Chronic itch is a common and distressing symptom that arises from a variety of skin conditions and systemic diseases. Despite this, there is no clinically based classification of pruritic diseases to assist in the diagnosis and cost-effective medical care of patients with pruritus. The proposed classification focuses on clinical signs and distinguishes between diseases with and without primary or secondary skin lesions. Three groups of conditions are proposed: pruritus on diseased (inflamed) skin (group I), pruritus on non-diseased (non-inflamed) skin (group II), and pruritus presenting with severe chronic secondary scratch lesions, such as prurigo nodularis (group III). The next part classifies the underlying diseases according to different categories: dermatological diseases, systemic diseases including diseases of pregnancy and drug-induced pruritus, neurological and psychiatric diseases. In some patients more than one cause may account for pruritus (category “mixed”) while in others no underlying disease can be identified (category “others”). This is the first version of a clinical classification worked out by the members of the International Forum for the Study of Itch (IFSI). Chronic pruritus, which can be distressing and often refractory to treatment, is associated with many diseases, the most common being chronic renal insufficiency, cholestatic liver diseases and atopic dermatitis (2–4). While many pruritic skin diseases can be diagnosed readily, this becomes more difficult for pruritus that occurs in apparently normal skin or accompanying secondary scratch-evoked lesions as a consequence of systemic disease. The quality, intensity and diurnal rhythm of itch are important factors that currently have limited diagnostic value.

There is no internationally accepted clinical classification of itch (5–7). A neuropathophysiological-based classification was proposed in 2003 (7). Twycross et al. (7) classified itch according to its origin: cutaneous (pruritoceptive – cutaneous nerves are activated by pruritogens at their sensory endings), neuropathic (diseased or lesioned pruritic neurones generate itch), neurogenic (itch induced by mediators acting centrally in the absence of neural damage), and psychogenic. This classification is beneficial mechanistically, but has the following limitations for clinical application: (i) it is retrospective, necessitating that the underlying cause of pruritus has already been diagnosed; (ii) several diseases, such as atopic dermatitis and cholestatic pruritus, fall into more than one category; and (iii) pruritus of unknown origin cannot be classified according to this scheme. This classification scheme is therefore of limited applicability in daily medical practice.

In recent years, new information about the neuronal basis and clinical course of pruritus has greatly improved the medical care and therapeutic options for patients with pruritus (8–15). These advances beg for consis-
tent definitions of clinical terms and classifications of pruritus befitting the enormity and complexity of this clinical problem. This is the first version of a clinical classification of itch formulated by the members of IFSI. It considers the origin and clinical manifestations of pruritus occurring in diseased and normal skin.

SKIN CONDITIONS IN CHRONIC PRURITUS (TABLES I–IV, FIG. 1): CLINICAL CLASSIFICATION OF PRURITUS

When dealing with patients with chronic pruritus, identifying the aetiology is a challenge. Before initiating laboratory and radiological examination, the most important step is to obtain a complete history and physical examination. Identifying recent changes in skin condition helps to guide the diagnosis of possible underlying diseases. Primary and secondary skin changes must be differentiated. Primary skin lesions originate from the causal disease. Secondary skin lesions are reactive lesions induced by manipulations (e.g. scratching or rubbing) of the skin due to chronic pruritus. We therefore suggest the following clinically-oriented classification scheme:

**Group I.** Many skin diseases are accompanied by itch. They comprise inflammatory, infectious, or autoimmune cutaneous diseases, genodermatoses, drug reactions, dermatoses of pregnancy and skin lymphomas, all of which lead to specific skin changes described elsewhere (Table II). This first group is named “pruritus on primary diseased, inflamed skin”. Due to scratching, the primary skin disease may be confounded by secondary scratch lesions. This may occur, for example, in excoriated forms of psoriasis, atopic dermatitis or bullous pemphigoid.

**Group II.** Patients with pruritic diseases of systemic, neurological or psychosomatic/psychiatric origin experience pruritus without any skin lesions except for possible secondary scratch lesions. Systemic diseases leading to itch include endocrine and metabolic disorders, infections, haematological and lymphoproliferative diseases, solid neoplasms and drug-induced pruritus (Tables III and IV). This second group is termed “pruritus on primary non-diseased, non-inflamed skin”. It has previously been named “pruritus sine materia”.

This term has multiple interpretations, such as pruritus without underlying origin (16), pruritus without any skin changes (17, 18), pruritus in systemic diseases without any initially visible skin changes (19), pruritus characterized by the “absence of specific cutaneous lesions of an itching dermatosis” (20) or even pruritus in the elderly (21). Besides there is a psychosomatic definition of pruritus sine materia in the ICD-10 classification of F45.8 as somatoform pruritus, which is the more acceptable term from the international classification system, but is not used by dermatologists (22). In the DSM-IV-R a similar category is not specifically defined, but can be classified as undifferentiated somatoform disorder (300.81) (23). Due to the confusion inherent in these various definitions, it is recommended that the term pruritus sine materia should no longer be used.

Another important point is that the presence of skin changes does not exclude the possibility of an underlying systemic cause, while the absence of a rash does not automatically mean that the underlying cause is a systemic disease (as, for example, in “invisible” dermatoses, such as mastocytosis). A skin examination by a trained dermatologist is therefore imperative in the evaluation of the patients.

| Table I. Clinical classification of chronic pruritus according to skin changes |
|---|
| Group | Clinical presentation and underlying disease | Diagnostics |
| I: Pruritus on primarily diseased, inflamed skin | Clinical picture: skin disease aetiology: mainly category I (see Table V) | Skin biopsy, laboratory investigation if necessary (e.g. IgE, indirect immunofluorescence) |
| II: Pruritus on primarily normal, non-inflamed skin | Clinical picture: normal skin aetiology: mainly category II, III, IV | Laboratory and radiological investigation, adapted to the patient’s history and pre-existing diseases |
| III: Pruritus with chronic secondary scratch lesions | Clinical picture: chronic secondary scratch lesions like prurigo nodularis aetiology: category I-IV | Skin biopsy, laboratory and radiological investigations, procedure adapted to the patients history and pre-existing diseases |

*Fig. 1. Clinical classification in the management of chronic pruritus patients. As a first step, patients are grouped according to their clinical picture and history. Although group I and II may already suggest a category, the classification of the patient is performed in a second step based on histological, laboratory and radiological investigation. If no category fits or several diseases are found (small arrows), the patients are classified into “mixed” or “others” (arrow on the right).*
Systemic solid tumours of the cervix, undetermined origin

Examples of diagnoses

- Bullous dermatoses, especially dermatitis
- Neuritic diseases (neuronal damage)
- Autoimmune dermatoses
- Genodermatoses
- Dermatoses of pregnancy
- Neoplasms

EB: epidermolysis bullosa.

**Table III. Category II: Systemic origin of chronic pruritus**

| Category | Examples of diagnoses |
|----------|-----------------------|
| Endocrine and metabolic diseases | Chronic renal failure, liver diseases with or without cholestasis, hyperthyroidism, malabsorption, perimenopausal pruritus |
| Infectious diseases | HIV-infection, helminthiosis, parasitosis |
| Haematological and lymphoproliferative diseases | Iron deficiency, polycythaemia vera, Hodgkin’s disease, Non-Hodgkin’s lymphoma, plasmocytoma |
| Visceral neoplasms | Solid tumours of the cervix, prostate, or colon, carcinoid syndrome |
| Pregnancy | Pruritus gravidarum with and without cholestasis |
| Drug-induced pruritus (selection) | Opioids, ACE-inhibitors, amiodarone, hydrochlorothiazid, estrogens, simvastatin, hydroxyethyl starch, allopurinol |

HIV: human immunodeficiency virus; ACE: angiotensin converting enzyme.

**Table IV. Category III/IV: Neurological and psychiatric/psychosomatic origin of chronic pruritus**

| Diseases | Examples of diagnoses |
|----------|-----------------------|
| **Group III.** Chronic pruritus frequently leads to mechanical reactions, such as scratching, rubbing or pinching. Scratching may induce variable damage of the skin, presenting as excoriations, crusts, lichenification, papules and nodules. These lesions may resolve, leaving hyper- or hypopigmentation and atrophic scars of the skin. Several lesions in different stages and sizes may co-exist in patients with chronic pruritus. Some of these clinical manifestations are summarized using terms such as lichen simplex chronicus, lichen Vidal, lichen amyloidosis, macular amyloidosis, and prurigo nodularis. All of these represent secondary acquired lesions induced by chronic scratching. The third group consequently comprises patients characterized by prominent severe chronic secondary scratch lesions, such as prurigo nodularis. The underlying origin may be a systemic disease or a skin disease. Patients in the third group have usually had chronic pruritus for years and rarely recall any initial skin changes. |

**CLASSIFICATION OF UNDERLYING DISEASES (TABLE V, FIG. 1): AETIOLOGICAL CLASSIFICATION OF PRURITUS**

After having performed a clinical examination, historical, laboratory and radiological investigations aim to identify underlying pruritogenic diseases. For differential diagnostic purposes, we propose the following categories of underlying diseases (Table V): Category I: Dermatological diseases; Category II: Systemic diseases including diseases of pregnancy and drug-induced pruritus; Category III: Neurological; and Category IV: Psychiatric/psychosomatic diseases. In quite a number of patients, more than one underlying disease may contribute to itch and should be categorized as “mixed” (Category V; for example, chronic pruritus presenting with dry skin in patients with renal insufficiency). In some patients no underlying disease

**Table V. Aetiological classification of chronic pruritus according to underlying origin**

| Category | Diseases |
|----------|----------|
| I. Dermatological | Arising from "diseases of the skin", such as psoriasis, atopic dermatitis, dry skin, scabies and urticaria |
| II. Systemic | Arising from "diseases of organs" other than the skin, such as liver (e.g. primary biliary cirrhosis), kidney (e.g. chronic renal failure), blood (e.g. Hodgkin’s disease), and certain multifactorial (e.g. metabolic) states or drugs |
| III. Neurological | Arising from "diseases or disorders of the central or peripheral nervous system", e.g. nerve damage, nerve compression, nerve irritation |
| IV. Psychogenic/ | Somatiform pruritus with co-morbidity of "psychiatric and psychosomatic diseases" |
| Psychosomatic | |
| V. Mixed | Overlapping and coexistence of several diseases |
| VI. Other | Undetermined origin |

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can be identified, and should be classified as “others” (Category VI). We suggest that chronic pruritus with no finding of the underlying origin following completion of diagnostic tests is called “pruritus of undetermined origin” (PUO). Definitions and clinical characteristics, which have to be included in the upcoming revisions and are currently discussed among the authors, but for which no consensus has been reached, include localization (localized vs. generalized), quality of itch (“flavouroir”), time domain (continuous, intermittent, diurnal rhythm) and response to treatment (“intractable”).

In summary, this classification aims to provide a practical and useful clinical approach to patients with chronic pruritus. We emphasize that not all forms of chronic itch are identical, and that it is important that healthcare providers do not regard itch as a singular uniform entity. The proposed classification also intends to improve the management of patients with chronic pruritus in a cost-effective manner. As our knowledge regarding neurophysiological and pathophysiological aspects of chronic pruritus develops, the present initial classification of chronic pruritus developed by IFSI will undoubtedly require future revisions.

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