as prolactinoma [5] or ACTH-secreting adenomas [2, 6]. Some studies suggest that prolactinoma with increased proliferation index, besides the risk of recurrence, is pituitary carcinomas precursors [6].

The data given in literature indicate low levels of proliferation marker Ki 67 in both gonadotropic hormone-secreting adenomas, and non-secreting ones [1, 6, 7].

In addition to existing data, the present study has demonstrated that polyhormonal adenomas including co-expression of LH present a low proliferation index.

# Conclusions

1. The heterogeneity expression of growth factors and corresponding receptors is dependent on hormonal profile of pituitary adenomas.

2. Secreting GH and PRL pituitary adenomas are the most active in terms of synthesis and release of growth factors.

# References

- 1. De Lellis RA, Lloyd RV, Heitz PU, et al. 2004. Pathology and genetics of tumours of endocrine organs. World Health Organization classification of tumours. Lyon: IARC Press.
- Saeger W, Dieter K, Buchfelder M, et al. Pathohistological classification of pituitary tumors: 10 years of experience with the German Pituitary Tumor Registry. *Eur J Endocrinol.* 2007;156:203-216.
- Pawlikowski M, Kunert Radek J, Radek M. Plurihormonality of pituitary adenomas in light of immunohistochemical studies. *Pol J Endocrinol.* 2010;61(1).
- Pawlikowski M, Gruszka A, Kurnatowska I, et al. Proliferating cell nuclear antigen (PCNA) expression in pituitary adenomas: relationship to the endocrine phenotype of adenoma. *Folia Histochem Cytobiol*. 2006;44(1):37-41.
- Chacko G, Ari George Chacko, Kalman Kovacs. Clinicopathologic correlates of giant pituitary adenomas. *Journal of Clinical Neuroscience*. 2009;16:660-665.
- Mastronardi L, Guiducci A, Spera C, et al. Ki-67 labelling index and invasiveness among anterior pituitary adenomas: analysis of 103 cases using the MIB-1 monoclonal antibody. *J Clin Pathol.* 1999;52:107.
- 7. Pizarro CB, Oliveira MB, et al. Measurement of Ki-67 antigen in 159 pituitary adenomas using the MIB-1 monoclonal antibody.

# The role of microflora in the pathogenesis of burns in different climatic conditions

# V. Babiuc

Department of Orthopedics and Traumatology, Nicolae Testemitsanu State University of Medicine and Pharmacy Chisinau, the Republic of Moldova

Corresponding author: babiucv@yahoo.fr. Manuscript received March 04, 2015; accepted July 15, 2015

#### Abstract

**Background:** In all the patients with combustions comprising more than 50% of the body surface, bacteremia takes place, and, during the shock period, its influence is minimal, then, during the toxemia period, when the autolysis process occurs in the affected area, microflora presents a particular danger. Microflora manifests its virulence completely depending on the state of the local and general immunity, which, in its turn, differs in different climatic conditions. Therefore, in order to determine the effective treatment, it is very necessary to study the microflora in patients with combustions in different diametrically opposed climatic conditions – tropical and continental.

**Material and methods:** The investigations were performed in 287 patients with combustions in tropical conditions (Cuba) and in 133 patients with combustions in continental conditions (Moldova, Moscow) in order to determine the role of microflora in the evolution of combustions in different climatic conditions. The following factors were determined: the microbial type, the sensibility degree to antibiotics, the conditions of favoring microbial invasion and the role of the medical staff in favoring patients with combustions affected by the microbial invasion.

**Results:** The obtained results showed that the conditions of the tropical climate are very favorable for microflora evolution, and the medical staff plays a very important role in favoring the microbial invasion, in the assessment of septicemia and also in the assessment of the microbial invasions in the pathogenesis of the combustion wounds.

**Conclusions:** Microflora presents a very big danger in the evolution of combustions. The virulence of microflora in the conditions of the tropical climate is much higher compared to the conditions of the continental climate. The medical staff and the necessary conditions for preserving the asepsis and antisepsis play a very important role in avoiding the microbial invasion in patients with combustions, both locally, and generally.

Key words: microflora, combustion wounds, septicemia, medical staff.

# Introduction

Microflora plays a special role in patients with burns. Artz C., Reiss E. (1957) affirm that microflora is one of the major problems in burn patients. A. Yakovlev (1967) considers that bacteremia develops in all patients with burns covering more than 50% of the body surface area, and while during shock its influence is minimal, during toxemia, when the autolytic process occurs in the affected area, microflora poses a particular danger. And not only in terms of bacteremia, that may occur at any time, but rather as a result of the absorption of microbial toxins from the affected area. The severely affected organs may easily decompensate following the local and general microbial invasion.

In all these cases, the microflora displays its virulence entirely depending on the local and general immune status. But both local and general immunity manifests itself differently in different climatic conditions. In tropical conditions, capillary permeability and plasmorrhea in the affected area are increased and the temperature of the surrounding environment is optimal for microflora vegetation.

Therefore, it was necessary to study microflora in these patients at different stages of burn disease dynamic evolution under absolutely different climatic conditions – tropical and continental.

## **Material and methods**

1147 investigations were performed in 287 patients with burns in tropical conditions and 526 investigations were performed in 133 patients in continental conditions. Microflora type, its sensibility to different local treatment remedies and antibiotics were studied. At the same time, the course of the local process, the general condition of the patient and the efficacy of the surgical interventions and blood culture were also investigated. Periodically, the microflora of the medical staff, instruments and surrounding environment were also studied.

# Results

The obtained results showed that all patients had infected wounds upon hospital admission. During the first 2-3 days following the trauma, in most cases, a microbial strain was found on the burn wounds. Shortly after that, its association with other strains increased dramatically. Out of the 287 patients studied in the tropical area, in 137 (48%) of them, staphylococcal microflora was found (tab. 1), in 62 (21.7%) – *Pseudomonas aeruginosa*, in 24 (8.3%) – *Proteus vulgaris*, in 29 (10%) – *Providencia* and 35 (12%) had various associated microflora on hospital admission.

The same situation, without much difference, was found on admission of patients in the continental climate areas (table 1).

## The methods of prophylaxis

In order to verify the evolution of pathological processes in burn disease excluding as much as possible the influence of microflora on these processes, in tropical conditions (Cuba), each patient (one or two per ward) was completely isolated and all the necessary conditions were created in the ward: an individual glass table with medicines, a special table for food, sterile conditioned air, individual WC in the ward, individual shower in the ward, sterile linen changed daily, additional ward preparation with quartz lamp, sterile gowns, covers and caps for medical staff daily, a metal medical dressing table sterilized by flame and alcohol and cooled with sterile saline solution after each application of dressing to a patient, and also complete isolation from relatives until patient's discharge. The contact between patients within the department was absolutely excluded. The patients who were able to move within the ward showered 2 or 3 times daily.

In continental conditions, the usual system form was applied: common ward, common dressing ward, common WC, free visitation etc.

# Study results and the divergence in appreciating the role of microflora in toxemic stage

During the treatment, the performed investigations showed that: in continental conditions, 4-5-7 days after

#### Table 1

#### The microbial type and frequency identified in burn patients in different climatic conditions

Climate area	Number of pa- tients	Microbial strain							
		Staphylococci	Pseudomonas aeruginosa	Proteus vulgaris	Providencia	Various associa- tions			
Tropical	287	137	62	24	29	35			
		48%	21.6%	8.3%	10%	12.1%			
Continental	133	63 47.4%	22 16.5%	15 11.3%	12 9%	21 15.8%			

Table 2

Microflora type and associations in burn patients in different climatic conditions

Climatic area	Num- ber of patients	On admis- sion	Dynamic evolution, on the 4 <sup>th</sup> -5 <sup>th</sup> -7 <sup>th</sup> day			Among them, associated						
		Form				Staph.+	Staph.+	Staph.+	Staph.+	Pseu-	Pseudom.	Proteus
		Non-asso- ciated	Asso- ciated	Non-as- sociated	Asso- ciated	Pseud. Aerug.	Coli bact.	Proteus vulgaris	Provid.	dom. Aerug.+ Provid.	Aerug.+ Proteus vulg.	vulg.+ Provid.
Tropical	287	252 87.8%	35 12.2%	195 67.9%	92 32.1%	18 19.5%	39 42.4%	13 14.9%	5 5.5%	12 13%	3 3.3%	2 2.1%
Continen- tal	133	112 84.2%	21 15.8%	17 12.7%	116 87.3%	26 22.4%	34 29.3%	7 6%	11 9.5%	18 15.6%	13 11.2%	7 6%

34

the trauma, the microbial association in the affected area increased dramatically (Table 2). While in the tropical area in the above-mentioned conditions, microflora association increased during the treatment from 12.2% to 32.1%, in the continental area, an extremely high virulence was established and its association increased from 15.8 to 87.3%.

In tropical areas, in 67.9% of the patients only one type of microbes remains during the treatment, while, in the continental area, this fact is established only in 12.7% of the patients. The rest of the patients (87.3%) from the continental area show an associated microflora form. This microbial invasion worsened a lot the dynamic evolution of burns in patients in continental conditions as a result of many complications caused by the microflora.

The most frequent microbial invasion in the affected areas, both in tropical and in continental conditions, is the staphylococcal microflora, *Pseudomonas aeruginosa* or *Coli bact.* in different associations. *Proteus vulgaris, Providencia* and others occur less frequently.

The most dangerous manifestation of microbial virulence was established from the 5<sup>th</sup> to the 9<sup>th</sup>-12<sup>th</sup> day after the trauma in both climatic conditions, when local autolytic processes of the necrotized tissues occurred. Once they are removed, the purulent process rapidly regresses and the regeneration in the affected area is clearly improved.

In this short time period, in both climatic conditions, an aggravated general condition of the patients is observed, especially in IIIA-IIIB and IV degree burns involving more than 15-20% of the body surface area. In these patients, 4-5 days after the trauma, the body temperature rises to 39-40-41°C. Patients develop very quickly drowsiness, stupor and delirium and some of them also develop reactive psychosis. At the same time, disturbances of internal organs and systems occur.

It was established that, in tropical conditions, after the removal of necrotized tissues from the wound, the mental lucidity of the patient is recovered in 2-3 days and the function of internal organs – somewhat slower. In continental conditions, this process is much slower, the aggravated general condition may persist up to 20-30 days after the trauma. The disturbance of internal organs function persists for a longer time and it is clear that the background for skin plasty in continental conditions is much less favorable.

That speaks that the main role in the second stage of burns is attributed to toxins accumulated in tissues as a result of increased catabolism and their absorption from the affected area.

There is no doubt that the microbial toxins are also absorbed from the wound, but their role is not so important. This fact was also confirmed during our investigations in tropical conditions, where patients were completely isolated and had their sterile linen changed daily, also having baths and showers daily, and asepsis was observed to the utmost degree. Out of 1286 patients, only 5 had microflora found in their blood, which represents 0.4% of the sepsis conditions. In continental area, under extremely unfavorable conditions as described above, microflora was detected in the blood of 39 out of 363 investigated patients, representing 10.7% of the patients with sepsis condition. The microflora identified in the blood was not always the same as the one in the wound, but it always matched the hospital microflora.

Though the role of microflora in tropical conditions in the studied patients was reduced to a minimum degree, the dynamic evolution of burn disease in tropical conditions is, however, very slowly progressive. Also, both in tropical and in continental conditions, when bacteremia occurred, the reaction of the organism to the infection and to the action of toxins after the reactive "explosion" went shortly after into a state of anergia, followed by patient's death due to the development of respiratory, cardiovascular, hepatic, renal failure etc.

Some authors affirm that sepsis in patients with burns is a persistent complication, but it can be minimized by observing aseptic and antiseptic techniques.

The investigations performed by some authors confirm that the clinical manifestations of the aggravation of the cardiovascular, respiratory, hepatic, renal and other systems' functioning are identical in severe lesions in patients with sepsis and without sepsis.

As a result of the investigations performed at the medical staff in continental conditions, pathogenic microflora was detected in oral and nasal cavities in 68.2% of the cases, on hands in 52.3% cases and on personal objects in 78.7% cases, as well as in the surrounding environment. This means that hospital microflora represents a major danger. In 83.4% cases, hospital microflora was resistant to most cephalosporin antibiotics.

Microflora, both in tropical and in continental conditions, remains to be an extremely dangerous factor in the aggravation of the course of burns. It is severe not only during the preoperative period, but during the postoperative period too, when, as a result of the virulent microflora invasion, a marginal lysis of transplant occurs or even a complete lysis.

Pneumonias, abscesses, phlegmons, thrombophlebitis, pyelonephritis etc. frequently occur as a result of generalization of infection (sepsis). Sometimes, on the general background of microflora invasion, multiple microabscesses in the intact skin areas with a marked marginal inflammation occurred.

These disorders disappear once the sepsis is under control. The result of the investigations we performed confirmed that microflora invasion can be reduced to minimum, once the asepsis and antisepsis are strictly observed, which was proved by our studies in tropical conditions.

# Conclusions

1. Both local and general microbial invasion is extremely dangerous in the dynamic evolution of burn disease.

2. The virulence of microflora in tropical climate conditions is much higher compared to the continental climate conditions.

3. The conditions required for maintaining the asepsis and antisepsis, described in this paper, allow avoiding the microbial invasion in patients with burns, both locally and generally. 4. At the second stage of burns, the main cause of patient's general condition aggravation is intoxication with autolytic products of the necrotized tissues from the affected area, but not microbial invasion, as it is stated by some authors.

5. The role of the living and treatment conditions of the burn patient is extremely important in avoiding both local and general microbial invasion.

6. The medical staff plays a very important role in intrahospital microbial invasion in burn patients.

#### References

- 1. Erency J, Renaud F. Manuel de bactériologie clinique. Paris: Elsevier, 1992;11.
- 2. Muir I. The treatment of severe burns. Drugs. 1971;1(6):429-433.
- Simonart A. Études expérimentales de la toxemia des brulés. Path. Biol. 1958;6:677-800.
- 4. Teot L. Les topiques antibacteriens dans le traitement des brûlures. *Soins*. 2019;55(742):42-44.

- 5. Vilain R. L'infection dirigée chez les brûlés. *Rev. hyg. et med. soc.* 1970;18:243-246.
- Bukowska D. Studies on antibacterial activity of convalescent sera after burns. *Pal. Tyd. Lec.* 1972;XXXII:513-516.
- 7. Carvajal H, Parks H. Burn in children. Jear book medical publishers. Inc. Chicago, London, Boca Raton, 1987.
- 8. Cristophe L. La mort des brûlés. These. Paris, 1939.
- 9. Davis J. Staphylococcal infection in burns. In: Research in burn. Ed. Curtis P. Artz. Philadelphia: F. Davis, 1962;212-218.
- 10. 1th International Congress on Burn Injuries. *Burns*. 1986;12(3):200-205.
  11. Mhahar P, Padiglione AA, Clteland H, et al. Pseudomonas aeruginosa bacteriaemia in burns patients. *Burns*. 2010;36(8):1228-1233.
- 12. Parkes A. Toxic shock syndrome in an adult burn patient. *Burns*. 2008;34(7):1057.
- 13. Peng YZ. Clinical characteristics and diagnosis of sepsis in pediatric burn patients. *Chinase Jurnal of Burns*. 2013;29(1):1-3.
- Touze A. Organisation des soins aux brûlés. Archives de Pediatrie. 2010;16(6):874.
- Zanii SR. Thermal burns and scalds: Clinical complication in the elderly. Consultant Pharmacist. 2012;27(1):16-22.
- Yang Z. Clinical study of the pathogeneses of mutiple failure after burns. *Chinese Journal of Plastic Surgery Burns*. 1992;8(1):8-12.

# Retroorbital pain and autonomic dysfunctions in patients with migraine

# C. Curca

Institute of Neurology and Neurosurgery, Department of Ophthalmology Nicolae Testemitsanu State University of Medicine and Pharmacy, Chisinau, the Republic of Moldova

Corresponding author: ccrist@mail.ru. Manuscript received March 21, 2015, accepted June 05, 2015

#### Abstract

**Background.** A part of migraine patients complain of unilateral or bilateral ocular pain during migraine access, which may be associated with some vegetative disorders: ptosis, mydriasis, conjunctival congestion, photo and phonophobia, lacrimation, unvoluntary periorbital muscle contractions, nasal hypersecretion. It is important to analyze the frequency of ocular pain in patients with migraine, laterality, character and their association with other autonomic manifestations.

**Material and methods:** 91 patients with migraine (9.9% men, 90.1% women), out of them 51.6% with chronic migraine, 34.1% with episodic migraine and 14.3% with rare episodic migraine. Patients' age was 18-63 years. The study included only patients with migraine without other associated neurological or ocular pathology. Ophthalmologic examination included assessment of visual acuity, perimetry, intraocular pressure measurement in migraine crisis and lucid period (air-push N 10-21 mm Hg), ophthalmoscopy, biomicroscopy, refractometry if necessary.

**Results:** According to the statistical analysis of data, 48.4% patients had bilateral ocular pain during migraine attack; 26.3% unilateral headache and eye pain, 25.3% did not experience pain during the migraine attack. By the type of eye pain 34.1% had non-pulsating retro-orbital pain; 18.7% –pulsating retro-orbital pain; 22% - had superficial eye pain. During the migraine attack 18.7% of migraine patients had unilateral conjunctival congestion, ipsilateral of headache; 33% bilateral congestion and congestion absent in 48.4% patients. Unilateral lacrimation – 11.4%, bilateral lacrimation in – 25.6%. Photophobia between attacks of migraine attacks of migraine attacks of patients. Unilateral ptosis – 8.4% during the attack, bilateral ptosis – 10.8%. Periorbital muscle tics during the migraine attacks were observed in 42.2% patients. We found a statistically significant correlation (P <0.001) between the type of eye pain and intraocular pressure values measured during the migraine attacks and between them.

**Conclusions:** Migraine attacks are often associated with different character of ocular pain, autonomic disorders and with increasing of intraocular pressure. **Key words:** ocular pain, migraine.

# Caracterul durerilor retroorbitale și tulburărilor vegetative la pacienții cu migrenă

## Introducere

O parte dintre pacienții cu migrenă acuză dureri oculare uni- sau bilaterale în timpul crizei migrenoase, care se pot asocia cu unele tulburări vegetative: ptoză, midriază, congestie conjunctivală, foto- și fonofobie, lăcrimare, contracții involuntare ale musculaturii periorbitale, hipersecreție nazală [1, 2, 5]. Durerile oculare pot fi uni- sau bilaterale, independent de localizarea cefaleei și se deosebesc după caracterul durerii și intensitatea acesteia. Varietatea senzațiilor oculare,