

# **NUTRITIONAL AND PHARMACOLOGICAL MODULATION OF THE METABOLIC RESPONSE OF SEVERELY BURNED PATIENTS: REVIEW OF THE LITERATURE (part III)\***

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**SUMMARY.** Severe burn patients are some of the most challenging critically ill patients, with an extreme state of physiological stress and an overwhelming systemic metabolic response. Increased energy expenditure to cope with this insult necessitates mobilization of large amounts of substrate from fat stores and active muscle for repair and fuel, leading to catabolism. The hypermetabolic response can last for as long as nine months to one year after injury and is associated with impaired wound healing, increased infection risks, erosion of lean body mass, hampered rehabilitation, and delayed reintegration of burn survivors into society. Reversal of the hypermetabolic response by manipulating the patient's physiological and biochemical environment through the administration of specific nutrients, growth factors, or other agents, often in pharmacological doses, is emerging as an essential component of the state of the art in severe burn management. Early enteral nutritional support, control of hyperglycaemia, blockade of catecholamine response, and use of anabolic steroids have all been proposed to attenuate hypermetabolism or to blunt catabolism associated with severe burn injury. The present study is a literature review of the proposed nutritional and metabolic therapeutic measures in order to determine evidence-based best practice. Unfortunately, the present state of our knowledge does not allow the formulation of clear-cut guidelines. Only general trends can be outlined which will certainly have some practical applications but above all will dictate future research in the field.

## **Part III Introduction**

Part I and II of this review examined the energy and nutrient requirements of healthy and critically ill patients and the metabolic and hormonal changes following severe burn injury, as well as the nutritional and metabolic therapeutic measures that can be undertaken to counter the effects of hypermetabolism in severely burned patients. Part III explores immunonutrition, specialized nutrition support, and protective nutrients as well as ways to monitor nutritional support. In conclusion an attempt to establish evidence-based best practice guidelines is made.

### **Immunonutrition, specialized nutrition support, and protective nutrients**

An accumulating body of evidence in animal models suggests that the addition of specific micronutrients, in

amounts above the accepted daily requirements, to enteral formulations can improve outcome with regard to immune function, septic morbidity, and overall mortality.<sup>1</sup> Recognition of this fact has provided a major impetus for the critical examination of dietary approaches with single or multiple nutrient supplements chosen to modulate the inflammatory response, enhance immune function, or improve the intestinal mucosal barrier.<sup>141</sup> Patients suffering the effects of hypercatabolism caused by surgery, cancer, or extensive burns are prime candidates for immunonutrition, as the intervention has come to be known,<sup>81,141</sup> even though some of the specialized nutritional support formulations do not exert action exclusively on the immune system.<sup>81</sup> Although a host of nutritional additives have been examined, glutamine, arginine, eicosapentaenoic acid, and docosahexanoic acid, omega-3 fatty acids, omega-3 fatty acid derivatives, and nucleotides (RNA) have received the greatest attention. Immune-enhancing diets/agents may include also antioxidants such as ascorbic acid (vitamin C), alpha-tocopherol (vita-

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min E), vitamin A, and zinc.<sup>1,141-143</sup> Progress made in the last decade in understanding the biochemistry and pharmacology of micro- and macronutrients, coupled with the accelerated progress in the fields of molecular biology and immunology, has resulted in the emergence of strong rationales for the use of such protective nutrients.<sup>141</sup>

#### *Glutamine*

Despite being the most abundant amino acid in the body, glutamine appears to become conditionally an essential amino acid in metabolic stress and in various critical care states.<sup>1,144</sup> During the stress reaction that follows surgery, major trauma, or infection, glutamine is promptly mobilized from muscle stores, with a resulting marked decrease in muscle and plasma concentrations.<sup>141,145</sup> Depletion of plasma and muscle glutamine is observed in acute burn injury contributing to muscle wasting, weight loss, and infection.<sup>144</sup> In addition to being used as a metabolic substrate by the intestine, glutamine is the major fuel source used at high rates by lymphocytes, neutrophils, and macrophages.<sup>146</sup> A deficiency of it can thus not only compromise the barrier function of the intestinal epithelium but also impair immunological function.<sup>1</sup> Interest in glutamine has grown out of the information linking this branched-chain amino acid to important biochemical cycles involved in the generation of crucial intermediates in purines, pyrimidines, glutathione, gamma-aminobutyric acid, and nucleotide synthesis. Glutamine also plays an important role in acid-base homeostasis by providing the backbone for ammonium generation in the kidney. In addition, it is a ubiquitous inter-organ nitrogen transporter.<sup>141,145</sup> Furthermore, it is now postulated that glutamine plays a role in intestinal surface integrity through its contributions to mucin formation via the synthesis of *N*-acetylglucosamine and *N*-acetylgalactosamine.<sup>141,147</sup> In burn patients, glutamine supplementation ameliorates wound healing, improves gut permeability, decreases plasma endotoxin levels, and results in a significant decrease in the incidence of gram-negative bacteraemia in severe thermally injured patients,<sup>148-151</sup> it is also associated with a reduction in the length of hospitalization and lower costs.<sup>150</sup> Systematic reviews and practice guidelines generally support glutamine supplementation in critical illness but vary in the level of recommendations for its use in burns.<sup>144</sup> The justification and safety of long-term glutamine supplementation are yet to be established.<sup>144</sup>

#### *Arginine*

Arginine is another nonessential amino acid that can become conditionally essential under conditions of stress and sepsis.<sup>1</sup> The metabolism of arginine, a dibasic amino acid, is closely related to that of glutamine. After glutamine is converted to citrulline in the intestine, this amino acid

is released into the portal circulation and later to the kidneys, where it undergoes transformation to arginine, an integral component of the urea cycle.<sup>141</sup> Arginine serves multiple roles in the pathophysiological response to burns.<sup>152</sup> Considering the wide range of vital metabolic activities for which arginine is needed, it is not surprising that supplementation with this amino acid was undertaken by nutritional scientists and clinical investigators seeking to enhance the immune competence of a host.<sup>141</sup> Administration of pharmacological doses of arginine has been shown to enhance the secretion of many hormones, including growth hormone, insulin-like growth factor, pituitary growth hormone, prolactin, and others. It is also a precursor for the synthesis of nitrates, nitrites, and nitric oxide, which seems to play an important role in macrophage-killing capacity.<sup>1</sup> In the early resuscitation stages of severe burn patients, the administration of enteral L-arginine effectively inhibits excessive increase in nitrogen monoxide (NO) level, improves blood supply to tissues, promotes oxygen transportation and metabolism, and alleviates the occurrence and damage of recessive shock.<sup>152</sup> Evidence regarding the use of arginine supplementation in enteral and parenteral solutions indicates that recommendations cannot be generalized from one population to another or from one catabolic state to another.<sup>141</sup> Because arginine can functionally be considered a pro-inflammatory substrate, much care is needed to avoid enhancing an immune response that could be deleterious in a given clinical setting (e.g., in disseminated sepsis).<sup>141</sup>

#### *Long-chain polyunsaturated fatty acids: eicosapentaenoic acid (EPA) and docosahexanoic acid (DHA)*

The omega-3 fatty acids (the so-called fish oils) have a number of advantageous properties compared with the more commonly used omega-6 fatty acids (vegetable oils). The latter are generally considered immunosuppressive (inhibiting antibody formation, lymphocyte and macrophage activity, and T-suppressor cell proliferation), whereas the former are less inflammatory and more immunostimulatory.<sup>1</sup> Omega-3 polyunsaturated fatty acid (PUFA) derivatives, specifically, eicosapentaenoic acid and docosahexanoic acid, have been studied extensively.<sup>141</sup> Their various biological effects on immune cells, vascular endothelial cells, and other tissues are thought to result, in part, from alterations in membrane lipid composition that affect the binding of ligands or signalling molecules. Furthermore, omega-3 PUFAs affect the expression of genes involved in immune modulation.<sup>141,153</sup> An important result of membrane enrichment with PUFAs is the increased susceptibility to lipid peroxidation, a factor that increases the requirement for antioxidants such as vitamin E, selenium, and vitamin C.<sup>141,154</sup> Enthusiasm surrounding the use of omega-3 PUFAs as immunomodulators, anti-cancer agents, and anti-inflammatory agents has been tempered by sev-

eral studies documenting possible detrimental effects.<sup>142</sup> Further studies are necessary to determine the appropriate amounts and proportions of PUFAs to total dietary fat that will enhance the beneficial effects and avoid the suppression of the host's immune defences.<sup>141</sup>

*Ascorbic acid (vitamin C), alpha-tocopherol (vitamin E), vitamin A, and purine and pyrimidine nucleotides*

The impact of vitamin C on oxidative stress-related diseases is moderate because of its limited oral bioavailability and rapid clearance. Parenteral administration can increase the benefit of vitamin C supplementation as is evident in critically ill patients.<sup>154</sup> The use of high doses of ascorbic acid in experimental burn-injured sheep was associated with decreased oedema and fluid requirements.<sup>155</sup> In a randomized trial of critically ill surgical patients, a combination of ascorbic acid and alpha-tocopherol reduced the prevalence of organ failure and ICU length of stay.<sup>156</sup> Early use of high-dose antioxidant therapy in injured patients seems to be beneficial; however, further clinical trials are required to confirm this potential effect and better define the timing and the required dose.<sup>157,158</sup>

Vitamin A in all its chemical forms (retinoic acid, retinol, and retinal) participates in important metabolic steps involved in immune competence and mucosal integrity. Consequently, vitamin A insufficiency can result in a broader range of clinical manifestations.<sup>141</sup> The direct effects of vitamin A deficiency on immune function have been clearly demonstrated in animal models and translate into an increased vulnerability to infections: impaired B-cell-mediated immunity, inhibition of interferon production, interference with antigen presentation and immunoglobulin responses, and defective phagocytosis by neutrophils.<sup>159,160</sup> Furthermore, hypovitaminosis A has been associated with serious complications and increased mortality in specific situations.<sup>141</sup>

The purine and pyrimidine nucleotides (adenine, guanine, thymidine, and uracil), being precursors for DNA and RNA, appear to be essential for cell energetics (adenosine triphosphate) and may also play a role as physiological mediators (cyclic adenosine monophosphate). Administration of these agents improves natural killer cell activity and enhances resistance to infection.<sup>1</sup>

The currently existing medical literature regarding enhanced enteral formulations in severely injured patients is characterized by small numbers of inconsistently defined patients who receive various non-comparable nutritional formulas for variable periods of time.<sup>1</sup> As can be expected, the cost of such specialized immunomodulating formulas is high and can only be recommended widely if claims are irrefutably proven.<sup>141</sup> Promising results and overly optimistic conclusions from individual studies have been quickly tempered by meta-analyses that have provided a more critical assessment of the value of those interven-

tions.<sup>141</sup> Whether the enhancement of standard enteral formulas with any of these micronutrients is beneficial in humans, and if so, in which patient populations, remains unclear.<sup>1</sup> Multiple studies looking at a combination diet of these agents have failed to demonstrate a benefit in critically ill patients.<sup>142,143</sup> The controversy regarding the use of immune-enhancing diets is ongoing, with many studies showing benefit and others showing no improvement in outcome. For instance, whereas many previous studies support the use of glutamine supplementation, a recent study demonstrated that the addition of glutamine to enteral feed did not improve outcome.<sup>161</sup> Moreover, although many studies in burned animal models show improvement with a specific immune supplementation, there are no human studies investigating the response in a clinical setting. As an example, supplementation of burned rats with omega-3 fatty acids improved protein metabolism and attenuated muscle breakdown.<sup>162</sup> No large human trial has confirmed these findings in burned patients.<sup>142,163</sup> Most researchers agree that an indiscriminate use of a combination formula immunonutrition diet in critically ill patients is not beneficial.<sup>142,163</sup> Therefore, a more selective approach is proposed, and there is a need for more clinical studies. Until larger studies with improved methodology are completed, only a relatively weak recommendation can be made in severely injured patients for the use of enteral formulations enhanced by the addition of arginine and/or glutamine. The specific impact of further supplementation with omega-3 fatty acids, nucleotides, and trace elements cannot be determined at this time. Similarly, the current literature gives no support to recommendations regarding the use of enhanced enteral formulas in patients with severe burns.<sup>1</sup>

### Monitoring of nutritional support

Some form of nutritional monitoring is essential in severely burned patients.<sup>1</sup> Multiple diagnostic tests are available and have been proposed to monitor the response to nutritional support. For classification purposes, these tests can be placed into one of the following categories: body measurements (e.g., weight change, anthropometric determinations), body composition studies (e.g., determinations of body fat, lean body mass, total body water), urine analyses for metabolic by-products (e.g., urea, creatinine), immunological tests (e.g., antibody production, delayed hypersensitivity skin tests), functional tests (e.g., handgrip strength), and serum chemistry analyses (e.g., albumin, pre-albumin). Many of these tests are insufficiently sensitive or specific for clinical use in any patient population, whereas others have been used primarily in research settings.<sup>1,164</sup> Unfortunately, there is no single available measurement for evaluating accurately the appropriateness of the nutritional support and the short-term re-

sponse to nutrition therapy provided to the patient.<sup>1,165</sup> Most nutrition laboratory testing relies on serum concentrations of ingested nutrients, their coenzymes, proteins, or lipids. Alternatively, functional tests measure a specific physiological process or biochemical reaction.<sup>166</sup> However, to be valid, any test must take into account the unique hypermetabolic response of the burned patient and the massive fluid shifts that occur.<sup>1</sup>

Nitrogen balance is a widely used and valuable nutritional indicator in the critically ill and is believed to be the single nutritional parameter most consistently associated with improved outcomes.<sup>164</sup> Nitrogen balance determination, if performed correctly, is the best currently available means of assessing the adequacy of nutritional support and is the standard to which all other monitoring tests should be compared.<sup>1</sup> However, its accurate determination is fraught with difficulty, both in terms of ensuring complete collection of nitrogenous waste (e.g., urine, faeces, wound exudate) and in the mathematical computation resulting in significant overestimation in nitrogen balance, particularly in burn patients.<sup>1</sup> One factor contributing to negative nitrogen balance in burn patients is protein loss through the burn wound.<sup>167</sup> Protein losses are affected by dressing type as well as wound care, they fluctuate throughout the post-burn course and are very difficult to quantify.<sup>1</sup> They are greatest in the first three days post-burn, being somewhat greater in full-thickness burns ( $0.98 \pm 0.82$  mg/cm<sup>2</sup>/h) than in partial-thickness burns ( $0.59 \pm 0.41$  mg/cm<sup>2</sup>/h).<sup>167</sup> Average daily protein losses during the first week post-burn can be estimated by the following equation: 24-h protein loss through burn surface (g) = 1.2 x body surface area (m<sup>2</sup>) x percentage burn. On subsequent days, protein is lost at approximately half this rate.<sup>167</sup>

Visceral proteins concentrations have been proposed as predictors of nitrogen balance.<sup>168</sup> By far the most commonly assayed serum proteins used in nutritional monitoring are albumin, pre-albumin, transferrin, and retinol-binding protein. Other proteins that have been used for monitoring purposes include somatomedin C (IGF-I) and fibronectin.<sup>1</sup> However, the correlation between nitrogen balance and serum albumin did not prove to be significant.<sup>169</sup> Plasma retinol-binding protein and pre-albumin concentrations, on the other hand, change earlier than albumin and transferrin levels and appear to correlate better with nitrogen balance during nutrition therapy.<sup>165</sup> Although concentrations of these plasma proteins have been shown to be affected by stress and renal and hepatic disease, they appear to be more sensitive indicators of the adequacy of nutrition support than other more commonly used assessment parameters.<sup>165</sup> However, the statistically significant correlations found between nitrogen balance and serum thyroxine-binding pre-albumin (TBPA), retinol-binding protein, and transferrin, even for the best correlation (retinol-binding protein,  $r = 0.388$ ), are too weak to per-

mit prediction of nitrogen balance.<sup>169</sup> These proteins may reflect severity of injury and prognosis in critically ill hospitalized patients, but they often do not accurately reflect nutritional status or adequacy of nutritional support.<sup>1,168</sup> Depressed albumin and TBPA concentrations in burn patients over the duration of hospitalization appear to be affected not only by nutritional status and adequacy of nutritional support but also by the extent and severity of the thermal injury.<sup>1,168</sup> Although the measurement of these proteins is of little value in the initial nutritional assessment of the critically ill and although static measurements of serum concentrations may be unreliable indicators in burn patients, serial measurements, particularly of plasma pre-albumin, seem to correlate reasonably well with nitrogen balance determinations in trauma and burn patients and may be useful in monitoring the response to nutritional support.<sup>1,164,166</sup> Also, serial determinations serum levels of acute-phase reactants (e.g., C-reactive protein, fibrinogen, alpha-1-glycoprotein), along with constituent proteins (e.g., pre-albumin, retinol-binding protein, transferrin) may improve the value of nutritional monitoring tools,<sup>1</sup> although there is no evidence to suggest that this practice improves clinical outcome.<sup>1</sup> Although there is no evidence available to recommend how often monitoring should be carried out, it has been suggested that ongoing assessment of the appropriateness of nutritional support is crucial in avoiding under- or overfeeding.<sup>1</sup>

Stepwise multiple regression analyses performed to determine which indices are most closely correlated with nitrogen balance show that a calculation using readily available information (nitrogen intake, post-burn day, percentage total body surface burned, and age) provides better prediction of nitrogen balance ( $r = 0.765$ ) than any of the visceral protein concentrations.<sup>169</sup> Much work, however, remains to be done in the field of nutrition monitoring. Serum protein markers, because of their simplicity, ready availability, and relatively low cost, are likely to remain the mainstay of nutritional monitoring tests in the future. Prospective, randomized studies are needed to identify the optimal serum protein marker and the frequency with which it should be assayed.<sup>1</sup>

## Conclusion

Our present health care environment requires a clearer delineation of the indications for nutritional or metabolic support and for unequivocal demonstrations of efficacy with regard to decreasing costs and improving outcomes. Important issues that should be examined include: 1. the nature of injury and its time course, with the goal of minimizing the effects of nutritional, especially parenteral, interventions; 2. the effects of macronutrient administration on cellular biology and organ function during critical illness; and 3. the identification of groups of patients who

will benefit from the administration of specific nutrients or growth factors, who needs them, what kind, and when.<sup>1</sup>

How nutritional therapy may affect real clinical outcomes is not readily apparent from a superficial reading of current data.<sup>81</sup> Nevertheless, the hypermetabolic state cannot persist indefinitely without adversely affecting the patient's outcome.<sup>16</sup> Nutritional support, both enteral and parenteral, has evolved over the last 30 years, with new formulations that incorporate many components believed to decrease inflammation and enhance the competence of the gut in preventing bacterial translocation and septic complications, thus shortening length of hospitalization and intensive care needs.<sup>141</sup> The evidence demonstrating the importance of nutritional measures in preventing infection and enhancing recovery from infection is encouraging.<sup>81</sup> We can now be more confident that nutritional modification can influence the outcome of our patients. In the future, through nutritional genomics, we may even be able to identify the patients most likely to benefit. It is perhaps important now for us to address these demonstrated standards of care thoroughly (such as early enteral nutrition, good nutrient provision combined with glycaemia control, and parenteral glutamine) so that a sound interpretation of the clinical studies on new and expensive therapies can be made.<sup>81</sup>

Whether enteral nutrition, containing pharmac nutrients or not, is the magic bullet in the treatment of ICU patients has been studied during the past few years. Empirically, nutrition along with intensive care prevents the development of malnutrition and associated complications. During recent years it has become more obvious that a proper use of parenteral and enteral nutrition in combination, taking the patient's condition into account, is most beneficial. It is apparent that the nutritional need is difficult to meet by enteral nutrition, and that the risk of overfeeding, with its associated complications, is a problem with parenteral nutrition. Hopefully, fundamentalism will be replaced by a balanced attitude.<sup>76</sup> Furthermore, the potential for harm from the use of supplements, which can intensify the immune response in a setting where suppression is more desirable, needs to be weighed carefully before routine administration is recommended.<sup>141</sup>

Patients with burns in less than 40% TBSA are not catabolic unless they become septic. Patients with burns greater than 40% are always catabolic, and this condition will affect their metabolic derangements and persist for at least a year after injury in most body tissues.<sup>14</sup> The accomplishments of the past decade have placed us in the midst of an exciting paradigm shift from what used to be a primary concern (i.e., mortality) to areas that are more likely to enhance burn survivors' quality of life.<sup>33</sup> Modulating post-burn hypermetabolism in the burn patient is of overwhelming importance in both the immediate care stage and the rehabilitative stage.<sup>33</sup> Moreover, beyond the gen-

eral immunonutrient approach, there is the development of a more specific approach to disease modification.<sup>82</sup> It is obvious, however, that burn-associated catabolism cannot be completely reversed but may be manipulated by both non-pharmacological and pharmacological means<sup>14</sup> and that nutritional support or hyperalimentation cannot in isolation reverse or prevent the persistent protein catabolism. In severely thermally injured children, this catabolism may result in growth delays for as long as two years.<sup>14,40</sup>

The state of the art in burn treatment is such that we are less concerned at present with how to provide adequate quantities of macronutrients. The bulk of available evidence suggests that - with the exception of the risk of overzealous overfeeding associated with derangements in hepatic, pulmonary, and immunological function that may lead to outcomes that are nearly as detrimental to the injured patient as malnutrition - we can currently provide patients with sufficient calories and proteins to avoid the detrimental effects of malnutrition. Our attention has shifted toward manipulating a patient's physiological and biochemical environment to his or her advantage through the administration of specific nutrients, growth factors, or other agents, often in pharmacological doses.<sup>1</sup> The recommendations of the Canadian Clinical Practice guidelines for nutrition support in critically ill patients strongly urge that enteral nutrition be used in preference to parenteral nutrition. The use of a standard, polymeric enteral formula that is initiated within 24 to 48 h after admission to an ICU is also recommended with patients being cared for in the semi-recumbent position. Arginine-containing enteral products should not be used and a glutamine-enriched formula should be considered for patients with severe burns and trauma.<sup>170</sup>

This systematic review has not found sufficient evidence to support or refute the effectiveness of early versus late enteral nutrition support in adults with burn injury. The trials showed some promising results that would suggest early enteral nutrition support may blunt the hypermetabolic response to thermal injury, but this is insufficient to provide clear guidelines for practice.<sup>25</sup> Exogenous continuous low-dose insulin infusion, beta blockade with propranolol, and the use of the synthetic testosterone analogue oxandrolone are the most cost-effective and least toxic therapies to date.<sup>14</sup> Moreover, the most striking nutrition-related effect on infection and outcome in severely burned patients has been tight glycaemic control combined with a best-evidence full nutrition protocol.<sup>81,171</sup> Our lack of detailed understanding of the cellular and subcellular biology of injury physiology, however, has so far limited our ability to modify it. But it seems likely that burgeoning research efforts in the molecular mechanisms behind this physiology of injury will lead in the future to an enhanced ability to control it.<sup>108</sup>

**RÉSUMÉ.** Les grands brûlés constituent un groupe de patients critiquement malades difficiles à traiter et exposés à un stress physiologique extrême et à une réaction métabolique systémique dévastatrice. La quantité augmentée d'énergie qu'il faut utiliser pour affronter cette condition requiert la mobilisation de grandes quantités de substrat provenant des réserves de graisse et du muscle actif pour la réparation et pour carburant, ce qui mène au catabolisme. La réponse métabolique peut durer jusqu'à neuf mois et même un an après la brûlure, associée à un procès altéré de la guérison des lésions, des risques d'infection augmentés, l'érosion de la masse corporelle maigre, une rééducation gênée et un retard dans la réintégration dans la société des patients non décédés. L'inversion de la réponse hypermétabolique, moyennant la manipulation de l'état physiologique et biochimique du patient, obtenu grâce à l'administration de substances nutritives spécifiques, de facteurs de la croissance et d'autres agents, souvent en doses pharmacologiques, commence à émerger comme composante essentielle de l'état de l'art pour ce qui concerne la gestion des brûlures sévères. Le support nutritif entéral précoce, le contrôle de l'hyperglycémie, le blocus de la réaction des catécholamines et l'emploi de stéroïdes anaboliques ont été proposés pour atténuer l'hypermétabolisme ou pour émousser le catabolisme associé aux brûlures sévères. Les Auteurs de la présente étude ont passé en revue la littérature relative pour ce qui concerne les mesures thérapeutiques nutritionnelles et métaboliques proposées dans le but de déterminer les pratiques meilleures sur la base de l'évidence. Malheureusement, l'état présent des connaissances ne permet pas la formulation de lignes directrices bien définies. Il est seulement possible d'indiquer à grands traits des tendances générales qui certainement auront des applications pratiques mais surtout dicteront les recherches futures dans ce secteur.

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## **G. WHITAKER INTERNATIONAL BURNS PRIZE-PALERMO (Italy) Under the patronage of the Authorities of the Sicilian Region for 2009**

By law n. 57 of June 14th 1983 the Sicilian Regional Assembly authorized the President of the Region to grant the Giuseppe Whitaker Foundation, a non profit-making organization under the patronage of the Accademia dei Lincei with seat in Palermo, a contribution for the establishment of the annual G. Whitaker International Burns Prize aimed at recognizing the activity of the most qualified experts from all countries in the field of burns pathology and treatment.

Law n. 23 of December 2002 establishes that the prize becomes biannual.

The next prize will be awarded in 2009 in Palermo at the seat of the G. Whitaker Foundation.

The amount of the prize is fixed at Euro 20,660.00.

The Adjudicating Committee is composed of the President of the Foundation, the President of the Sicilian Region, the Representative of the National Lincei Academy within the G. Whitaker Foundation, the Dean of the Faculty of Medicine and Surgery of Palermo University or his nominee, a Representative of the Italian Society of Plastic Surgery, three experts in the field of prevention, pathology, therapy and functional recovery of burns, the winner of the prize awarded in the previous year, and a legal expert nominated in agreement with the President of the Region as a guarantee of the respect for the scientific purpose which the legislators intended to achieve when establishing the prize.

Anyone who considers himself to be qualified to compete for the award may send by **January 31st 2009** his detailed curriculum vitae to: Michele Masellis M.D., Secretary-Member of the Scientific Committee, G. Whitaker Foundation, Via Dante 167, 90141 Palermo, Italy.