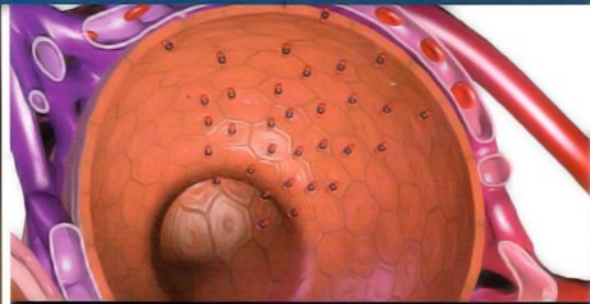


MEDICAL UPDATES



Issue No.:2 July 2010



**Antileukotriene Drugs in
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Safety in
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Control in Dental Health-
Care Settings**



Pregnancy outcome following gestational exposure to azithromycin

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Background: Azithromycin is an azalide antibiotic with an extensive range of indications and has become a common treatment option due to its convenient dosing regimen and therapeutic advantages. Human studies addressing gestational use of azithromycin have primarily focused on antibiotic efficacy rather than fetal safety. Our primary objective was to evaluate the possibility of teratogenic risk following gestational exposure to azithromycin.

Methods: There were 3 groups of pregnant women enrolled in our study: 1) women who took azithromycin. 2) women exposed to non-teratogenic antibiotics for similar indications, and 3) women exposed to non-teratogenic agents. They were matched for gestational age at time of call, maternal age, cigarette and alcohol consumption. Rates of major malformations and other endpoints of interest were compared among the three groups.

Results: The outcome of 123 pregnancies with gestational use of azithromycin was ascertained as well as 123 in each of two comparison groups. In the azithromycin group, 88 (72%) exposures occurred during the first trimester, 23 (19%) in the second trimester, and 12 (9%) in the third trimester. Five women used the drug more than once, due to recurrent infections during the pregnancy.

The indication for azithromycin use among the exposed group, were for the most part, respiratory infections (82%) including bronchitis, sinusitis and pneumonia, whereas only 18% of the women used azithromycin for genitourinary infections. Treatment for chlamydia was with a single one-gram oral dose of azithromycin, with no further recurrences. The average treatment for URTI's was for 5 days: day one 250 mg 2/d and day 2-5 250 mg 1/d. There were no differences in the maternal characteristics between the study group and the two comparison groups.

Gestational exposure to azithromycin is not associated with an increase in the rate of major malformations above the baseline of 1-3%.

Table 1: Pregnancy Outcomes

Variables	Azithromycin		Disease-matched		Non-teratogens		Azithromycin vs. antibiotics		Azithromycin vs. Non-teratogens		Three groups	P-value overall
	N	%	N	%	N	%	χ^2 (df = 1)	P	χ^2 (df = 1)	P	χ^2 (df = 2)	P
Live Birth	113	91.9	117	95.1	114	92.7	0.01	0.92	0.95	0.33	0.58	0.75
SA	6	4.9	3	2.4	8	6.5	0.92	0.34	0.04	0.85	2.34	0.31
Fetal Distress	19	16.8	24	20.5	26	22.8	5.70	0.02	0.64	0.42	1.72	0.42
Major malformation	3	3.4	2	2.3	3	3.4						0.89
	Mean	SD	Mean	SD	Mean	SD					χ^2 (df = 2)	
Gest age @ birth (wks)	39	2	39	2	40	1					0.56	0.76
Birth wt (g)	3460	587	3522	491	3546	501					1.29	0.52

The outcomes in the exposed group were 113 live births; 6 spontaneous abortions; 3 fetal deaths and 1 therapeutic abortion (for which no anomalies were detected). There were no significant differences in the rates of major malformations between women exposed to azithromycin (3.4%), and those in the disease-matched and non-teratogen (2.3% and 3.4%, respectively). Table 1 The details of the major malformations are documented in Table 2. Of note, the three malformations in the exposed group, were in the children of mothers who were treated with azithromycin for URTI. Statistical analysis of secondary outcomes did not detect differences among the three groups in terms of pregnancy

outcome, fetal distress, preterm delivery rates, and mean birth weight. Table 1

Table 2: Malformations

AZITHROMYCIN-EXPOSED GROUP	<ul style="list-style-type: none"> • Sensory neural deafness (profound congenital) • Tracheomalacia, incompetent oesophageal sphincter and gastroesophageal reflux
DISEASE-MATCHED GROUP	<ul style="list-style-type: none"> • Congenital diaphragmatic hernia • Ductus arteriosus persistence • Hydronephrosis of the left kidney • VSD
NON-TERATOGEN GROUP	<ul style="list-style-type: none"> • Hypospadias • Diaphragmatic hernia

Conclusion: The results of this prospective study of 123 pregnant women exposed to azithromycin do not suggest that there is a greater risk for major malformations above the baseline rate of 1%–3%. This evidence-based data will be particularly useful for health care providers in their decision making, regarding the treatment of pregnant women for infections such as chlamydia when azithromycin is considered to be the drug of choice.

Antileukotriene drugs in the treatment of asthma

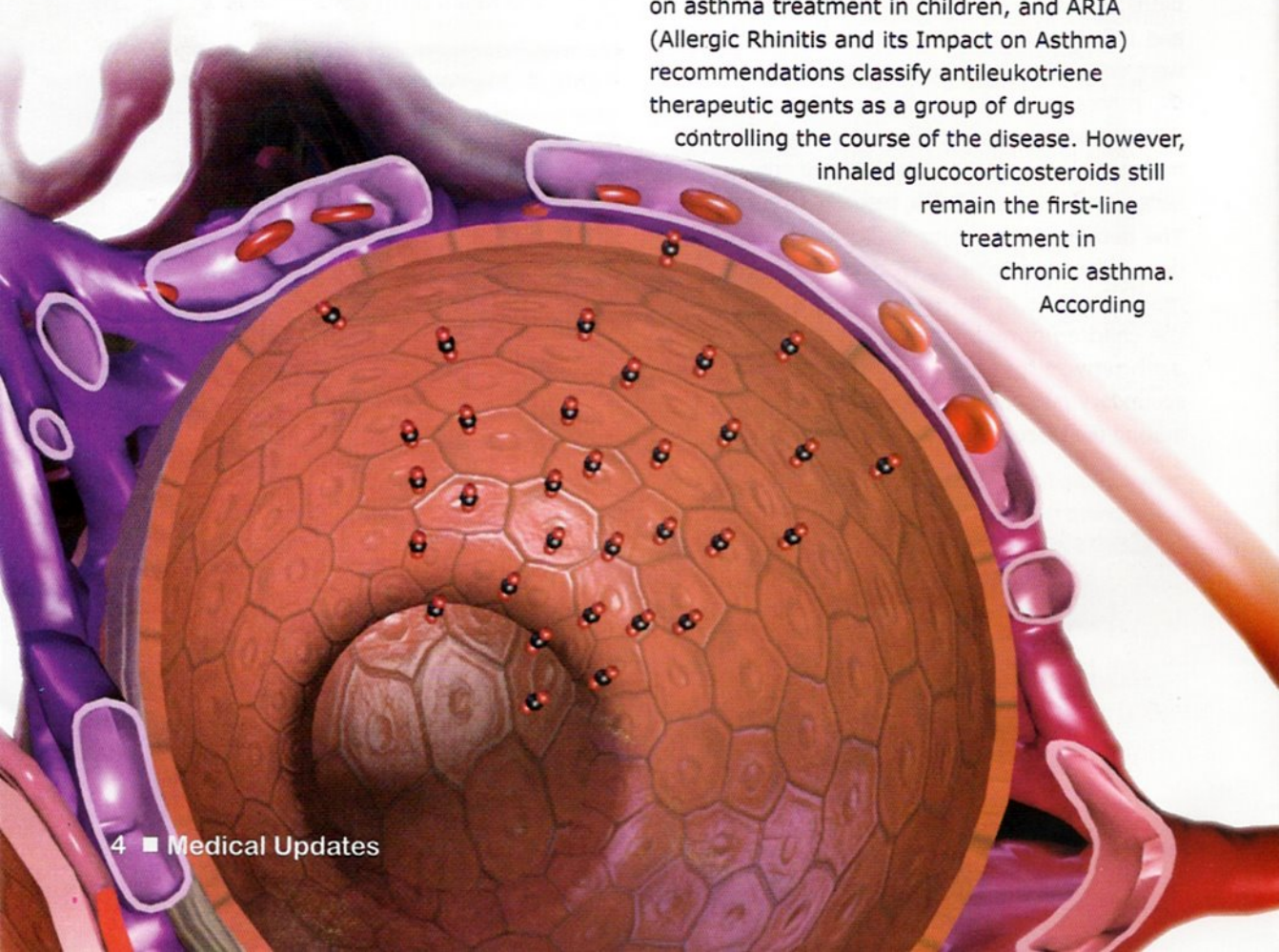
Lucyna Mastalerz; Jagoda Kumiłk

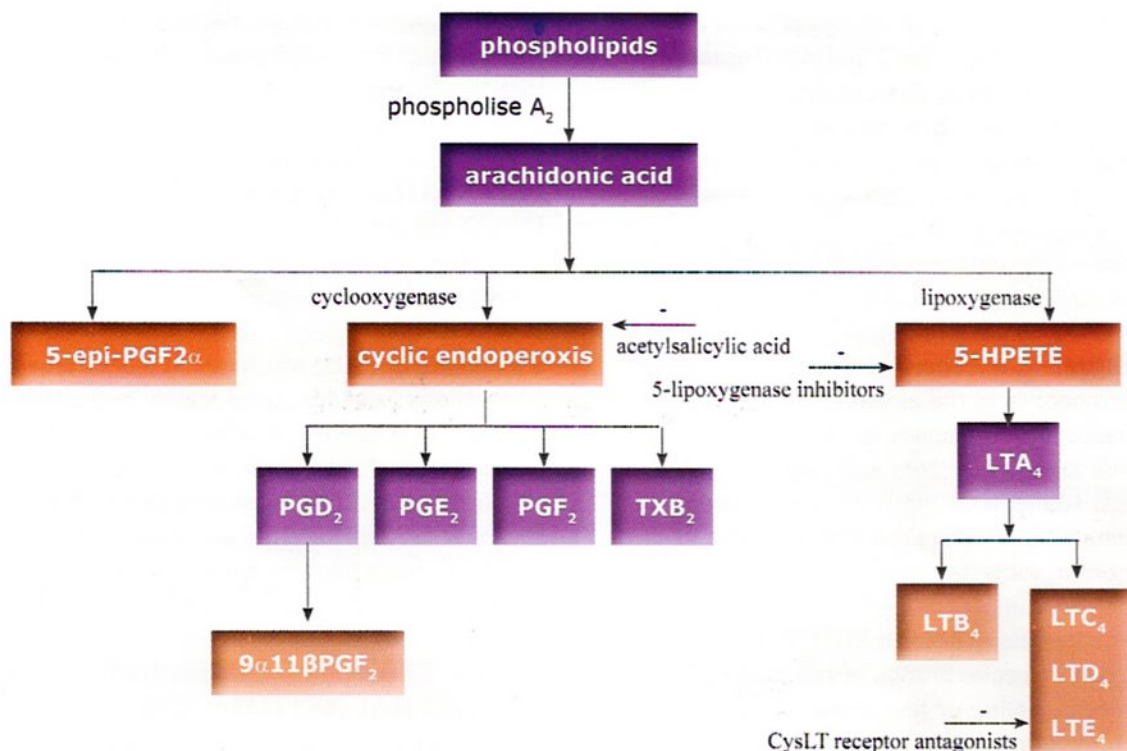
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Recommendations classify antileukotriene therapeutic agents as a group of drugs controlling the course of the disease.

ABSTRACT

Antileukotriene medications that have been implemented into clinical practice of bronchial asthma and allergic rhinitis include specific leukotriene receptor antagonists (montelukast, zafirlukast, pranlukast) and leukotriene biosynthesis inhibitors (zileuton). The current GINA (Global Initiative for Asthma) guidelines, the PRACTALL (Practicing Allergology) report on asthma treatment in children, and ARIA (Allergic Rhinitis and its Impact on Asthma) recommendations classify antileukotriene therapeutic agents as a group of drugs controlling the course of the disease. However, inhaled glucocorticosteroids still remain the first-line treatment in chronic asthma. According





to current guidelines, antileukotriene drugs are recommended as alternative treatment to low-dose inhaled glucocorticosteroids in the second level of asthma severity and as complementary treatment to inhaled and/or oral glucocorticosteroids, starting from the third level of asthma severity. Recently, clinical efficacy of antileukotriene drugs has been suggested in the treatment of isolated allergic rhinitis, chronic cough in the course of asthma, as a sole symptom of the disease, and as the therapy for episodes of wheezing caused by viral infections.

LEUKOTRIENES AS MEDIATORS OF ASTHMA

Leukotrienes are biologically active 5-lipoxygenase (5-LO) lipid mediators of arachidonic acid (FIGURE). They include 2

classes: an unstable leukotriene A4 (LTA4), which is further converted into leukotriene B4 (LTB4), and a separate category of leukotrienes that contain cysteine and are termed collectively as cys-LTs – leukotriene C4 (LTC4), D4 (LTD4), and E4 (LTE4). Cys-LTs can be produced via 5-LO pathway by a variety of inflammatory cells such as eosinophils, basophils, alveolar macrophages, monocytes, and mast cells. Endothelial cells do not express 5-LO but contain LTC4 synthase and can therefore participate in leukotriene production via a transcellular mechanism.

Eosinophils and mast cells produce mainly LTC4, while neutrophils – LTB4. Cys-LTs, which cause bronchoconstriction in asthma patients and are a potent chemoattractant for leukocytes (LTB4), exert their biological

actions through interactions of specific receptors. There are 2 separate receptors for cys-LTs called Cys-LT1 and CysLT2. Bronchoconstriction induced by cys-LTs appears to be caused by selective activation of the CysLT1 receptors. Growing evidence suggests that leukotrienes play an important role in the pathogenesis of bronchial asthma and allergic rhinitis. They cause smooth muscle contraction, impair mucociliary clearance, enhance mucus secretion, attract eosinophils to the airways, and increase vascular permeability producing edema. Moreover, in patients with asthma, the airways are 100 to 1000 times more sensitive to inhaled LTD4 and LTE4 than the airways of normal subjects.

Furthermore, inhaled LTC4 and LTD4 increase bronchial reactivity to methacholine or histamine. Such response to exogenous leukotrienes indicates the biological role of these compounds in asthma. In addition, leukotrienes have been identified in urine, plasma, nasal secretions, induced sputum, and bronchoalveolar lavage fluid from patients with asthma. Urinary LTE4 measurements can be used to monitor systemic production of cys-LTs. During spontaneous exacerbations of bronchial asthma, following exercise, allergen, and aspirin challenge, urinary LTE4 excretion increases.

The effects of leukotriene biosynthesis inhibitors (inhibitors of 5-LO) or specific leukotriene receptor antagonists in patients with asthma have suggested that interventions in the 5-LO pathway may be of therapeutic use in the treatment of asthma and rhinitis. These drugs inhibit not only the early but also

the late phases of allergic response, which implicates an anti-inflammatory component of such treatment.

CLINICAL DIVISION OF ANTILEUKOTRIENE DRUGS USED IN ASTHMA AND RHINITIS

Antileukotriene drugs used in asthma and rhinitis include:

- 1 inhibitors of 5-LO, which inhibit leukotriene biosynthesis: zileuton, used mainly in the USA
- 2 CysLT1 antagonists: montelukast, zafirlukast, and pranlukast, which is used mainly in Japan. Still investigated (not yet in clinical practice) are the so called FLAP inhibitors that inhibit the 5-LO-activating proteins.

LONG-TERM TREATMENT OF BRONCHIAL ASTHMA AND RHINITIS VS. ANTILEUKOTRIENE DRUGS

The current GINA (Global Initiative for Asthma) guidelines, the PRACTALL (Practicing Allergology) report on asthma treatment in children, and ARIA (Allergic Rhinitis and its Impact on Asthma) recommendations classify antileukotriene therapeutic agents as a group of drugs controlling the course of the disease. The choice of medication used in long-term asthma management depends on the level of disease control.

From a clinical point of view, the most significant problem concerns the possibility of applying antileukotriene drugs in the long-term treatment of asthma. Depending on life activity limitation, day and night symptoms, need for use of a short-acting β_2 -agonist, lung function (peak expiratory

flow/forced expiratory volume in 1 second [PEF/FEV₁]), and the number of exacerbations requiring treatment intensification, asthma can be divided into:

- 1 controlled
- 2 partly controlled
- 3 uncontrolled, which may cause exacerbation of the disease.

Similar criteria are applied to assess the efficacy of treatment (including antileukotriene agents) in the long-term management of asthma. According to the GINA guidelines, 5 steps in the intensity of asthma management can be distinguished depending on the severity level of asthma and its control. In all steps a short acting β_2 -agonist may be used as needed:

step 1

- short-acting β_2 -agonist as needed

step 2

- low-dose inhaled glucocorticosteroid **or**
- antileukotriene

step 3

- low-dose inhaled glucocorticosteroid plus long acting β_2 -agonist **or**
- medium- or high-dose inhaled glucocorticosteroids

or

- low-dose inhaled glucocorticosteroid plus antileukotriene

or

- low-dose inhaled glucocorticosteroid plus sustained release theophylline

step 4

- medium- or high-dose inhaled glucocorticosteroid plus long-acting β_2 -agonist plus antileukotriene

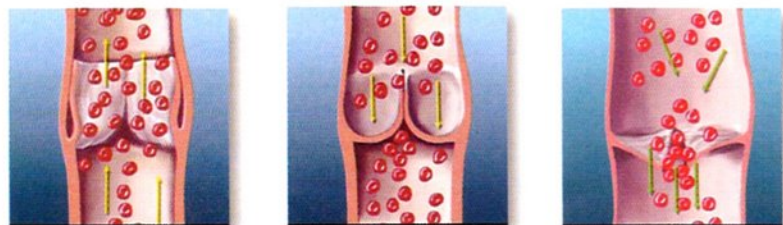
or

- medium- or high-dose inhaled glucocorticosteroid plus long acting β_2 -agonist plus sustained release theophylline

step 5

- same as step 4 and additionally oral glucocorticosteroid (lowest dose) and/or anti-immunoglobulin E antibodies.

Antileukotrienes are classified according to standing guidelines as a group of drugs controlling the course of asthma. However, inhaled glucocorticosteroids still remain the first-line treatment in chronic asthma. Antileukotriene agents are recommended as alternative treatment to low-dose inhaled glucocorticosteroids in the second level of asthma, or as complementary treatment to glucocorticosteroids, starting from the third level of asthma.



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The impact of psychosocial factors on adherence to compression therapy to prevent recurrence of venous leg ulcers

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AIMS: To identify self-care activities undertaken and to determine relationships between self-efficacy, depression, quality of life, social support and adherence to compression therapy in a sample of patients with chronic venous insufficiency.

BACKGROUND: Up to 70% of venous leg ulcers recur after healing. Compression hosiery is a primary strategy to prevent recurrence; however, problems with adherence to this strategy are well

documented and an improved understanding of how psychosocial factors influence patients with chronic venous insufficiency will help guide effective preventive strategies.

DESIGN: Cross-sectional survey and retrospective medical record review.

METHOD: All patients previously diagnosed with a venous leg ulcer that healed between 12-36 months prior to the study were invited to participate. Data on health, psychosocial

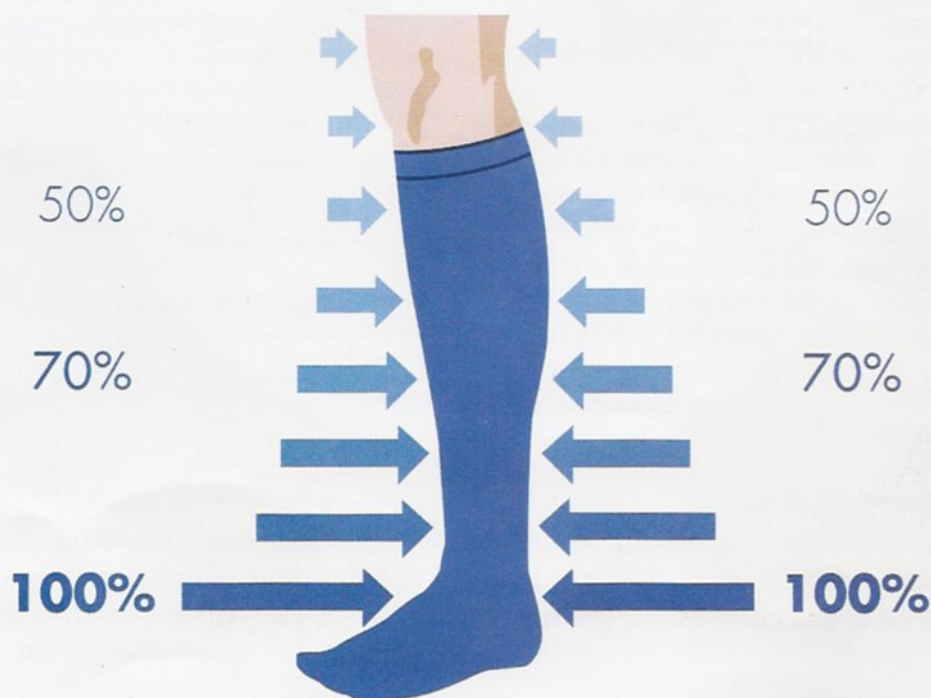
variables and self-care activities were obtained from a self-report survey and data on medical and previous ulcer history were obtained from medical records. Multiple linear regression modelling was used to determine the independent influences of psychosocial factors on adherence to compression therapy.

RESULTS: In a sample of 122 participants, the most frequently identified self-care activities were application of topical skin treatments, wearing compression hosiery and covering legs to prevent trauma. Compression hosiery was worn for a median of four days/week (range 0-7). After adjustment for all variables and potential confounders in a multivariable regression model, wearing compression hosiery was found to be significantly positively associated with participants' knowledge of the cause of their condition ($p = 0.002$), higher self-efficacy scores ($p = 0.026$) and lower depression scores ($p = 0.009$).

Depression is significantly related to adherence to compression therapy

CONCLUSION: In this sample, depression, self-efficacy and knowledge were found to be significantly related to adherence to compression therapy.

RELEVANCE TO CLINICAL PRACTICE: These findings support the need to screen for and treat depression in this population. In addition, strategies to improve patient knowledge and self-efficacy may positively influence adherence to compression therapy.



Medicina (B Aires). 2010;70(3):284-92.

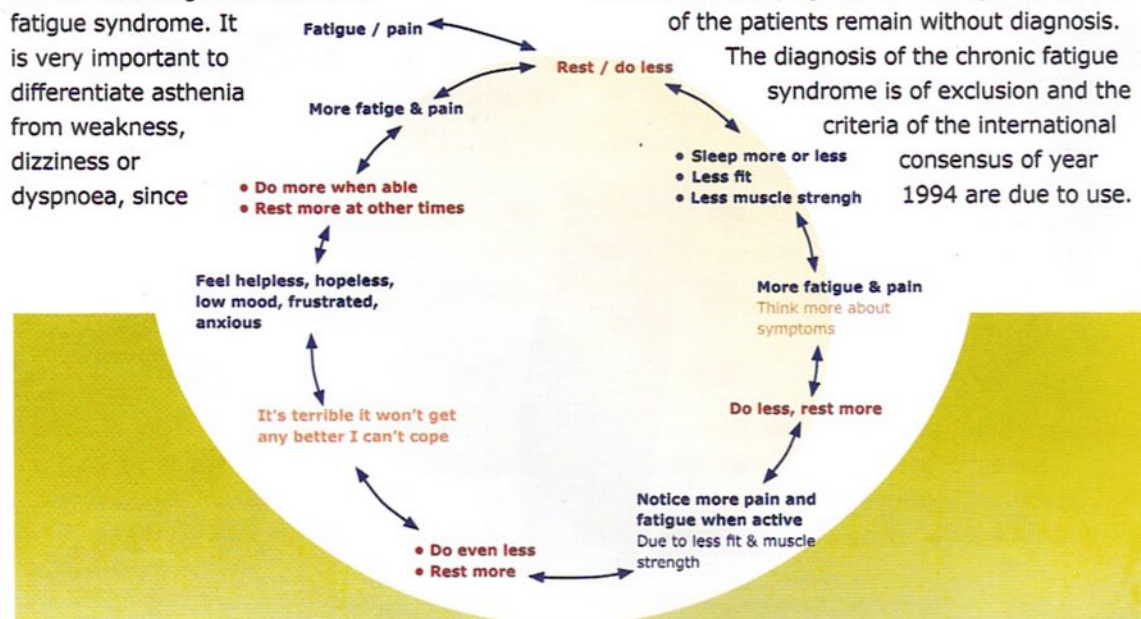
The chronic asthenia syndrome: a clinical approach

Young P, Finn BC, Bruetman J, Pellegrini D, Kremer A.

The term asthenia comes from the Greek (censqsneia, a: privation, without; esthénos: vigor, force), it means absence of strength, vigor or force. It is a symptom, difficult to define, with a set of vague sensations, different for each patient. It is a frequent cause of consult, almost 30% in ambulatory settings. The chronic fatigue represents up to 10% of these cases, and the 0.2-0.7% belongs to the chronic fatigue syndrome. It is very important to differentiate asthenia from weakness, dizziness or dyspnoea, since

patients may confuse them. The factor time in asthenia is very useful for its characterization, it was defined to the prolonged fatigue when it lasts for more than a month and chronic when the duration is greater than 6 months. The depression is the commonest fatigue cause, representing approximately half of the cases. The most effective treatment of the asthenia is to solve the underlying cause, although up to 20% of the patients remain without diagnosis.

The diagnosis of the chronic fatigue syndrome is of exclusion and the criteria of the international consensus of year 1994 are due to use.



The high frequency of the symptoms of chronic asthenia syndrome, entails an enormous social and economic cost. That's why it is so important for the physicians to have a correct management of these symptoms.

Guidelines for Infection Control in Dental Health-Care Settings



Clinical Contact Surfaces

Clinical contact surfaces can be directly contaminated from patient materials either by direct spray or spatter generated during dental procedures or by contact with DHCP's gloved hands. These surfaces can subsequently contaminate other instruments, devices, hands, or gloves. Examples of such surfaces include

- light handles,
- switches,
- dental radiograph equipment,
- dental chairside computers,
- reusable containers of dental materials,
- drawer handles,
- faucet handles,
- countertops,
- pens,
- telephones, and doorknobs.

Barrier protection of surfaces and equipment can prevent contamination of clinical contact surfaces, but is particularly effective for those that are difficult to clean.

Barriers include clear plastic wrap, bags, sheets, tubing, and plastic-backed paper or other materials impervious to moisture. Because such coverings can become contaminated, they should be removed and discarded between patients, while DHCP are still gloved. After removing the barrier, examine the surface to make sure it did not become soiled inadvertently. The surface needs to be cleaned and disinfected only if contamination is evident. Otherwise, after removing gloves and performing hand hygiene, DHCP should place clean barriers on these surfaces before the next patient. If barriers are not used, surfaces should be cleaned and disinfected between patients by using an EPA-registered hospital disinfectant with an HIV, HBV claim (i.e., low-level disinfectant) or a tuberculocidal claim (i.e., intermediate-level disinfectant).

Intermediate-level disinfectant should be used when the surface is visibly contaminated with blood or OPIM. Also, general cleaning and disinfection are recommended for clinical contact surfaces, dental unit surfaces, and countertops at the end of daily work activities and are required if surfaces have become contaminated since their last cleaning. To facilitate daily cleaning, treatment areas should be kept free of unnecessary equipment and supplies.

Manufacturers of dental devices and equipment should provide information regarding material compatibility with liquid chemical germicides, whether equipment can be safely immersed for cleaning, and how it should be decontaminated.

