

UNIVERSITY OF MEDICINE AND PHARMACY OF CRAIOVA

Ph.D SCHOOL

ABSTRACT OF Ph.D PAPER ENTITLED:
**CUTANEOUS MANIFESTATIONS
INDUCED BY STREPTOCOCCAL TONSILLAR
FOCAL INFECTION**

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Abstract

The theme of my PhD dissertation concerning ‘Cutaneous manifestations induced by outbreak of streptococcal etiology of tonsillar infection’ represents an interesting and important issue from a doctrinary point of view, and also from the practical point of view for almost all specialities, especially when we think that dermatology ranks first. It is essential to remind that the founders of the focal infection theory in Romania were the representatives of the Medical School of Cluj (I. Goia, I. Hateganu, A. Moga) who demonstrated the causality relation between focal infection and numerous severe conditions like rheumatic fever, slow malignant endocarditis, diffuse or focal glomerulonephritis, bronchial asthma, etc.

From the large list of cutaneous manifestation due to focal infection we mention: impetigo (most frequent), erythema nodosum, erythema multiforme, dyshidrotic eczema, eczematid-like eruptions, guttate psoriasis. Atopic skin is more prone to chronic prurigo, nummular eczema, neurodermatitis, vasculitis associated or not with purpura, urticaria, Quincke’s edema, etc.

The group of diseases caused by group A beta-haemolytic streptococcal tonsillar infection is extensive, we monitored only the most frequent conditions that occurred in our 204 patients study group who committed to the dermatology department of Craiova, over a period of 3 years (2010-2012) compounded by the outpatients’ dermatology department.

We find it useful to insist more over the morphoclinical, etiopathogenic and evolutive features of these conditions which are relatively frequent and often make difficult to put the correct diagnosis and especially to recommend to most suitable therapy and to prevent relapses.

With this occasion, I want to pay my respect to professor doctor Elena Ioniță, who stood by me all along the line, offering me all the support I needed.

I want to thank particularly to professor doctor Ion Țolea for the valuable guidance in selecting and ordering the documentary.

I also want to thank to doctor Simona Ianoși and doctor Ion Florea of the Dermatology Department for the advices and the colaboration in obtaining the iconography.

The author

Craiova, 2014

In the first part of my paper I have tried to bring up to date the information concerning the focal infection and its implications in the general pathology and in particular in the cutaneous pathology.

A general accepted definition establishes that focal infection represent a local inflammatory process, usually, secluded, without possibility for drainage, that periodically disseminates microorganisms, their toxins or other products of tissue disintegration to distal locations.

The focal infection theory is ancient and was described (Ebers și Ninive – 650 î.e.n) when it was reported the cure of some organic disease after treating the focus of infection. Later on authors like Kocher (1828), Possler (1906) and Billings (1912) spoke in their articles about the implications of the focal infection in development and sustainance of certain systemic conditions. The Romanian School of Medicine (professors Goia, Hațeganu and Moga from Cluj –in 1930's) introduced and developed the focal infection theory publishing a complete set of papers regarding rheumatic fever induced by of focus of infection.

In this so called foci are mainly identified streptococcus species with variate biologic features, partially acquired through their prolonged existence into organism. The dissemination of microorganisms or their toxins can initiate, sustain, or worsen systemic diseases. In other words, any chronic infection, regardless of its location in the body, can act at some point as a focus of infection.

In view of the above and analysing existing literature data, currently we cannot talk yet about a complete classification. Current medical practice shows that the sites particularly susceptible to focus of infection are the following:

- tonsills – being the most comun focal infection called tonsillar foci;
- facial sinuses: maxillary, ethmoidal, frontal – rhinosinusal foci;
- middle ear – ear foci;
- teeth – dental foci;
- tracheobronchial tree – bronchopulmonary foci;

- gall bladder - gallbladder foci;
- digestive system – intestinal foci;
- urinary tract – anaxial foci

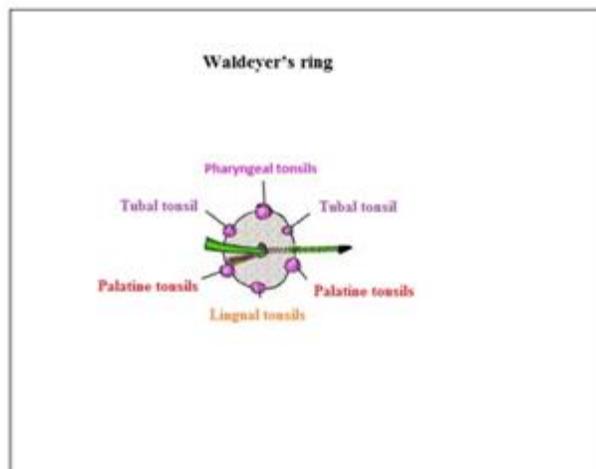
and the list could continue because, as we have seen earlier, any cutaneous or visceral infection can become at a time a focus of infection.

We must underline the fact that over 90% of the foci are located at the cephalic extremity, the most aggressive being the tonsillar, dental and sinusal foci.

The tonsillar focal infection is one of the most frequent foci, accounting about 60-70% of the cases.

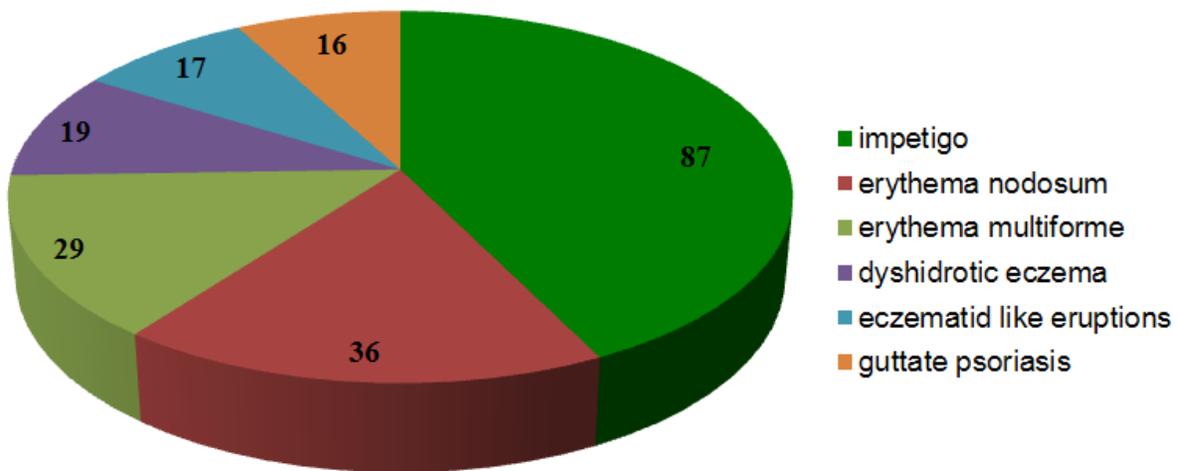
In the pharynx, the lymphoid tissue implicated in the immune response of the body is describing an annular arrangement (Waldeyer's lymphatic ring) composed of large lymphoid aggregates called tonsills, with lymphoid follicles dispersed into the pharyngeal mucosa.

Waldeyer's ring consist of two parts: a inner ring and a outer ring. The cervical lymph nodes form the outer ring, while the inner ring is composed of: Luschka's pharyngeal tonsils, Gerlach's tubal tonsil, palatine tonsils, Francke's lingual tonsils. All these structures are interconnected and represents secondary lymphoid organs producing lymphocyte T cells implicated in cell-mediated immunity and lymphocyte B cells implicated in immune mediated response by producing antibodies like IgG, Ig A and Ig M.



In the second part of my paper, which contains the personal contributions, we started to correlate the tonsillar focal infection with the cutaneous manifestations, conducting a complex retrospective and prospective study, which consisted of 204 cases with various pathology, represented by patients who checked in and outpatients' dermatology department of Craiova, over a period of 3 years (2010-2012). Based on the diagnosis, our cases were distributed as following:

- impetigo occupying the first place with 87 patients accounting for almost half of the study group;
 - second is erythema nodosum with 36 cases;
- and in descending order:
- erythema multiforme – 29 cases;
 - dyshidrotic eczema – 19 cases;
 - eczematid like eruptions – 17 cases;
 - guttate psoriasis – 16 cases. (see graph 1)

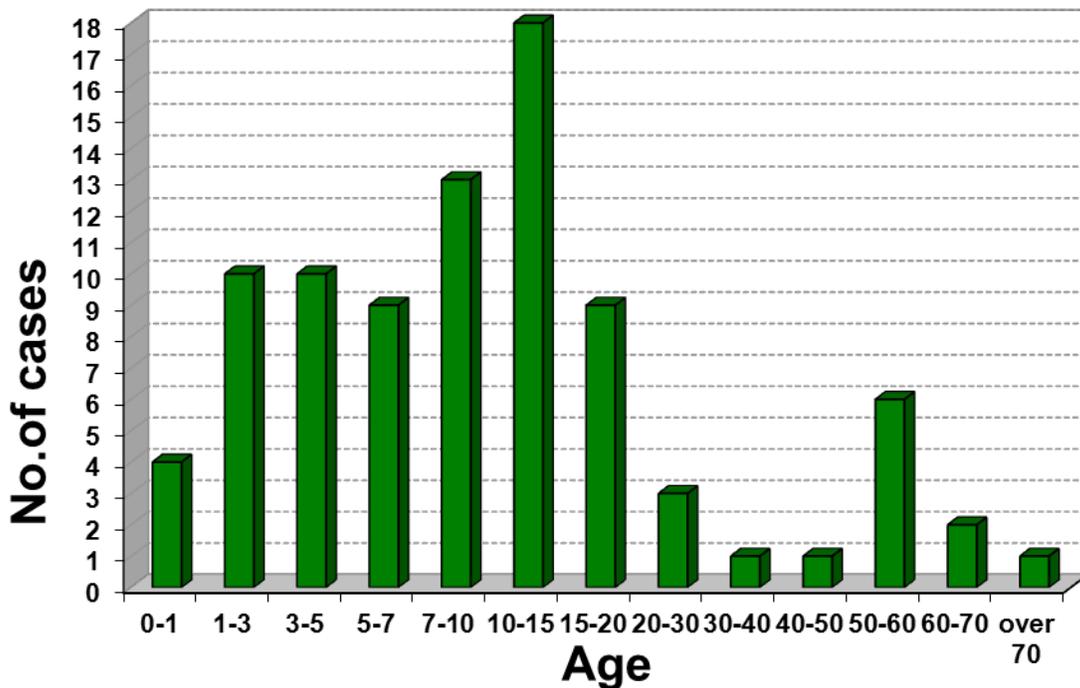


Graf. 1 Patients' distribution according to cutaneous manifestation

As we have seen, the pathology related to focal infections includes many other cutaneous manifestations (erythroderma, eczemas especially nummular eczema, pityriasis lichenoides chronica, etc) but we didn't take them into account because they didn't occur in our study group.

Regarding impetigo's distribution we can conclude:

- The distribution by age is very important because is more than obvious that most of the patients, meaning 64 from 87 counting over 70% (73,56%) are under the age 15. (see graph 2)

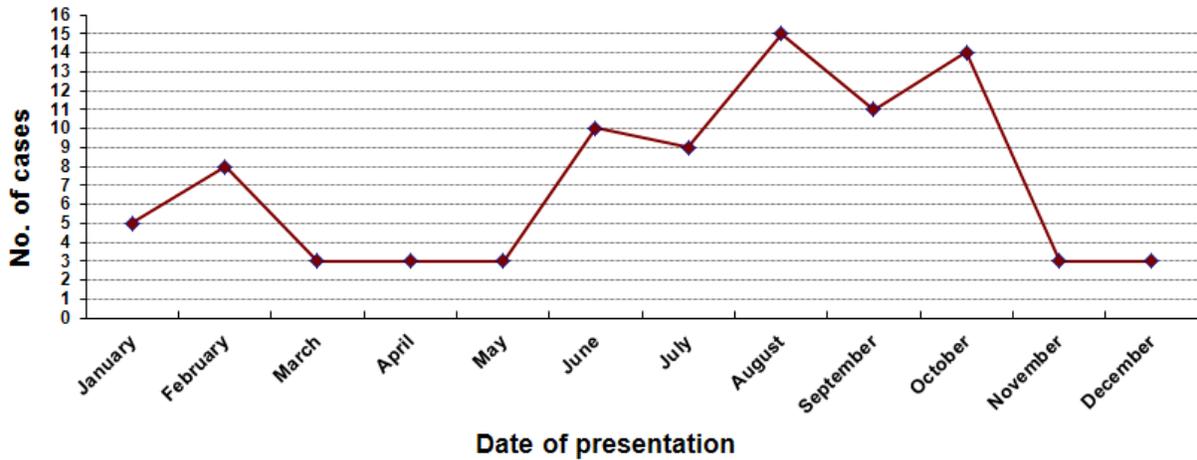


Graph. 2 Patients' distribution by age

- The patients' distribution by sex showed no statistically significant differences (42 females and 45 men), although is slightly more common in men (51,72% towards 48,27%) . The studies conducted for a long period confirm this fact.

- According to check-in date, the number of cases is highest in the summer and autumn period and lower in spring, opposite to our expectations. For example, in March, April

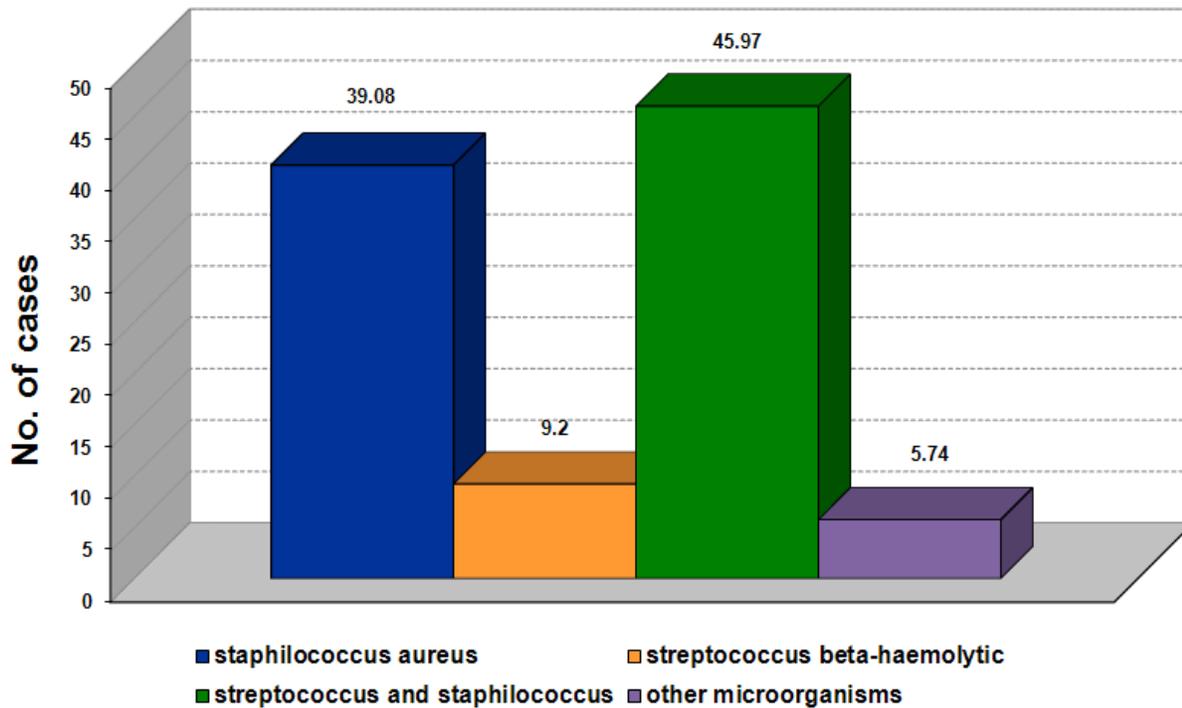
and May, the overall cases were 9, meaning 10,34% in comparison with June, July and August when were registered almost 4 times more cases (39,08%). If we add the other 25 cases registered in September and October (28,73%) to the latter, we notice that approximately 70% of the cases presented to the doctor in this period. (see graph 3). These clinical – statistical data seems unreal, but it is important to underline that specialized literature reports superimposable values.



Graph. 3 Patients' distribution by date of presentation

The bacteriological investigation shows:

- staphylococcus aureus in pure culture in 34 patients (39,08%)
- streptococcus beta-haemolytic in pure culture in 8 patients (9.19%),
- both bacteria in 40 patients (45,97%)
- in 5 patients (5,74%) were discovered other microorganisms (other staphylococci types, corynebacterium, candida, etc) (see graph 4).



Graf. 4 Bacteriological investigation results

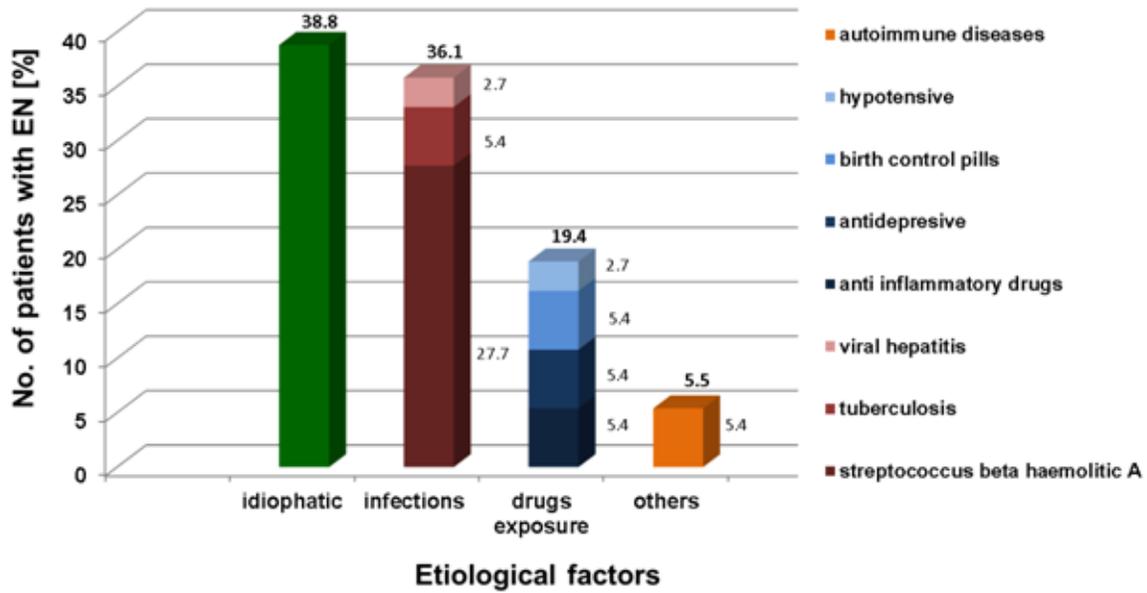
The group with erythema nodosum (EN) consisted of 36 patients, aged 16 – 76 years, the majority being owned by patients aged between 18 and 34 years. It's important to mention that nearly all were females, 33 cases (91,6%).

In more than a third of the cases studied we couldn't identify the etiologic agent, the rest of the cases being distributed as following:

- infections: post-streptococcal EN was responsible for 10 out of 13 infections, the other being diagnosed with EN secondary to ganglionic and pulmonary tuberculosis and another with HBs antigen and HCV antibodies present.

- in 7 cases (19,4%) EN secondary to chronic drug exposure. Drugs responsible for inducing EN were found to be: anti-inflammatory drugs, birth control pills, antidepressive drugs, hipotensors.

- other causes: 1 case of chronic lupus erythematosus, 1 case of hypothyroidism (Hashimoto's thyroiditis). (see graph. 5)



Graph. 5 Cases distribution according to etiological factors

Regarding erythema multiforme, this condition with extremely variable clinical appearance, was represented in our study group by 29 patients, showing almost all the clinical presentation described in literature, ranged from minor papulovesicular eruptions located on the photoexposed areas to severe forms with mucosal involvement and extended lesions like ectodermosis pluriorificialis or Steven Johnson syndrome. Statistically, the majority of the cases occurs in adults, whereas 72.4% of the patients were aged between 21 and 60 years, meaning that were exposed to most of the etiologic factors. It's important to mention that there are no significant differences concerning the distribution by age and by area of residence.

We also been interested in discovering conditions induced by streptococcal tonsillar infection and we found 3 cases with repeated pharyngotonsillitis and 3 cases with acute infections of the upper respiratory tract.

The cases with dyshidrotic eczema studied (19 cases) displayed lesions on the palms (16 cases), 3 of them reporting feet involvement. These data confirms the rarity of the cases which presents eruption affecting both the hands and feet. In 6 cases the patients recalled repeat pharyngotonsillitis, some being treated more or less empirically, other being neglected for a long period.

We must stress that 7 out of all 19 cases presented interdigital tinea pedis, some patients completely ignoring these manifestation.

The 17 cases with eczematid-like eruptions could be correlated with streptococcal and staphylococcal focal infections. Between them the pityriasiform and microbial eruptions were the most, each with 5 cases, followed by seborrheic eruptions with 4 cases and last psoriasiform eruption with 3 cases. The distribution by age, area of residence and sex has nothing specific whereas this has no relevance.

Another clinical entity, being a part of our study, was represented by the 28 cases of psoriasis, aged under 20 years from which 16 cases presented with classic form of guttate psoriasis. From those, in 9 cases we were able to demonstrate the presence of tonsillar focal infection. These data was verified along time by the beneficial effect that tonsillectomy may have on different variants of psoriasis, especially in streptococcal carrier and in patients with recurrent streptococcal pharyngitis or tonsillitis.

That being mentioned, we recommended tonsillectomy to all guttate psoriasis cases associated or not with hypertrophic tonsils and frequent relapses.

Based on our results and on clinical observations supported by de statistical data and inonography, we conclud:

1. Our study reveals the leading role played as an etiologic factor by the focal infection. The large number of these clinical manifestation with unpredictable evolution, with tendency to relapse and sometimes difficult to treat, confirms the practical significance of this paper for the practitioner regardless of his specialisation.

2. The large number of patients studied, accounting over 200 people, allowed us to obtain accurate results, the majority being superimposable with the specialised literature data, noting that the study group was heterogeneous, aged between 2 months and 76 years.

3. Considering the theme of our paper, we tried to find in each case a correlation between a focal infection and the cutaneous manifestation and we always noticed the sequence between the focus of infection and clinical skin lesion, highly variable in time, with worsening of the local phenomena whenever the activation of the foci occurred.

4. Given the importance of the bacteriological investigation especially in cases of impetigo, we managed to identify in more than a third of the cases (40%) *Staphylococcus aureus* in pure culture, streptococcus beta-haemolytic in pure culture in 9%, and mixed infection in 46%.

5. The bacteriological data allowed us to notice that staphylococcal involvement in triggering impetigo is not mandatory, the bacterium being present in cultures due to its high virulence by developing exotoxin that inhibits the growth of streptococci.

6. In chronic infectious foci developed streptococcus species with variate biologic features, partially acquired through their prolonged existence into organism. Those bacteria can initiate systemic diseases and/or dermatological symptomatology (sometimes discrete) according to patient's immune system. In other words, any chronic infection, regardless of its location in the body, can act at some point depending on patient's immunity as a focus of infection.

7. Erythema nodosum represented in our study by 36 cases, exceeded by a multitude a etiologic factors often impossible to identify. Concerning the subject of my paper, we were able to demonstrate that streptococcal infection was responsible for almost one third of cases (27,7%).

8. The predilection of erythema nodosum for females (91,6%) was partially explain by the large consumption of drugs, the self medication custom, associated with an impressive variety of pathologies, and/or the worldwide usage of birth control pills, that are known to produce a lot of side effects.

9. Erythema multiforme is a condition with a incompletely understood etiopathogenesis, being ultimately considered a cutaneous and mucosal reaction triggered by a variety of stimuli: acute and chronic infections, repeated drug administration, prolonged corticotherapy, immunosuppression, collagen diseases, etc which appears to be a delayed hypersensitivity cell mediated reaction (type IV).

10. The recurrences of erythema multiforme at the same individual, in the following years, usually in spring, can't be etiopathogenically classified for now.

11. Taking into consideration that aproximatevely one third of the cases were preceded by herpes virus infection type I or II, it worth trying prophylactic measures for 6-12 months by reccomanding immunomodulators.

12. Dyshidrotic eczema has a multifactorial etiology (unknown cause) which contribute in different ways from case to case both endogenous and exogenous factors.

13. Regarding the etiopathogenesis of our 19 cases we mention:

- Streptococcal and staphylococcal infections were responsible for aproximatevely one third of the cases, figures much higher than those reported in the specialised literature

- Cutaneous hypersensibility reported by most patients is due to the atopic dermatitis identified in more than a half of cases.

14. Eczematid like eruptions represent cutaneous manifestations frequently induced by a focus of infection, with similar clinical appearance, without subjective symptoms and highly variable evolution. The proposed classification is incompletely justified and difficult to make mainly due to the clinical resemblance and because they constantly change aspect day by day.

15. Our cases match the current classification and are distributed like following:

- pityriasiform eruptions - 5 cases;
- psoriasiform eruptions – 3 cases;
- seborrheic eruptions - 4 cases
- microbial eruptions -5 cases.

16. Regarding psoriasis, our data shows 28 cases of psoriasis, aged under 20 years from which 16 cases presented with classic form of guttate psoriasis (tear drop or rain drop psoriasis). From those, in 9 cases we were able to demonstrate the presence of streptococcal

tonsillar infection; the treatment of the focus of infection led to remission of the psoriatic eruption.

17. Both our data and specialised literature mention the beneficial effect of tonsillectomy in improving psoriasis and/or long term antibiotic treatments.

18. In cases with guttate psoriasis we consider that a local and systemic treatment addressing both rash and combating any infectious process is mandatory even if it does not fit perfectly into the classic definition of a focus of infection.

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