ICD has traditionally grouped diseases by aetiology and by affected organ system. For ICD11 the creation of a new chapter for multisystem disorders has been proposed. The following text sets out the rationale for and the possible scope of a multisystem disorders chapter.

The concept of multisystem disorders is not new, however the meaning of “multisystem” as used in the literature is largely implicit and rarely defined explicitly except for case definitions of the CDC, and a mention in Webster’s Medical Dictionary. There is an important group of significant disorders which have varied manifestations and can affect so many organs that it is not possible to tie them to a single predominant organ system. Examples include systemic lupus erythematosus, dermatomyositis, Behçet disease, polyarteritis nodosa, sarcoidosis, Wegener granulomatosis, mitochondrial disorders and many complex heredofamilial and developmental disorders. In contrast, there are many disorders which have an impact on several body systems but which normally have a predominant effect on only one (e.g. rheumatoid arthritis).

In the definition of “multisystem” the important point is that there is no dominant system affected, and not how many systems are affected. This aspect of predominance of a system would be pragmatically assessed according to whether a patient presenting to the healthcare system would normally be managed in a specific specialist department or not. Patients who have a multisystem disorder may present with such a complex phenotype that they cannot be handled in a single specialist department. Although they will often be managed within the ambit of internal medicine\(^1\), they may need input from multiple specialists (e.g. nephrologist, neurologist, rheumatologist, dermatologist, paediatrician, medical geneticist). Alternatively the systems affected by the disease process can vary markedly from patient to patient. Thus although sarcoidosis commonly affects the lungs, it regularly presents with ocular, skin or CNS symptoms in the absence of pulmonary symptoms. The services which will be involved in its management will thus vary. Although many multisystem disorders are rare, some, such as sarcoidosis, are not.

As a result, we define “multisystem” as diseases that regularly manifest

- **without involvement of a common single system**
  this would apply to SLE, sarcoidosis, Behçet disease, systemic sclerosis, vasculitis (including Wegener granulomatosis, Churg-Strauss allergic granulomatosis etc.)

- **with concomitant major involvement of several systems**
  this would again apply to all the above and also to dermatomyositis; there would also be many genetic syndromes (e.g. ataxia telangiectasia, tuberous sclerosis) to which this would apply

The regrouping to a multisystem chapter would be applied to diseases that at present reside in a specific organ chapter and that have no sensible and satisfactory home there. By using multiple parents, however, it will be possible to find the organ-specific children of multisystem disorders, e.g. pulmonary sarcoidosis, both in the multisystem chapter and in the appropriate organ-specific chapter. Diseases residing in any of the aetiological chapters, being infections, neoplasms and injuries, would not be considered for this proposed chapter.

In consequence:
The point of origination versus manifestation does matter less than the aspect of treatment, because treatment would deal with manifestation and aetiology pending on the individual disease. It is important to highlight the fact that a disease included here does regularly have a variety of very different presentations depending on which of several systems is involved. For example, Sarcoidosis of skin (D86.8) (which usually is not associated with pulmonary involvement) is currently classified under diseases of the blood and blood-forming organs as “certain disorders involving the immune mechanism” which is not any more appropriate for sarcoidosis than it would be for leprosy.

Defining “by departments” might need to be verified for its applicability on a global scale.

We need to explain why we are doing this:
1. to facilitate users finding the relevant diseases
2. to recognize the multiple disciplines that are involved in treatment
3. to have a taxonomically more correct representation of the diseases in the reference linearizations for international comparison.
4. to make it clear that these diseases may present in very different ways depending upon which system is affected. The inclusion of Behçet disease within musculoskeletal diseases, for example, does not inform that this condition most commonly affects skin, eye and oral mucosa: musculoskeletal symptoms do not feature at all in the 1990 International Criteria Behçet disease.
5. The subgrouping of diseases in the chapter will have to be pragmatic because the aetiology is frequently not known. Consideration should be given to including some of the metabolic diseases (e.g. amyloidosis) in such a chapter. Most of the “connective tissue” diseases would be more appropriate here, though preferably under an alternative title (to be discussed further).

Whether the notion of multisystem disease would be useful for international comparison needs to be discussed. For health services planning and morbidity (including casemix) “multisystem” may mean high resources and at any rate means involvement of multiple disciplines; for mortality it means “complicated”, for prevention “multisystem” means nothing, for casemix multisystem may mean “complex”.

For a linearization of ICD this would mean that multisystem disorders would
1. list explicitly the systems they involve
2. be referenced to and from the relevant system-based chapters
Disambiguation and classification is necessary for:

2. Multisystem organ involvement, multisystem manifestation, multisystem reaction
2.
2. CDC definitions for multisystem (depending on the context of the disease):
2. # Multisystem involvement -- three or more of the following:
   • # Gastrointestinal
   • # Muscular
   • # Mucous membrane
   • # Renal
   • # Hepatic
   • # Hematologic
   • # Central nervous system
   .
   . Literature search (118.348.467 Articles of 32 databases):
   . (Derwent, EMBASE, Medline, Cochrane, Hogrefe, Karger, Krause, Thieme, Ethmed, Gobal Health, ISTP, Scisearch, SOMED, NHS-CRD, HECLINET, and more)
   . Keywords and their frequencies in articles:
   . "multisystem diseases" 225
   . "multisystemic diseases" 148
   . "multisystemic disease" 1226
   . "multisystem disease" 3184
   .

Keywords in titles:
TI="multisystem diseases" 39
TI="multisystemic diseases" 8
TI="multisystemic disease" 85
TI="multisystem disease" 185

“OR” link of above results and eliminating duplicates, results in 121 matching articles that are listed at the end of this document.

A broad review of the titles indicates reference to a restricted range of diseases, so that an extensive review would guide probably compilation of a list of diseases that usually are referred to as “multisystem”. Size and content of that list will further inform the decisions
Literature


20. Manigand, G., ACCIDENTS DES TRAITEMENTS MEDICAMENTEUX DE FOND DES RHUMATISMES INFLAMMATOIRES CHRONIQUES ET DE D’OR - D-PENICILLAMINE MALADIES SYSTEMIQUES. I. SELS D’OR- D. PENICILLAMINE


28. Rodes, J., M. Bruguera, and A. Pares, CIRROSIS BILIAR PRIMARIA, UNA ENFERMEDAD MULTISISTEMICA. PATOGENESIS Y TRATAMIENTO


118. Luyten, P. and B. Van Houdenhove, Treatment of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), a multisystem disease, should target the pathophysiological aberrations (inflammatory and oxidative and nitrosative stress pathways), not the psychosocial "barriers" for a new equilibrium - Response to Maes and Twisk. 2010, ELSEVIER IRELAND LTD, ELSEVIER HOUSE, BROOKVALE PLAZA, EAST PARK SHANNON, CO, CLARE, 00000, IRELAND. p. 147-147.

