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## Commentary

**Proposed classification for koebner, wolf isotopic, renbok, koebner nonreaction, isotopic nonreaction & other related phenomen.**

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## Abstract

Students of skin diseases have long noted a variety of disease responses and non-responses to trauma and the presence of structural abnormalities. This article will review the series of these responses including: Koebner phenomenon, Wolf isotopic response, Renbök response, Koebner nonreaction, isotopic nonreaction, and other related skin reactions. Because most of these reported phenomena have similar morphological features the diagnosis is often made on the basis of differences in the clinical presentation. Note that some of the cutaneous reactions of similar phenomena have been described using varied nomenclature, further adding to the confusion. In view of this, we believe that at present there is a robust need to define each cutaneous reaction accordingly and classify the various types of these phenomena under a broad universal term or terms. Respecting the idea of differences might facilitate a better understanding of the pathophysiology of these entities. We then will propose an alternative classification system.

## Introduction

### Definitions of Currently Recognized Conditions

*Koebner phenomenon:* The “Koebner phenomenon,” also called the “Koebner response,” the “isomorphic phenomenon”, and the “isomorphic response,” is well known to clinicians [1-5].

The term “Koebner phenomenon” is used to describe the appearance of typical skin lesions of an existing dermatosis at sites of injuries [2-4]. Trauma to an unaffected area of skin in a psoriatic patient can produce new, similar psoriatic lesions in the distribution of the trauma. Because of their similarity, this cutaneous response is also known as an "isomorphic reaction," meaning a reaction in the same form.

Heinrich Koebner (alternative spelling Köbner) was a renowned German dermatologist of the 19th century. In 1872, at a meeting of the Silesian Society for National Culture, Koebner reported his observations and studies that resulted from having seen patients

who had developed psoriasis at sites of diverse trauma including horse bites, suppuration of lymphadenitis, and tattoos.. These same findings were published in 1876 and caused considerable diverse discussion about the origin of psoriasis in the following years [6]. Today the “Koebner phenomenon” is well documented in a broad array of skin diseases and still of considerable interest among the research community because the pathophysiology remains unclear [7-10].

*Koebner nonreaction:* In contrast to this well-known observation in which skin disease is produced in the site of injury, infrequently disease may be spared in the distribution of trauma. Cochran and colleagues in 1981 first described a maculopapular drug reaction which spared the sites of previous X-irradiation in a patient who had been treated for Wilm’s tumor [11]. Bernhard et al later introduced the term “Koebner nonreaction” or “Isomorphic nonresponse” to refer to the absence of a drug reaction at the site of the previous x-irradiation.[12]

*Reverse Koebner response:* The Reverse Koebner response is the nonappearance or disappearance of the lesions of particular dermatoses at the site of injury. It was first described in psoriasis patient with only few cases reported to date [13-15].

*Wolf’s Isotopic Response:* The term "isotopic response" was introduced by Wolf et al in 1995 to describe the occurrence of a new skin disease at the site of another unrelated and already healed skin disease [16-17]. Subsequently it was changed to "Wolf’s isotopic response” because literature searches for "isotopic response" generated hundreds of references that were linked with radioactive isotopes [18].

*Isotopic Nonresponse:* In analogy to the isomorphic nonresponse the term “isotopic nonresponse,” related to the isotopic response was introduced in the original contribution by same authors [16]. It is defined as the absence of an eruption at the site of another unrelated and already healed skin disease or the sparing of the sites of another unrelated and already healed skin disease [19-23].

*Renbök Phenomenon:* Happle et al. first introduced the term “Renbök phenomenon” or “Inverse Koebner Phenomenon” to describe the observation of normal hair growth in psoriatic plaques in patients with co-existing psoriasis and alopecia areata [24]. Later, additional cases with alopecia areata sparing nevus flammeus and congenital melanocytic nevus were described [25-33]. Mansur et al., suggested that a dermatosis sparing another co-existing unrelated previous skin disorder including Renbok phenomenon could be defined as a “reverse isotopic response” [34].

*Remote Reverse Koebner Phenomenon:* The “remote reverse Koebner phenomenon” is described in vitiligo patients, in which spontaneous repigmentation is seen in distant patches after autologous skin graft surgery [35].

## Miscellaneous Related Conditions

*Sparing Phenomenon:* Clinical observation of purpuric lesions apparently inhibited by an existing tattoo in a young patient was described under the recently introduced “sparing phenomenon” by Pinal-Fernandez and others [36]. Wang TS and Tsai TF have recently published a very interesting phenomenon in which a 67-year-old man who had generalized psoriasis exhibited complete sparing of the post-polio residual paralysis of his lower leg [37].

*Deep Koebner Phenomenon:* “Deep Koebner Phenomenon” or "deep Koebner effect" has been introduced to describe traumatic injury or physical stress as a trigger for the subsequent development of psoriatic arthritis. This relationship has been suggested by several case reports and case series [38-40].

*Radioisotopic response:* The term used to describe the phenomenon of secondary dermatosis arising in an ionizing radiation field. (Conventional electron beam radiotherapy and ultraviolet radiation also included to the list subsequently)[41-42].

## Rationale For New Categorization

As clinicians we believe that there is a need for a more precise classification of “Koebner phenomenon” and other related entities to bring uniformity to their description, categorization, and documentation. Although we are honoring those who described these various phenomena, the key element is that these cutaneous responses must share some particular aspects of their pathophysiology.

In order to devise a unifying classification these phenomena, we propose the following questions.

1. Is the second skin disease occurring in or sparing the particular area of skin component?

2. Is this an isomorphic (appearance of the same disease at another location) or isotopic phenomenon (appearance of a new disease at the same place)?
3. What is the nature of first cutaneous insult (a skin disease, physical injury, genetic mosaicism)?
4. What is the nature of second skin insult (a skin disease, physical injury)?
5. Are the two skin insults (e.g. first skin disease & second skin disease /physical injury & second skin disease/ genetic mosaicism & second skin disease) concomitantly present or not?
6. If two skin diseases are concomitantly present, do they occur on same site or not?

## New Classification Proposal

To simplify this nosology, we propose to unify these disparate observations and terms under two major divisions.

- A. *Cutaneous Affinity Phenomenon*: The affinity to develop a skin disease on an area previously or presently affected by another skin disease, physical or chemical insult, or site of genetic mosaicism.
- B. *Cutaneous Sparing Phenomenon*: The sparing of specific skin disease on an area previously or presently affected by another skin disease, physical or chemical insult, or site of genetic mosaicism.

We also need to define several new terms that will link together observed phenomena. These include the isotopic co-response, the isotopic co-nonresponse, the reverse isotopic response, and the inverse isotopic response. To understand the utility of this classification, see table I.

*Reverse Koebner response*: Reverse Koebner response to be further classified to following sub groups according to the type of cutaneous insult

*Post vaccination reverse Koebner response*: is the nonappearance or disappearance of the lesions of particular dermatoses at the site of vaccination

*Post radiation reverse Koebner response*; is the nonappearance or disappearance of the lesions of particular dermatoses at the site of radiation [15]

*Post traumatic reverse Koebner response*: is the nonappearance or disappearance of the lesions of particular dermatoses at the site of trauma [14]

*Post neural reverse Koebner response*: is the nonappearance or disappearance of the lesions of particular dermatoses at the site of neurological deficits [43]

*Isotopic co-response*: If the second skin disease appeared on the site of previous active disorder there is no available descriptive term in the present nomenclature. Hence, we introduce "isotopic co- response" for such instances [44-48].

*Isotopic co-nonresponse*: The term "isotopic co-nonresponse" should be included in the nomenclature to describe the disappearance of the already existing skin disorder by a second unrelated new skin disease, which appeared on the primary cutaneous disease.

*Reverse isotopic response*: "Reverse isotopic response" denotes a dermatosis sparing another co-existing unrelated previous skin disorder (inflammatory or infectious in origin).

*Inverse isotopic response*: We also propose a new term "inverse isotopic response" for a dermatosis sparing existing genetic mosaicism (e.g., nevus) - "primary inverse isotopic response" or physical insult (e.g., Tattoo) - "secondary inverse isotopic response" [32,36].

**Table I: Proposed Categorization for Cutaneous Affinity and Sparing Phenomena**

Cutaneous Affinity Phenomena	Cutaneous Sparing Phenomena
<p><b>Isomorphic Affinity Phenomena</b></p> <p>a. Koebner response (Koebner phenomenon, Koebner reaction, isomorphic response ,isomorphic phenomenon, isomorphic reaction)</p> <p>b. Remote reverse Koebner response (phenomenon)</p> <p>c. Deep Koebner effect (phenomenon)</p>	<p><b>Isomorphic Sparing Phenomena</b></p> <p>a.Reverse Koebner response (reverse Koebner phenomenon, reverse isomorphic response, reverse isomorphic phenomenon)</p> <p>1.Post vaccination reverse Koebner response</p> <p>2. Post radiation reverse Koebner response</p> <p>3. Post traumatic reverse Koebner response</p> <p>4. Post neural reverse Koebner response</p>
<p><b>Isotopic Affinity Phenomena</b></p> <p>a.Wolf's isotopic response (isotopic response)</p> <p>1.Post herpetic isotopic response (Wolf's post herpetic isotopic response)</p> <p>b. Post vaccination isotopic response</p> <p>c. Post radiation isotopic response(radioisotopic response)</p> <p>d. Post traumatic isotopic response</p> <p>e. Post neural isotopic response</p> <p>f.Post genetic mosaicism isotopic response</p> <p>g. Isotopic co-response</p>	<p><b>Isotopic Sparing Phenomena</b></p> <p>a. Isotopic nonresponse</p> <p>1. Post herpetic isotopic non response</p> <p>b. Post vaccination isotopic non response</p> <p>c. Post radiation isotopic non response(Koebner nonresponse ,Koebner nonreaction, isomorphic nonresponse, isomorphic nonreaction))</p> <p>d. Post traumatic isotopic nonresponse</p> <p>e. Post neural isotopic non response</p> <p>f. Post genetic mosaicism isotopic nonresponse</p> <p>g. Isotopic co-nonresponse</p> <p>h.Reverse isotopic response (Renböök phenomenon)</p> <p>i. Inverse isotopic response</p> <p>1. Primary inverse isotopic response</p> <p>2. Secondary inverse isotopic response</p>
<p><b>Combine isomorphic – isotopic affinity phenomena</b></p>	<p><b>Combine isomorphic – isotopic sparing phenomena</b></p>

We would also like to propose the following sub classifications under the Isotopic Affinity Phenomenon according to the course of the cutaneous insults that leads to subsequent occurrence of new skin disease at the subjected site. (vaccination, radiation, trauma and neurological deficits)

*Post vaccination isotopic response:* the occurrence of a new skin disease at the site of previous vaccination [49-50]

*Post radiation isotopic response:* the occurrence of a new skin disease at the site of previous radiation [41, 42]

*Post traumatic isotopic response:* the occurrence of a new skin disease at the site of previous trauma [51,52]

*Post neural isotopic response:* the occurrence of a new skin disease at the site of previous neurological deficit [53, 54]

*Post genetic mosaicism isotopic response*: the occurrence of a new skin disease at the site of nevus

In analog to the above Isomorphic Affinity Phenomenon sub classifications of following sub headings should be included under the Isotopic Sparing Phenomenon according to the primary cutaneous insults such as:

*Post vaccination isotopic nonresponse*: the absence or sparing of a cutaneous eruption at the site of vaccination [55]

*Post radiation isotopic nonresponse*: the absence or sparing of a cutaneous eruption at the site of radiation [11-12,15]

*Post traumatic isotopic nonresponse*: the absence or sparing of a cutaneous eruption at the site of trauma [56]

*Post neural isotopic nonresponse* the absence or sparing of a cutaneous eruption at the site of neurological deficit [37]

*Post genetic mosaicism isotopic nonresponse*: the absence or sparing of a cutaneous eruption at the site of nevus[57]

Various combination responses

*Combined isomorphic – isotopic affinity phenomenon*: This new term should be added to the dermatology glossary to document the simultaneous existing cutaneous reactions related to the isomorphic affinity phenomenon and isotopic affinity phenomenon [57-60].

*Combined isomorphic – isotopic sparing phenomenon*: Analogous to the combined isomorphic – isotopic affinity phenomenon the term combines isomorphic- isotopic sparing phenomenon and is defined as both isomorphic affinity phenomenon and isomorphic sparing phenomenon in an individual at the same time.

We believe that this new classification scheme will simplify the broad understanding of these diverse phenomena. As new and unique observations continue to be reported and classified, modifications and revisions in the proposed new classification may become mandatory. Nevertheless, this simplifies a broad range of phenomena into four major categories. We propose those notions of the isomorphic and isotopic affinity phenomena and the isomorphic and isotopic sparing phenomena to help in our global understanding of these conditions.

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