling of being cold and off balance; an increase in nausea and diarrhea; and the limiting of social interactions to activities of particular significance. Participants who reported fatigue said that they "pushed on" despite these problems. An important feature of fatigue is the increased effort required to manage the changes described. The requirement to do so comes at a time when individuals have less energy available. Fatigue is hypothesized to indicate a declining ability to adapt to stressors that occur during the resistance phase of the GAS. The antecedent of fatigue is a nonadaptive response to tiredness. If an effective adaptive response can be mounted at this stage, an individual can move back to tiredness and, eventually, to no tiredness. If adaptation is not effective, the outcome is eventual progression to exhaustion.

Exhaustion

Exhaustion is characterized by confusion that resembles delirium, emotional numbness, sudden loss of energy in the absence of any identifiable energy expenditure, difficulty staying awake and sleeping, an inability to control body processes, and complete social withdrawal. Exhaustion indicates an almost complete inability to respond to stressors and is hypothesized to occur during the exhaustion phase of the GAS. The antecedent of exhaustion is an ineffective adaptation to fatigue. If an effective adaptive response becomes possible, an individual can move back to fatigue, tiredness, and, eventually, to a normal state of no tiredness. If an adaptive response cannot be mounted, however, exhaustion cannot be sustained for very long before death takes place.

Discussion

The new definitions suggest that fatigue is not a continuum but rather a state along a continuum (labeled adaptation for now). Tiredness and exhaustion are not anchors at either end of a fatigue continuum but are distinct states that have important clinical meaning; they are located at the ends of the adaptation continuum.

One of the most important findings of the current study was that decreased control over body processes and decreased social interactions did not appear until individuals manifested the behavioral patterns associated with fatigue in the other four domains. This finding suggests that the behavioral patterns for tiredness with respect to sleep quality, stamina, cognition, and emotional reactivity could serve as very early markers, perhaps even an early warning system, for impending fatigue. Similarly, the behavioral patterns for fatigue with respect to body processes and social networks could serve as behavioral markers that an individual has entered fatigue. These findings are consistent with the early work of Bartlett (1953), who noted that the sensations associated with fatigue arrive too late to be of any value as an early warning sign of excessive energy expenditure.

The transitions from tiredness to fatigue and from fatigue to exhaustion require further investigation. At this point, the process by which individuals move among these states is not clear, but within all study populations, the energy required for adaptation increased at the same time as the adaptational challenges became more complex. The adaptation that was required during exhaustion occurred when participants perceived that they had almost no energy left. In each state, the order of changes in each domain seemed to be related to the nature of the stressor. For example, weakness occurred before changes in the other domains in cachexic patients with cancer, whereas sleepiness occurred first in shift workers.

Understanding the distinctions among tiredness, fatigue, and exhaustion is important for at least two reasons. First, if tiredness is a precursor to fatigue and if fatigue is a precursor to exhaustion, the transition points from tiredness to fatigue and from fatigue to exhaustion are prime targets for nursing interventions that could protect patients from or at least delay the progression to fatigue and exhaustion. Second, failure to understand the relative places of tiredness, fatigue, and exhaustion in the adaptation process might result in the use of inappropriate interventions that inadvertently promote fatigue and exhaustion. For example, mild exercise, which might be appropriate for someone experiencing tiredness, might be an additional stressor (and therefore harmful) for a person experiencing exhaustion.

Implications for Nursing

The conceptual definitions of tiredness, fatigue, and exhaustion described in this article were sufficiently robust

to withstand reintroduction into the original interview texts in samples from five populations that experience them for various reasons. A screening tool to facilitate the identification of individuals with tiredness, fatigue, and exhaustion is currently under development, and plans for pilot studies based on the transitions between tiredness and fatigue and between fatigue and exhaustion are under way. The core principles for those studies were drawn from previous research of patients with cancer who, unexpectedly, did not develop fatigue (Olson et al., 2002) and from self-care theory (Orem, 2001).

Many possible physiologic mechanisms for fatigue have been proposed, and some correlations have been identified, but clear biologic markers have yet to be established (Payne, Piper, Rabinowitz, & Zimmerman, 2006; St. Pierre, 1992). Plans to examine relationships among common markers associated with the stress response based on qualitative work and controlling for possible changes in circadian rhythms are under way. Increasing lack of coordination among these markers is expected as patients proceed to fatigue and exhaustion.

Once the studies are complete, a clearer direction for the construction of nursing interventions will be apparent. In the meantime, nurses are advised to focus on eliminating stressors where possible and on increasing the resistance of patients to stressors. Suggestions for protecting individuals from fatigue or delaying its onset include assessing symptoms and other stressors with a view to their alleviation or reduction and establishing daily routines that eliminate unnecessary activities and create a new routine around at least one enjoyable activity and any treatment-related plans. Suggestions for protecting individuals from exhaustion or delaying its onset include assessing symptoms and other stressors; modifying daily routines to minimize energy loss further; exploring complementary therapies designed to remove energy blockages or provide energy; avoiding, when possible, any medications (e.g., amphetamines, methylphenidate, modafinil) or other substances (e.g., caffeine) that induce stimulation and, thus, require unnecessary expenditure of energy.

Conclusion

The elaboration of conceptual boundaries among tiredness, fatigue, and exhaustion and the Fatigue Adaptation Model have provided a new way of thinking about how fatigue and exhaustion can be prevented or delayed. Future studies will examine connections among the new conceptualizations, the relationships embedded in the model, and various health outcomes. If exhaustion can be delayed, for example, increasing survival may be possible, at least in cancers with short natural histories.

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