OBJECTIVES:

To examine symptom clusters in oncology patients; to determine if these symptom clusters might share a common biologic mechanism; and to describe potential biologic mechanisms that warrant investigation.

DATA SOURCES:

Synthesis of the theoretical and research papers on symptom clusters.

CONCLUSION:

Definitive conclusions about whether there is a biologic basis for the clustering of symptoms cannot be determined at this time. The animal model of sickness behavior holds promise as a potential biologic mechanism for clustering symptoms.

IMPLICATIONS FOR NURSING PRACTICE:

Until more definitive studies of symptom clusters are performed, clinicians need to monitor patients for the co-occurrence of multiple symptoms and develop appropriate management plans.

KEY WORDS:

Symptom clusters, symptom assessment, cluster analysis, mechanisms

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IS THERE A BIOLOGICAL BASIS FOR THE CLUSTERING OF SYMPTOMS?

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PATIENTS with cancer rarely experience a single symptom as a result of their disease or its treatment. However, most symptom management studies have taken a reductionistic approach and focused on the assessment or management of a single symptom like pain, fatigue, depression, or nausea.[1-3] In 2001, Dodd et al[3] suggested that symptom management research needed to focus on multiple symptoms that are related to each other but are not required to share the same etiology. However, this definition did not address the issue of whether or not the symptoms within a cluster could or needed to share a common biological mechanism.

The article by Dodd et al[3] launched a series of studies[4-12] and conceptual reviews[13-17] on a variety of symptom clusters in oncology. Within a concept analysis of symptom clusters, Kim et al[14] extended the definition of a symptom cluster as follows: "A symptom cluster consists of two or more symptoms that are related to each other and that occur together. Symptom clusters are composed of stable groups of symptoms, are relatively independent of other clusters, and may reveal specific underlying dimensions of symptoms. Relationships among symptoms within a cluster should be stronger than relationships among symptoms across different clusters. Symptoms in a cluster may or may not share the same etiology."[14, p278] Again, this expanded definition does not address the focus of this article, namely whether or not symptoms within a cluster could or should share a common biological mechanism.

The purposes of this article are: to examine the symptom clusters identified to date in oncology patients; to determine if these symptom clusters might share a common biologic mechanism; and to describe potential biologic mechanisms that might be investigated in subsequent research on cancer-related symptom

clusters. Although symptoms contained within a cluster may share a common etiology (eg, nausea, diarrhea, and anorexia may occur as a result of a gastrointestinal tumor or cancer chemotherapy), that does not mean they share a common biologic mechanism. The converse may be true as well: symptoms within a cluster that have different etiologies (eg, pain from bone metastasis, fatigue from radiation therapy, and depression from the loss of a spouse) may share a common biologic mechanism.

SIMILARITIES AND DIFFERENCES IN SYMPTOM CLUSTERS IN ONCOLOGY PATIENTS

The studies on symptom clusters in oncology patients can be categorized into two groups. In one group (summarized in Table 1),[3,4,8] the investigators created an a priori cluster of symptoms and evaluated the impact of that symptom cluster on a patient outcome. In the second group (summarized in Table 2),[4-12,18] oncology patients completed a symptom inventory and in some of these studies, symptom clusters were identified empirically using either cluster analysis or factor analysis procedures.

In the first group,[3,4,8] pain and fatigue were the common symptoms across all three studies. In all but one of these studies,[8] sleep disturbance was the third symptom in the cluster that was created a priori. In all three studies, the rationale for the a priori selection of these symptoms was that they are highly prevalent in oncology patients. However, none of these articles discussed the idea that these symptoms could share a common biologic mechanism.

Some of the studies listed in Table 2 used either cluster analysis or factor analysis procedures to empirically derive symptom clusters.[6,10-12,18] This group of studies, which used analytic procedures to derive symptom clusters, has the potential to more easily identify symptoms that may share a common biologic mechanism because these statistical procedures examine the inter-relationships among variables and disentangles those relationships to identify clusters of variables that are closely linked.[19,20]

Two of the studies enrolled patients with a single cancer diagnosis (ie, lung cancer[6] or breast cancer[10]), while the other three studies enrolled inpatients with a variety of cancer diagnoses.[11,12,18] It is interesting to note that in the two studies with samples from a single cancer diagnosis,[6,10] a single symptom cluster with six or seven symptoms was identified using either factor analysis or cluster analysis. The symptoms shared across the two studies were fatigue and weakness. Symptoms in the single cluster that were unique to the patients with lung cancer were nausea, vomiting, loss of appetite, weight loss, and altered taste sensations. Symptoms in the single cluster that were unique to the patients with breast cancer were lack of energy, feeling depressed or blue, feeling nervous or anxious, and loss of concentration. The differences in the specific symptoms within the single cluster solution may relate to differences in symptoms associated with specific cancers or cancer treatments or in the questionnaires and methods that were used to assess and create the symptom cluster. Bender et al[10] noted in their discussion that additional studies are needed to identify the physiologic mechanisms that underlie these symptom clusters.

The three studies that enrolled patients with a variety of cancer diagnoses derived two,[18] three,[12] or seven[11] symptom clusters. While the studies by Cleeland et al[18] and Chen and Tseng[12] both used the M.D. Anderson Symptom Inventory and similar analytic methods, the symptom clusters identified in these studies were not identical. However, in both studies, within one symptom cluster, the symptoms of pain, fatigue, sleep disturbance, and drowsiness did overlap. In addition, in both studies, a gastrointestinal symptom cluster (ie, nausea and vomiting) was identified. In addition, the study by Walsh and Rybicki,[11] of palliative care patients (n = 922), identified a gastrointestinal symptom cluster with the same symptoms of nausea and vomiting. However, pain, fatigue, and sleep disturbance did not cluster together in their sample. Variations in the number of symptom clusters, as well as in the particular symptoms within each cluster, may be attributable to the instruments used to measure the symptoms, the methods used to create the symptom clusters, and/or the heterogeneous nature of the patients in terms of cancer diagnoses, stages of disease, and current treatment regimens.

The authors of the most recent studies (listed in Table 2)[11,12] noted that further research is needed on symptom clusters because this work may promote our understanding of the etiology and pathophysiology of multiple symptoms in patients with cancer. Chen and Tseng[12] proposed that one potential mechanism to explain certain symptoms