HABILITATION THESIS

INVESTIGATION AND PERSONALIZED ANALYSIS OF HEALTH LEVEL ASSOCIATED WITH METHODS OF TREATMENT, RECUPERATION AND RE-EDUCATION IN THE DYSPHONIAE INDUCED AT THE PROFESSIONS WITH INTENSE USER VOICE (DISFONOTEST)

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2014
Habilitation Thesis

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Abstract of Habilitation Thesis

My name is Mihail Dan Cobzeanu, I have been an ENT consultant since 1998 and a general surgery registrar since 1991. I sustained my doctoral research PhD thesis at UMF Gr T Popa Iasi in 1996 on the following subject: “Vertical partial laryngectomies intake on the complex treatment of the glotic neoplasm”. I have also been Associate Professor since 2004, head of the ENT Department of Sf.Spiridon Emergency Hospital since 2010 and in 2014 I was named Professor (decision nr.2/21.03.2014 of the Senate of UMF Gr.T.Pop Iasi). This thesis represents a synthesis of my career as a researcher after sustaining my doctoral research thesis at UMF Gr.T.Pop Iasi, confirmed by diploma number 440/15.10.1996 issued by the Education and Research Ministry.

After sustaining my thesis, I channeled my activity on 3 directions:

1. Didactic activity
2. Scientific and research activity
3. Medical activity

1. Didactic activity

My didactic activity was and is dedicated to the universities and post-universitary learning cycles and consists in course and practical teaching of the 5th year students of UMF Gr.T.Pop Iasi in 3 different languages (Romanian, English and French). Regarding the postuniversitary activity, it was focused on the ENT resident doctors as well as teaching young specialists through two courses of continuous medical training: endoscopic laryngeal surgery and endoscopic rhinologic surgery.

With the purpose of supporting my didactic activity I authored 11 books for universitary and postuniversitary studies.

My objectives for the future development of my academic career are:

1. Axiological orientation of the educational process.
2. Anticipation of the educational objectives
3. Evaluation of the efficiency of the education process in order to improve this process

To achieve these objectives I plan to:

- improve the teaching methods with the direct implication of the student and by allowing a national and international informational exchange
- enroll the resident doctors and young specialists in the research activities of the clinic
- intensify the collaboration efforts between different ENT departments from Romania and from other countries in order to implement new surgical and research methods
- improve the learning experience through the E-learning platform
- organize courses for continuous medical education for resident doctors and young ENT specialist

2. Scientific and research activity:

My scientific and research efforts are directed towards the following pathologies:
hypopharyngolaryngeal oncology, rhinosinusal allergies and gastroesophageal and hypopharyngolaryngeal reflux affecting the larynx.

Concerning the laryngeal neoplasm, I continued the research started in my PhD thesis, focusing on evaluating the factors that favor its genesis in order to be able to put an early diagnosis and assure an efficient treatment.

The study of foreign bodies in children, with a major impact on their health, materialized in an international grant. My scientific activity took form by writing 152 scientific papers (author and co-author) that were published in full in national and international journals, as follows: 10 in ISI journals, 11 proceeding ISI, 32 in Pubmed, Index Copernicus and Med Line, 7 in CNSIS journals and 92 in national and international congress books.

I sustained over 100 oral presentations at national and international ENT congresses and have also actively participated at organizing different ENT events with international participation (national congresses, conferences and symposiums).

I have organized and I have been:

- President of the National Congress of ENT and Cervico-Facial Surgery with international participation, 22-25 September 2010, Iasi, Romania.
- President of the 2nd Congress of the Romanian Society of Rhinolgy with international participation, September 2013, Piatra Neamt, Romania

I have moderated and have been speaker at over 25 round tables at national and international congresses.

Throughout my entire research career, I have been actively implicated in 5 grants, for one of which I was project manager.

Also, I was member in 3 projects won in competitions, POSDRU.

Research development focuses, as up until now, on attending national and international scientific events, on establishing new scientific collaborations with other specialists and on developing new methods and techniques.

In order to substantially increase the impact of my scientific papers I intend to submit a research project for PN-II-PT-PCCA -Methods of investigation and personalized analysis of the health status associated with voice recovery and reeducation in disphonia found in professionals with intense vocal effort in order to continue the research started in the internal grant of UMF Gr.T.Popa Iasi.

Another research which I’ll propose is a collaboration with N.Testemitanu University, Republic Moldova.

**Mixing educational and researching activities**

Career development of young researchers by introducing new fields of activity.

Skill improvement by continuous medical learning.

The results of the studies will be found in articles and books that I will publish within the research projects that I will coordinate. These projects will encourage young PhD’s and master students to participate at research activities and to present their results at different conferences.
3. Medical activity
I have never forgotten the essence of my work, always trying to assure the best treatment for my patients. To do this, I had to implement new diagnosis and surgical techniques in our ENT clinic in order to make an early diagnosis and to give a better treatment. So, I introduced the endoscopic techniques that allowed minimally invasive surgery and a more accurate diagnosis process.
Rezumatul Tezei de abilitare


După sustinerea tezei de doctorat, activitatea mea s-a axat pe trei directii principale:
1. Activitate didactica.2. Activitate stiintifică si de cercetare.3. Activitatea de asistenta medicală

1. Activitatea didactica

Activitatea didactică a fost si este dedicata invatamantului universitar si post-universitar si constă în coordonarea de cursuri si seminarii pentru studentii Facultății de Medicină, U.M.F. Grigore T.Popa - Iasi, anul V (serii limba romana, engleza si franceza) cit si anul IV colegiu. Activitatea postuniversitara, s-a axat pe formarea rezidentilor ORL, precum si instruirea specialistilor ORL în domeniul chirurgiei endoscopice laringiane si rinosinusale.

În scopul sustinerii activității didactice, am participat în calitate de autor la elaborarea si publicarea a 11 cărți in domeniul ORL.

Obiectivele dezvoltării în viitor a activității educationale, academice

Realizarea acestor obiective se bazează pe:
- imbunatatirea metodologiei de predare cu implicarea directa a studentilor si prin asigurarea unui schimb de informații la nivel național si international
- implicarea in următorii ani a medicilor rezidenti si a doctoranților in activitatea de cercetare a clinicii.
- intensificarea eforturilor de colaborare cu diverse servicii O.R.L.din tara si strainate in scopul introducerii unor tehnici noi chirurgicale si de cercetare.
- imbunatatirea activității didactice prin intermediul platformei E-learning.
- organizarea de cursuri de specializare in cadrul educatiei medicale continue, pentru medicii rezidenti si specialistii ORL din zona Moldovei.

2. Activitatea stiintifică si de cercetare.

Cele mai importante directii ale activității mele stiintifice sunt constituite de cercetările in domeniul patologiei oncologice ORL, a alergiei rinosinusale si a refluxului gastroesofagian implicat in patologia laringiana.În acest scop am efectuat cercetări multidisciplinare cit si cu specialişti din alte institute tehnice si de arta, in scopul diagnosticării si rezolvării terapeutice a disfoniilor datorate bolii de reflux gastro esofagian la grupuri de pacienți cu profesii ce
implica un efort vocal intens.

O directie de cercetare ce a continuat tema tezei de doctorat, a fost evaluarea factorilor favorizanti in geneza neoplasmului laringian, alaturi de diagnosticul precoce si tratament. Studiul corpurilor straini la copii, cu implicatii majore in starea de sanatate, s-a materializat printr-un grant international.

Activitatea stiintifică s-a concretizat prin redactarea a 152 lucrari stiintifice publicate in extenso in calitate de autor sau coautor, in reviste nationale si internationale, din care, 10 in reviste cotate ISI, 11 in publicatii proceeding ISI, 32 in publicatii din baze de date (PUBMED, INDEX COPERNICUS, MED LINE), 7 in reviste nationale recunoscute CNCSIS si 92 lucrari prezentate si publicate in volume de rezumate congrese nationale si internationale.

Am realizat peste 100 de prezentări orale in cadrul Congreselor ORL. Am participat activ la organizarea de congrese si conferinte nationale cu participare international.

In aceasta perioada am fost ales: Presedinte al 32 lea Congres National ORL, 2010, Iasi; Presedinte al 2-lea Congres al Societatii Romane de Rinologie, 2013, P.Neamt; Presedintele Societatii Romane de Rinologie, 2013-1015. Am moderat si am fost speaker la peste 25 de mese rotunde la congrese nationale si internationale. Am fost implicat in mod activ in 5 granturi de cercetare, din care la unul ca manager de proiect, 4 nationale si unul international si deasemenea in 3 proiecte POSDRU.

Dezvoltarea activitatii de cercetare se axeaza ca si pana acum, pe: participarea la evenimente de specialitate internationale si nationale ; participare la proiecte de cercetare cu publicarea si diseminarea rezultatelor obtinute; dezvoltarea si introducerea a noi metode de cercetare.

In acest context, voi depune un proiect de cercetare, in idea continuarii cercetarii a grantului intern UMF Iasi, intitulat : Metode de investigare si analiza personalizata a sanatatii asociata cu recuperarea si reeducarea personalului in patologia disfoniilor depistate la profesiile cu solicitare intense,

O alta linie de cercetare o reprezinta colaborarea transfrontaliera cu Universitatea N.Testimitanu, Republica Moldova, in domeniul alergiei rinosinusale.

Corelarea activitatii de cercetare cu ceea educationala, se va realiza prin : optimizarea planurilor de invatamint in acord cu tematica europeana ; introducerea unor noi directii de perfectionare medicala continua a specialistilor din reteaua medicala primara.

3. Activitatea de asistentă medicală.

Nu am uitat nici o clipă esența meseriei, aplecându-mă temenic asupra optimizării protocoalelor terapeutice. Implementarea in clinica a tehniciilor de endoscopie ORL, a permis diagnosticul precoce a neoplasmelor din sfera ORL. Abordarea chirurgiei minim invazive rinosinusale si faringolaringiene, alaturi de cea clasica a permis imbunatatirea calitatii vietii si prognosticul pacientilor. Munca in echipe multidisciplinare a permis pe linga imbunatatirea rezultatelor medicale, obtinerea unor rezultate stiintifice superioare.
PART 1.(b)- Profesional and scientific research realization and development of my career

PART 1.(b.i)
My name is Mihail Dan Cobzeanu, I have been an ENT consultant since 1998 and a general surgery registrar since 1991. I sustained my doctoral research PhD thesis at UMF Gr T Popa Iasi in 1996 on the following subject: „Vertical partial laryngectomies intake on the complex treatment of the glotic neoplasm”. I have also been Associate Professor since 2004, head of the ENT Department of Sf.Spiridon Emergency Hospital since 2010 and in 2014 I was named Professor (decision nr.2/21.03.2014 of the Senate of UMF Gr.T.Popa Iasi ).
This thesis represents a synthesis of my career as a researcher after sustaining my doctoral research thesis at UMF Gr.T.Popa Iasi, confirmed by diploma number 440/15.10.1996 issued by the Education and Research Ministry.

Abstract of PH.D thesis
The role of partial vertical laryngectomy in the complex treatment of laryngeal carcinoma
This doctor’s degree paper has been conceived in the ENT Clinic of Sf.Spiridon Hospital Iasi, under the scientific tutelage of Prof.Dr.Cezar Dinu. It was finished and presented in 1995, confirmed by diploma no Nr.440/15.01.1996 issued by the superior comitee.
The partial vertical surgery in the tumoral laryngeal pathology needs a thorough knowledge of the anatomy because of its neuromuscular and vasculolymphatic independence. Each hemilarynx has conjunctive structures that constitute barriers against the spreading of the neoplastic process.
804 patients where included in the study, out of which 330 were found with supraglottic localization and 259 with glotic localization. The main risk factors were also studied.
It was insisted on the importance of early stage diagnosis using all means of investigation (videofibroscopy, suspension laryngoscopy, CT scan, MRI), which allows performing partial laryngectomies.
Out of 259 glotic neoplasms, 129 could benefit from different techniques of partial vertical excisions. We preferred the median approach. Checking the ganglia areas was necessary in case of ventricular invasion.
Larynx luminal remodeling is a key step in assuring a good functional outcome and was done by several surgical procedures: cordectomy, Hautant hemilaryngectomy, fronto-lateral of fronto-anterior laryngectomy, Mayer-Piquet crico-hyoido-epiglottic plasty, Labayle cricohyoidopexy.
Functional laryngeal surgery can only be approached by an experienced surgeon, who must choose the technique after assessing the intraoperative situation.
The most frequent postoperative complications where bleeding, subcutaneous emphysema, pharyngeal fistula, laryngeal stenosis, and breathing and swallowing problems.
Excisions made without enough safety margins lead to local recurrences which required total laryngectomy as soon as possible.
One of the advantages of partial functional larynx surgery is having an eye-view of the lesion
and of the excision, with extemporaneous anatomopathological result and, according to this result, a possible decision to continue with a total laryngectomy if necessary.

After sustaining my thesis, I channeled my activity on 3 directions:

2. Didactic activity
3. Scientific and research activity
4. Medical activity

1. Didactic activity
My didactic activity was and is dedicated to the universitary and post-universitary learning cycles and consists in course and practical teaching of the 5th year students of UMF Gt.T.Popaiasi in 3 different languages (Romanian, English and French). Regarding the postuniversitary activity, it was focused on the ENT resident doctors as well at teaching young specialists through two courses of continuous medical training: endoscopic laryngeal surgery and endoscopic rhynologic surgery.

With the purpose of supporting my didactic activity I authored several books for universitary and postuniversitary studies.

Book author/Chapters

Books

For the last academical position:

A.- Book author

B.- Coauthor/Chapters
2. Scientific and research activity:
My scientific and research efforts are directed towards the following pathologies: hypopharyngolaryngeal oncology, foreign body at the children, gastro esophageal and hypopharyngolaryngeal reflux affecting the larynx.

Researching the effects of gastroesophageal and hypopharyngolaryngeal reflux on the larynx required the help of our gastroenterology and pneumology colleagues from UMF Gr T Popa Iasi and also from the specialist of the Technical University and the Conservatory. Together we formed a team that studies dysphonia caused by reflux in patients with professions that require intense vocal effort.

Concerning the laryngeal neoplasm, I continued the research started in my PhD thesis, focusing on evaluating the factors that favor its genesis in order to be able to put an early diagnosis and assure an efficient treatment.

The study of foreign bodies in children, with a major impact on their health, materialized in an international grand.

Larynx Neoplasm Pathology

-ISI articles

ISI proceeding articles
Articles published in BDI journals


The larynx oncological pathology was my continuous main field after I finished PH degree, so I wrote many articles which were published in ISI or BDI publications.
LARYNGOTRACHEAL NONHODGKIN’S LYMPHOMA

M. D. Cobzeanu, V. Costinescu, Carmen Daniela Rusu, Sultana Mihailovic, M. Grigoras,
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aENT Department, „Gr. T. Popa” University of Medicine and Pharmacy Iasi, Romania
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Abstract

Objectives. Malignant lymphomas of larynx and trachea are rare tumors and require special diagnostic and therapeutic attention. The authors present an unexpected case of non-Hodgkin Lymphoma localized in the subglottic larynx and upper cervical trachea. The clinical presentation, diagnostic and therapeutic approach, evolution and prognosis are discussed. Method. We report a case of 25-year-old man patient, with anamnestic progressive dyspnea, presented in our ENT Department with severe airway obstruction caused by a large subglottic tumoral mass migrated in glottic space during an accidental fall of patient. An emergency tracheotomy was performed. The flexible endoscopy and CT-scan revealed a large pedunculated mass arising from the subglottic larynx and anterior wall of upper cervical trachea with the obstruction of 2/3 from laryngotracheal lumen. Results. After a complex assessment, the tumor was excised by external approach (median thyrotomy). The histopathologic exam of surgical specimen showed malignant non-Hodgkin lymphoma and the immunohistochemical profiles were evaluated in order to establish the therapeutic strategy including combination chemotherapy in the Department of Oncology. Conclusions. Involvement of the subglottic larynx and trachea by lymphoma is an uncommon problem which can cause severe airway obstruction and requires multidisciplinary approach (ENT, pneumology, oncology/hematology). The clinicopathologic features of this case have been described and compared with previously reported cases. Keywords. Non Hodgkin Lymphomas, Larynx, Trachea, Immunohistochemy, Chemotherapy

Introduction

Malignant Non Hodgkin’s Lymphoma of the larynx represent a rare disease (there were only 90 cases mentioned in the anglo-saxon literature until 2006). (1) The first case of laryngeal non-Hodgkin lymphoma was mentioned in 1934 by Mac Kenty and Remacle, the diseases being more frequent amongst adult and having the histopathologic aspect of a type B lymphocitary cells. (2)

The symptomatology in the laryngeal localisation is represented by dyspnea, dysphonia or dysphagia, only rarely causing acute respiratory failure phenomena. In time, it can determine extralaryngeal extention in the respiratory tract, skin and stomach. (3,4,5) The diagnosis includes ENT exam (indirect and direct laryngoscopy, fibroscopy), radiological exams (CT, MRI) and histopathological confirmation.

The updated Keil classification is used nowadays for dividing the non Hodgkin’s Lymphoma in 4 stages as follows: Stage I E – strictly laryngeal localization of non Hodgkin’s lymphoma; Stage II E – laryngeal and regional lymphatic nodes involvement; Stage III E – generalized head and neck disease; Stage IV E – secondary laryngeal affection inside of a generalized disease.

The treatment options depend on a variety of factors including the grade of lymphoma, the stage and extent of disease, the patient status. (6,7,8)

Material and methods

The authors present a case of I.F., a 25 year old man patient admitted in our ENT Department with a severe acute respiratory insufficiency by transfer from the Pneumology Hospital Iasi. The emergency tracheotomy was required. Previously, the patient had been suspected with astma due to the presence of progressive dyspnea, dysphonia, productive caughing. The tracheobroncho-fibroscopy identified a vegetative pedunculated tumoral mass, arising from subglottic larynx and trachea. During an accidental fall of the patient, the tumour migrated between the vocal cords causing airway obstruction, required the tracheotomy. (fig. 1) The CT scan confirmed the presence
of the tumour originating from the subglottic larynx and anterior wall of upper cervical trachea (first tracheal ring) protruding into the larynx tracheal lumen. Systemic screening found no other extralaryngeal tumoral lesions. (fig. 2)

Results
The surgical management was decided in order to excise the tumoral mass, under general anesthesia, by external approach. The median thyrotomy was performed with the oulining of the mobile pediculated tumour located in the subglottic region on the anterior side of the cricoid cartilage and the first tracheal ring. (fig. 3,4,5,6,7,8)
Fig. 9. In lamina propria of larynx mucosa there is large atypical anaplastic cells, X10

Fig. 10. CD 30 staining is usually strong in the large cells, with characteristic Golgi and membrane pattern, x 10

Fig. 11. In this case ALCL, CD 3 was positive focal in some tumoral cells, x 20
The tumour was excised with electrocauter and the tracheotomy was suppressed after 48 hours due to favorable postoperatory progress with normal breathing and disappearance of dysphonia. The histopathological exam of surgical specimen showed an anaplastic large cell B lymphoma with a proliferation in the lamina propria of large atypical cells with vesicular chromatin, proeminent nucleoli and bizarre shaped nuclei. These aspects can lead to other types of malign lymphoma and carcinoma, requiring the immunohistochemical exams (fig. 9,10,11).

The phenotype was identified in the paraffin sections and included CD 30+ (fig. 10)CD 30 /g114 focal and CD 20 (fig. 12).

The differential diagnosis is important for no be mistaken, for other cell non lymphoid malignancies.

The absence of other extralaryngeal lesions and lymphadenopathy included the patient in the stage IE.

In present, the most used prognosis classification of diffuse lymphoma with large cells is the International Prognostic Index (I.P.I.) that allows the precision of evolution of patients with aggressive non Hodgkin’s lymphoma.

Five factors are the same value and have independent influence on the patient’s survival: age > 60 years, values LDH > 2, Ann Arbor stage III or IV, the presence of > 2 extranodal sides. According to I.P.I., this patient with 0 risk factors was included in the good risk category with ≈ 80% chances of survival 10 years after the treatment. (10,11,12)

After surgery, the treatment was completed with combined chemotherapy and radiotherapy.

The chemotherapy consists on 4 cycles of CHOP (Cyclophosphamide, Adriamycine, Vincristine), Prednisone) every 21 days, followed by local external radiotherapy in dose of 30 Gy involve field type. The first 4 cycles of chemotherapy were well tolerated by the patient without any notable hematologic toxicity (grade 1). At the review exams, the patient maintains a very good general status without any biological modification.

After radiotherapy, the patient has been reviewed and underwent 2 more CHOP chemotherapy cycles.

**Discussion**

In the presented case of subglottic laryngeal non Hodgkin’s lymphoma (NHL), the initial symptomatology was confound with pseudoasthmatic phenomena because of progressive dispnea, productive coughing.

In evolution, the laryngeal obstruction caused by lymphoma may be mistaken for other tumoral lesions.
The histopathological exam of the surgical pieces can confirm the diagnosis of type B malignant lymphoma, with large anaplastic cells, having a high malignancy, classified as follows NHL classification.

Lymphoma with B lymphocytic cells: low malignancy: lymphocytic, lymphoplasmocytic, plasmocytic, centroblastic type; high malignancy: centroblastic, immunoblastic, lymphoblastic and with anaplastic cells type.

Lymphoma with T lymphocytic cells: low malignancy: lymphocytic and pleomorphic with small cells type; high malignancy: lymphocytic, immunoblastic, pleomorphic with large cells type.

The Ann Arbor classification was used to specify the treatment of laryngeal NHL:

a) NHL strictly localized requires locoregional radiotherapy 35-40 Gy. (13,14,15);

b) NHL in stage IE and IIE with a large tumoral mass requires chemotherapy associated with radiotherapy;

c) NHL in stage IIIE, IVE requires polichemotherapy;

d) NHL in localized form requires surgical excision.

The prognosis of NHL located form is favourable. The lymphatic spread with cervical lymphadenopathy and different secondary lesions determine a poor prognosis. (16,17,18)

Conclusions

1. Involvement of the subglottic larynx and trachea by lymphoma is an uncommon localization which can cause severe airway obstruction and requires a multidisciplinary approach.

2. Laryngeal NHL was represent less than 1% from primitive malignant laryngeal tumours, the most part of these having lymphocite B cells development.

3. Laryngeal NHL can remain located for a long time and the extent can occur later in the lymph nodes, respiratory tract, orbit, skin.

4. The CT scan, the histology as well as the immunohistochemical exam confirm the tumoral form and extent in order to perform the complex therapy.

5. The characteristic feature of the presented case was the acute obstructive laryngeal syndrom caused by the protruding of pediculated mobile subglottic tumour into glottic space requiring an emergency tracheotomy.

6. This case of laryngotracheal non Hodgkin’s lymphoma with low grade of cellular differentiation (anaplastic cells) required both surgical excision of strictly located tumour, combined by chemotherapy and radiotherapy.

List of references


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IMPLICATIONS OF ENVIRONMENTAL AND INDIVIDUAL FACTORS IN GENESIS AND MANAGEMENT OF ADVANCED LARYNX NEOPLASMS

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Abstract

The purpose of this paper was to analyze and discuss the main factors that influence the evolution, prognostic, management and life quality of the patients affected by larynx neoplasms. Larynx carcinoma is one of the most frequent tumors of the head and neck. The external factors such as environmental and life factors (excess of alcohol, coffee, welfare, diet, professions) were found to influence the prognosis of the advanced larynx carcinoma patients. A correct management of these cases would ensure a better quality of life, even if the cure management of the patients often leads to ethical conflicts with direct effects on patient satisfaction. It was highlighted the difficulty to apply a standard therapy as the extension of laryngeal cancer in stages III - IV requires complex oncological solutions.

Key words: environment, external factors, larynx carcinoma, therapeutic management

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1. Introduction

Ecological studies linked the risk of laryngeal cancer in different populations to the tobacco smoke and alcohol. Neck cancers are associated with drastic functional problems, such as pain and difficulties in breathing, eating and speaking (Tschesner et al., 2009).

Increasing interest and awareness are given in recent years to the behavioral and functional impact of the specific treatment on the patients overall life. Health-related quality of life and the environmental factors associated to cardiovangelic diseases have become secondary endpoints in outcome assessment of patients with head and neck cancer (Aaronson and Beckmann, 1986; List and Stracks, 2000; Rogers et al., 2007; Tschesner et al., 2009).

The International Agency for Research on Cancer has prepared estimates of the global cancer burden for the last 30 years (Parkin et al., 2005).

Broad estimates of numbers of new cases for 12 common types of cancer in different areas of the world were analyzed starting with 1975, being able to supply exhaustive country-specific estimates of incidence, mortality, and prevalence, by sex and age group for 26 types of cancer in the year 2000 (Parkin et al., 1984; Parkin et al., 2001; Farley et al. 2000). The numbers of new cancer cases range from 2.2 million cases in China (20.3% of the world total) and 1.6 million in North America (14.4%) to about 1,400 in Micronesia/Palynesia.

Fig. 1 shows the number of new cases, deaths, and persons living with cancer by continent and for several larger countries (Parkin et al., 2005). Larynx carcinoma is one of the most common tumors of the head and neck. The care management of larynx advanced carcinoma must be a complex one, including surgery, radiotherapy, chemotherapy or palliative treatment, often leading to ethical conflicts with direct effects on the life quality of the patients.
Proper resolution of ethical issues, through open doctor-patient discussion helps take the most appropriate therapeutical decisions to improve the life quality of the patients (Storne et al., 2002).

In 1950, laryngeal cancers caused the death of 1661 male and 191 female in United States (Winder et al., 1956). Larynx cancer, which reached almost 159,000 new cases and 90,000 deaths in 2001, has a prevalent incidence in men, for whom it means 2.4% of cases and 2.1% of deaths (Fig. 2) (Parkin et al., 2005; Torres, 2007). The disease frequency proved to have a large geographic variability, marked by some high-risk countries in Southern Europe (France, Italy, Spain), Eastern Europe (Russia, Ukraine), South America (Uruguay, Argentina), and Western Asia (Turkey, Iraq) (Fig. 2) (Parkin et al., 2005; Torres, 2007).

Therefore, there is a large socio-economic variability in the frequency of this malady, which can be associated to environmental factors and lifestyle of the patients. The improvement of the survival rate and quality of life of patients with larynx cancer remains a challenge despite recent advances in treatment schemes and resources (Bernier, 2011; Torres, 2007).

2. Relevance of environmental factors in the prevalence of larynx cancer

The concept of environment is frequently used with an extensive scale in the medical literature, including all non-genetic factors such as diet, lifestyle and infectious agents (Petti, 2009). In this large sense, the environment is involved in generating the greater part of human cancers.

Exposure to a number of environmental carcinogenic factors has definitely been linked with an increased risk of cancer in humans. In a strict sense, environmental carcinogens include outdoor and indoor air pollutants, as well as soil and drinking water contaminants (Bernier, 2011; Boffetta and Nyberg, 2003).

The relationship between cancer outcome and the environment was summarized by Parkin et al. (2011) as to estimate the numbers (and percentages) of incident cancer cases in the UK in 2010 that are attributable to the 14 everyday life and environmental exposures considered (Fig. 3).

The four most important daily life exposures such as tobacco smoking, dietary factors, alcohol drinking and bodyweight, accounted for 34% of the cancers occurring in 2010, which represent almost four-fifths of the total from all 14 exposures (Parkin et al., 2011). However, the dominant association between alcohol drinking and risk of laryngeal cancer was suggested in the early 1990s by case-series and
was first reported in a case-control study in the 1950s (Islami et al., 2010; La Vecchia et al., 2008; Wynder et al., 1956).

The frequency is higher in males 420 cases (85.8%) than females 63 cases 14.8% and average age is 55-65 years, with variability between 28-78 years.

According to the topographic localization, these cases can be classified as: 107 glottic, 91 supraglottic, 20 subglottic, 112 transglottic and 153 plathyngolaryngeal cases (Fig. 5).

![Fig. 5. Topographic localization of patient lesions](image)

Some environmental and external factors involved in laryngeal cancer were taken into account in the study, as promoters of this disease.

- **Smoking and alcohol**

Smoke inhalation is associated with the introduction of more than 30 carcinogenic compounds, such as nitrates, polycyclic aromatic hydrocarbons, tars. The number and type of cigarettes smoked is associated with time, age and profession, as well as other factors (Chen and Halpern, 2007). It is important to highlight that the percentage of nonsmokers among the laryngeal cancer patients was small.

A similar result was reported by Wynder et al., (1976), which made a retrospective study of larynx cancer during 1956-1974. They found that only 2% of male patients and 14% of female patients were nonsmokers. However, the large sex difference noted in the study performed in 1956 (male:female ratio of 14.9:1) diminished considerable in 1974 (4.6:1), because more and more women became cigarette smokers (Wynder et al., 1956; Wynder et al., 1976).

Consumption of alcohol is among the main factors involved in the genesis of most superior respiratory digestive neoplasms. Alcohol is an important factor that, in association with smoking enhances the risk of cancer. Wynder et al. (1976) found that, among males, alcohol drinkers represented 55% of the glottic cancer patients and 70% of the supraglottic cancer patients.

Vincent and Marchetta (1963) found that, out of 106 patients with carcinoma of the oral cavity, pharynx or larynx interviewed concerning their use of alcoholic beverages and tobacco, 92 per cent reported that they drank significant amounts of alcohol daily. A history of heavy consumption of alcohol was given by 62 per cent of the patients, and 85 per cent smoked the equivalent of one or more packs of cigarettes a day (Vincent and Marchetta, 1963).

This combination results in the depletion of antitumor substances, vitamins, minerals with increased carcinogenic risk in these patients. In the statistics of our clinic, we found that out of 483 cases, more than 2/3 cases were smokers and more than 1/3
cases were associated with chronic alcohol consumption.

- **Diet**
  Diet diversity represented by the number of different foods consumed has been considered an indicator of a healthy diet and was related to the risk of several digestive tract cancers (Garavello et al., 2009). The study has proven the involvement in carcinogenesis of a diet low in Fe, Se, vitamins, fruits, vegetables, dairy products. Moreover, in a polluted environment, professional effort can interfere with the different mechanisms involved in immune defense. Among these factors, low living standards with poor nutrition as direct influence should also be noted.

  A study carried out by Garavello et al. (2009) suggests that a diet not only rich but also varied in fruit and vegetables is related to a decreased risk of laryngeal cancer. Some evidences highlighted that non-starchy vegetables, fruits, and foods containing carotenoids decrease the risk of cancer of larynx (Fitzgibbon and Stolley, 2010).

- **Individual factors**
  Various studies showed the family related character of the laryngeal cancer with implication of different genetic factors and enzymes, such as aryl hydrocarbon hydroxylase (AHH), p53 protein, associated with gastroesophageal reflux and Lynch or Bloom syndrome.

- **Profession**
  Chronic exposure of patients to pollutants such as dust and powders, paints and thinners, gas exhaust, asbestos compounds, tar and hydrocarbons in association with chronic alcohol consumption and tobacco promotes carcinogenesis (Boscetti et al., 2006; Chen and Halpern 2007; Lango, 2009; Terhaard, 1992; Thawley et al., 1999). Although occupational exposure is obviously important, the effects of various exposures are difficult to quantify and isolate (Wynder et al. 1976).

4. **Analysis of data**

  The first group of patients (A) was treated by surgical therapy (Table 1). Thus, 166 cases were solved by total laryngectomy, which was associated to functional neck dissection in 117 cases and radical neck dissection in 24 cases. Lymph node metastasis after anatomicopathological examination on uncertain oncological limits of excision was found in 147 cases, which determined the need of complementary radiotherapy.

  In 12 cases total laryngectomy and partial pharyngectomy were practiced with different types of flaps pharyngeal reconstruction, followed by radiotherapy. In 13 cases palliative treatment with tracheostomy was practiced followed by radiochemotherapy. In 166 cases solved by surgery, the complications were as follows: 36 swallowing disorders, 43 pharyngeal fistulas, and 28 wound suppurations. In 39 cases, the tumoral local recurrences at the level of tracheostoma were observed. The solution was surgery with excision of the relapse and complementary radiotherapy in 22 cases, while in 17 cases only palliative treatment was performed. The survival rate of this group was 83 at 3 years representing (50 %) (Agrowal and Goldberg, 2008; Genden et al., 2007; Koufman and Burke, 1997; Tufaro and Staffor, 2008).

  In group B of study, radiochemotherapy was applied in 320 cases. From these, 299 cases were treated by primary radiotherapy and 21 cases by chemotherapy, followed by complementary radiotherapy (Table 2). Tumoral recurrences were found in 31 patients from group B: 12 cases with metastasis in the thyroid gland and peripharyngeal soft tissue; 11 cases with pharyngeal metastasis; 8 cases with lymph node metastasis.

**Table 1. Results of advanced larynx cancer surgical treatment in patients in group A**

<table>
<thead>
<tr>
<th>Method of treatment</th>
<th>Total laryngectomy+functional neck dissection+radiotherapy=117 cases</th>
<th>Total laryngectomy+radical neck dissection+radiotherapy=24 cases</th>
<th>Total laryngectomy partial pharyngectomy+radical neck dissection+radiotherapy=12 cases</th>
<th>Palliative therapy+Tracheotomy+Chemoradiotherapy=13 cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complications</td>
<td>Trouble of swallowing=36 cases</td>
<td>Pharyngeal fistula=43 cases</td>
<td>Wound suppuration = 38 cases</td>
<td>Local recurrences=39 cases</td>
</tr>
<tr>
<td>Recurrences</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 2. The results of the radiochemotherapy in the treatment of group B**

<table>
<thead>
<tr>
<th>Method of treatment</th>
<th>Radiotherapy+tracheotomy=299 cases</th>
<th>Chemotherapy + radiotherapy=21 cases</th>
<th>Thyroid recurrences=12 cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complications</td>
<td>Pharynx recurrences=11 cases</td>
<td>Lymph node recurrences=8 cases</td>
<td></td>
</tr>
<tr>
<td>Survival rate at 3 years</td>
<td>112 cases (35%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Complications were represented by an intense process of radioepiteliata in 21 cases and also by pharyngeal fistula in 6 cases. The survival rate at 3 years in group B was 112 patients (35%) (Costinescu et al., 1996; Sessions et al., 2002). The study sought to highlight the main etiological factors involved in the development of laryngeal cancer, emphasizing on the action of external environmental factors as well as of the daily habits.

Cobzeanu et al. (2001) insisted on the multidisciplinary therapeutic management, presenting curative and prophylactic measures applied in order to improve quality of life in line with the global efforts in the field of oncology.

5. Conclusions

In cases of advanced larynx carcinoma it is difficult to apply a standard treatment because the extension of the lesions and individual factors were different. There were environmental and external factors involved in the larynx cancer pathology, which will determine the prognosis and evolution of these patients.

The open discussions between doctor and patient in taking the most appropriate therapeutic decisions are a very important step in improving quality of life. The care management of the patients after treatment can lead to ethical conflicts with direct effects on patient satisfaction.

The permanent follow up of the patients with advanced larynx cancer offered the possibility of performing efficient interventions in case of therapeutic failure and tumoral recurrences.

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BIOETHICAL ASPECTS IN QUALITY OF LIFE AT PATIENTS TREATED FOR ADVANCED LARYNX NEOPLASM


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**** Legal Medicine, Medical Deontology and Bioethics Department; „Gr.T.Popa” University of Medicine and Pharmacy, Iași, Romania

Introduction. Diagnosis and treatment of the larynx cancer in late stages present several features which result in a superior survival rate compared to other localization in ENT sphere. Maintaining an adequate social life, getting a higher quality of life and an optimal bioethical relationship between patient and physician, all represent the main directions in a correct management addressed to the patients with larynx cancer.

Material and method. The authors made a retrospective study on a number of 63 patients with advanced staged laryngeal neoplasms treated in the ENT clinic of „Sf.Spiridon” hospital from Iasi, Romania in the 2005 – 2006 period. 27 cases received a complete radiochemotheraphic treatment (CHIM-RT), while the other 36 cases received a radiosurgical treatment (CHIR-RT). The scales of the performance status where observed using the Karnofsky and ECOG/OMS/Zubrad indicator, as well as the general health status using the short SF 36 formula and the EORTS QL0-H&N35.

Results and discussions. Comparative studies were conducted in the 2 groups of patients, one group treated by radical surgery followed by RT and the other treated by CHIM-RT, showing a high survival rate in the first group and a better quality of life in the second group. HNQOL and SF 36 tests specific to head and neck cancer were applied.

Conclusions. The quality of life and the bioethics issues of patients diagnosed and treated for larynx cancer depends on the individual factors and the type of applied treatment. The applied questionnaires, representing the means of assessing the status of each patient, offer details on the disease as well as on the patient involvement in the decision-making processes in order to increase the treatment compliance.

Keywords: quality of life, bioethics, SF 36, EORTS QL0-H&N35, larynx cancer.

INTRODUCTION

Laryngeal cancer is one of the commonest of all head and neck malignant tumors. These are usually squamous cell carcinomas, most commonly arising from the glottis. Both the disease and the effects of therapy (surgery, radiation, chemotherapy) interfere with basic human functions (eating, speaking, breathing) and with the psycho-social life of the patient. This is why the bioethical aspects as well as the multimodal treatment are important goals to achieve.[2, 5] The medical team members are directly responsible for the obtained results. Open discussions are important before taking therapeutic decisions. The cancer patient care management often raises ethical problems with different effects on patient satisfaction as well as the morbidity and mortality indicators. These problems should be reviewed by ethics committees.[10, 15]
MATERIAL AND METHODS
Between January 2005 and December 2006, in ENT Clinic of „Sf. Spiridon” Hospital Iași 63 patients with late stages larynx cancer were diagnosed and treated. They were divided into 2 groups: one group with surgical treatment followed by RT and another group treated with CHIM-RT, which were eventually associated with life-saving surgery.

Baseline demographics and clinical characteristics including age, sex, TNM tumor stage, Karnofsky status, race, occupation, and level of education were obtained from retrospective studies.

Patients included in this study were divided into 2 groups: 36 cases applying surgery followed by RT and 27 cases treated with CHIM followed by RT.

The statistical study was carried out using the data on the performance status by Karnofsky index and by ECOG/OMS/ZUBROD index, as well as the tests from Short-Form 36 (SF 36) regarding the general health status and the Quality of Life in Head and Neck Cancer Patients Form (EORTCQLQ – H&N 35), along with following the bioethical desideratum of the physician - patient relation in the diagnosis and therapy of the larynx cancer.[12, 13, 14]

The comparison between the studied groups of patients was made using the $\chi^2$ test, the student test, the $t$ paired test and also the Kaplan Meier method for studying the survival rate.[9, 18]

RESULTS AND DISCUSSIONS
Standardized questionnaires applied before and after the therapy where used in order to select the 63 patients included in the study.

Group A consisted in 36 patients who had undergone radical surgery and radical neck dissection followed by external RT in dose of 70 Gy.

Group B was comprised of 27 patients who underwent concomitant chemotherapy and radiotherapy, 7 cases needing radical salvation surgery due to the failure of oncological treatment.(Graph I).

![Graph I. Type of treatment](image)

Patients were between 30 and 75 years old, mean age was 55, 3 ± 11, 4 SD years.
Thus, we had 7 patients between the ages of 30 and 40, 12 patients between 41 and 50, 24 patients between 51 and 60, 15 patients between 61 and 70 and 5 patients over 70 (Graph II).
Male preponderance was noticed – 57 male cases facing 6 female cases (Graph III).

Discussion and the realization of the therapeutical procedure was made taking in consideration the anatomopathological exam performed on the biopsy samples which showed 19 cases of well differentiated squamous cell carcinoma, 19 cases of moderate differentiated squamous cell carcinoma and 28 cases of undifferentiated squamous cell carcinoma and the TNM tumor staging (T3 - 41 cases and T4 - 22 cases) (Graph IV).
The general health status was investigated using the Short-Form 36 (SF 36) in which the standardized scores were noted on a scale between 0 for the worst score and 100 for the best. [8, 16]

Table 1

<table>
<thead>
<tr>
<th>Patients/ Domain 63</th>
<th>Meaning of Score</th>
<th>Slightly modified score (70-100)</th>
<th>Moderate modified score (40-70)</th>
<th>Profound modified score (&lt; 40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. PF</td>
<td>Limitations of physical activities</td>
<td>29</td>
<td>21</td>
<td>13</td>
</tr>
<tr>
<td>2. RP</td>
<td>Problems with work or other daily activities as a result of physical health</td>
<td>23</td>
<td>28</td>
<td>12</td>
</tr>
<tr>
<td>3. BP</td>
<td>Extent of pain or limitations due to pain</td>
<td>32</td>
<td>21</td>
<td>10</td>
</tr>
<tr>
<td>4. GH</td>
<td>Perception of personal health</td>
<td>19</td>
<td>33</td>
<td>11</td>
</tr>
<tr>
<td>5. VT</td>
<td>Level of energy</td>
<td>34</td>
<td>19</td>
<td>10</td>
</tr>
<tr>
<td>6. SF</td>
<td>Extent and frequency of interference with social activities due to physical and</td>
<td>41</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>emotional problems</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. RE</td>
<td>Problems with work or other activities due to emotional problems</td>
<td>36</td>
<td>20</td>
<td>7</td>
</tr>
<tr>
<td>8. MH</td>
<td>Feelings of nervousness and depression</td>
<td>33</td>
<td>21</td>
<td>9</td>
</tr>
</tbody>
</table>

Respecting the patients inherent dignity as a human being is of utmost importance. The consent must be fully informed, authentic and free of coercion.

What gives the care of cancer patients its special moral quality is the complexity and emotional potentials of a diagnosis of cancer, factors which depend on the patients vulnerability and corresponding the clinician’s ethical obligations.

The negative impact and most of the harm attributed to truth telling arise from clumsy,
rashed disclosure. The oncologist has the obligation to evaluate his personal ability of mastering the art of truth telling.

The patient must understand the importance of the decision that needs to be taken, its alternatives and its urgency. So, all the clinicians/oncologists who are not capable of sharing time, affection and sacrifice should reevaluate their capacity of taking care of a patient with cancer.

Compromise can sometimes be made if it does not bring any moral loss to any of the concerned parties.

Elimination of pain is a moral obligation in cancer treatment. Patient suffering is often related to a physical and mental depression, with feelings of alienation, of family and social abandonment.

The treatment of suffering requires a psychological, social and spiritual integration that together with the alienation of pain represent the palliative care of cancer patients.

Futility is considered a moral obligation of the doctor not to treat patients outrun by the evolution of the disease, as they will no longer have any benefit.

The futility criterion can be morally applied only when both parties agree that no treatment is beneficial for the patient.

The patient has the right to his inherited human rights no matter the disease they suffer from and the degree of vulnerability, especially in incurable diseases. In these conditions, the patient has the right to be fully informed and to be able to freely choose his future, this including his agreement with the therapeutical act, which has to be informed, authentic and free willed.

In the patient-doctor relation, both come with their own knowledge and values. The doctor has medical knowledge and must use them in the best way as to propose the best treatment method which will serve the best interests of the patient. On the other hand, the patient has his own values and principles in life by which he will judge the treatment proposed by the doctor. He will finally take his own decision. This decision might not be the same as the doctor’s, thus generating and ethical conflict. The secret of solving this conflict lies in knowing the patient and understanding the reason of his choice. The doctor is obliged to accept this choice if the patient is fully rational and competent.

Throughout the whole therapeutical process, the patient has to agree based on the information presented by the doctor. He must be fully aware of the importance of his decision, the therapeutical alternatives, as well as the urgency with which his neoplastic affection must be treated. So, all the oncologists who are not capable of sharing time, affection and sacrifice should reevaluate their capacity of taking care of a patient with cancer.

Pain relief should represent the main moral obligation of the doctor and should be a medical goal that must be achieved or at least dealt with the best way possible. Patient suffering is mostly comprised of pain unsolved by the treatment, as well as of physical and mental depression and feelings of alienation, social and familial abandonment. A study carried out in Holland on the moral portrayal of the patient soliciting euthanasia proved that most of these request were motivated by pain, depression, as well as other disorders that could be solved by modern medicine, thus offering an at least acceptable quality of life.

Treatment of suffering needs psychological and social integration, as well as spiritual support which along with pain relief represent the main pillars in the palliative care of cancer.
patients. When the theraupeutical stage is surpassed and surgery can no longer be successfully and usefully applied, palliative care remains the last ethical resort which can offer quality to the remaining life if the patient, time having no importance in this case. We now arrive at the delicate subject of medical futility, with all it’s negative aspects. Even if in theory the doctor should not treat patients surpassed by their illness, in practice this futility criterion can be applied only if the medical team, the patient and eventually the family of the patient come to an agreement. By this, the doctor fulfills his deontological duty of not abandoning his terminal patients who feel as human beings and not just as some symptoms carriers.[10, 11, 17]

Thus, the Karnofsky index had the following graphic representation (Graphic V): 28 patients – 80; 23 patients – 70; 12 patients – 50.

![Graph V. Karnofsky score](image)

The ECOG/OMS/ZUBROD index (Graphic VI):
- 45 patients – 2;
- 18 patients – 3.

![Graph VI. ECOG/OMS/ZUBROD index](image)

After this retrospective study, the survival rate and social insertion were observed and the quality of life was evaluated. We have insisted on the 4 areas, including speech, nutrition,
social and some aesthetic deficiencies as well as 20 other questions relating to certain symptoms of larynx cancer.

We considered the quality of life scores divided into 3 groups representing high quality (70 – 100), intermediate quality (31 – 69) and low quality (0 – 30), representation scale of results being from 0 to 100.

**Duration of survival**

In the first year: 52 followed from 63 = 12 deaths (5 CHIR-RT and 7 CHIM-RT).

In the second year: 41 followed from 63 = 11 deaths (4 CHIR-RT and 7 CHIM-RT).

**Grafic VII. Duration of survival**

**Quality of life**

**Table 2**

<table>
<thead>
<tr>
<th></th>
<th>Well</th>
<th>Influenced</th>
<th>Chi-square test (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Speech</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgery+Radiotherapy</td>
<td>21</td>
<td>15</td>
<td>$X^2 = 1.66$</td>
</tr>
<tr>
<td>Radiochemotherapy</td>
<td>20</td>
<td>7</td>
<td>$p = 0.198$</td>
</tr>
<tr>
<td><strong>Deglutition</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgery+Radiotherapy</td>
<td>23</td>
<td>13</td>
<td>$X^2 = 2.36$</td>
</tr>
<tr>
<td>Radiochemotherapy</td>
<td>12</td>
<td>15</td>
<td>$p = 0.1242$</td>
</tr>
<tr>
<td><strong>pain</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgery+Radiotherapy</td>
<td>31</td>
<td>5</td>
<td>$X^2 = 3.37$</td>
</tr>
<tr>
<td>Radiochemotherapy</td>
<td>17</td>
<td>10</td>
<td>$p = 0.0663$</td>
</tr>
<tr>
<td><strong>Emotions</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgery+Radiotherapy</td>
<td>17</td>
<td>19</td>
<td>$X^2 = 4.40$</td>
</tr>
<tr>
<td>Radiochemotherapy</td>
<td>5</td>
<td>22</td>
<td>$p = 0.0359$</td>
</tr>
</tbody>
</table>
Graph VIII. Quality of life

a. Speech:
   Group A (CHIR-RT): good – 21 patients, influenced – 15 patients
   Group B (CHIM-RT): good – 20 patients, influenced – 7 patients

b. Deglutition:
   Group A (CHIR-RT): good – 23 patients, influenced – 13 patients
   Group B (CHIM-RT): good – 12 patients, influenced – 15 patients

c. Pain:
   Group A (CHIR-RT): good – 31 patients, influenced – 5 patients
   Group B (CHIM-RT): good – 17 patients, influenced – 10 patients

d. Emotions:
   Group A (CHIR-RT):
   - with emotional changes – 17 patients
   - without emotional changes – 19 patients
   Group B (CHIM-RT):
   - with emotional changes – 5 patients
   - without emotional changes – 22 patients

Treatment results
The conclusions of the emotional modifications shows that the patients treated by radical surgical excision had more frequent emotional modified aspects like in patients treated by radiochemotherapy.[3, 4, 6]

Table 3

<table>
<thead>
<tr>
<th></th>
<th>Survival</th>
<th>Died</th>
<th>Number of complications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>One year</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgery+Radiotherapy</td>
<td>11</td>
<td>10</td>
<td>18</td>
</tr>
<tr>
<td>Radiochemotherapy</td>
<td>7</td>
<td>7</td>
<td>20</td>
</tr>
<tr>
<td><strong>Two year</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgery+Radiotherapy</td>
<td>11</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Radiochemotherapy</td>
<td>9</td>
<td>8</td>
<td>-</td>
</tr>
</tbody>
</table>
Chi-square test (95% CI)  \( X^2 = 2.91, p = 0.0746 \)

Complications and recurrences after therapy Group A and Group B:

- **CHIR** (total laryngectomy) and RT – 36 patients:
  - after 1 year:
    - peristomal recurrences – 6
    - pharyngeal recurrences – 3
    - local lymphatic recurrences – 2
    - deaths – 10
    - complications: surgery plaque infection – 6, pharyngo-cutaneous fistula - 12
  - after 2 years:
    - local recurrences – 5
    - local lymphatic recurrences – 6
    - deaths – 3
    - complications: pharyngeal stenosis - 3

- **CHIM + RT** – 27 patients:
  - after 1 year:
    - local recurrences (therapeutic failure) – 7:
      - rescue surgery – 4
      - palliative treatment - 3
    - deaths – 7
    - complications: radiodermatitis – 16, stenosis - 4
  - after 2 years:
    - local recurrences (therapeutic failure) – 9:
      - rescue surgery – 3
      - palliative treatment - 6
    - deaths – 8 [1, 7, 17]

**CONCLUSIONS**

The aspects related to localization, tumoral stages, loco-regional metastases as well as the coexistent morbidity influence the prognosis and the surviving rates.

Bioethical aspects and the quality of life in patients with larynx neoplasm in advanced stages depend on some individual factors and methods of multidisciplinary treatment that can be applied.

The proposed questionnaires were used in order to assess the health status of each patient, to offer details both on the existing diseases and on the need of patient involvement in the decision-making processes, thus achieving increased treatment compliance.

The study showed that there was no significant difference of life quality and survival in the 2 groups taken in the study.

Postoperative complications were significantly higher in patients with failure of therapy, salvage surgery showing a greater frequency particularly for faringo-cutaneous fistula and infection of wounds.
Local changes and functional disorders determined by postradiochemioterapy often cause feeding's disorders, local pain, but presenting however a better mental status as well as a better voice.

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Gastroesophageal reflux disease
- Internal U.M.F.Gr T Popa grant:
The implication of the gastroesophageal reflux disease in the genesis of ENT pathology, with application in the dysphonia of professions of intense voice user.

ISI articles


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ENVIRONMENTAL FACTORS ASSOCIATED WITH DYSPHONIA IN PROFESSIONAL VOICE USERS

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³University of the Arts “George Enescu” Iasi, Romania

Abstract

Gastro-Esophageal Reflux Disease (GERD) seems to be frequently associated with laryngeal lesions and the occurrence of disphonia. The aim of the study was to evaluate the environmental factors associated with dysphonia in professional voice users. We prospective studied 50 intense voice users’ subjects (actors, singers, teachers, priests) with dysphonia in order to identify the environmental factors which may be involved in the alteration of voice. We demonstrated the importance of the risk factors (environmental and biologic factors) in the occurrence of dysphonia.

Keywords: intense voice users; gastroesophageal reflux; environmental factors; dysphonia.

1. INTRODUCTION

Data on the Gastro-Esophageal Reflux Disease (GERD) implication in the genesis of the laryngeal lesions and the occurrence of disphonia are extensively presented in the recent medical literature. Approximately 4-10% of patients with ENT diseases may have symptoms induced by reflux (Ahmed T.F.et al., 2006). GERD is widely present in the general population. As much as 15-20% of the population may present at least once a week symptoms evoking gastro-esophageal reflux (Stanciu C.et al, (2001). Among the patients with laryngitis and dysphonia, symptoms of reflux are extremely frequent. Thus, 73% of those patients may show symptoms of GERD and 50% may have pathologic pH measurements (Drug V.et all, 2005). That represents a much higher incidence of reflux symptoms than in the general population. Additionally, a recent study made in patients with GERD indicated a prevalence of symptoms suggesting concomitant laryngeal diseases in 10.4% of cases (M. D. Cobzeanu et all, 2012). Moreover, evidence in favor of the implication of GERD in the appearance of laryngitis is also demonstrated by therapeutic trial, that is, an improvement in the ENT condition after administration of proton pump inhibitors (Sataloff R.T. et all,2010). The treatment of reflux in those patients also improves the objective parameters of the voice (Sataloff R.T. et al, 2010). A particular aspect is represented by voice alteration in patients with professions requiring high vocal strain, such as, actors, priests and even professional singers (Voineag M et all,2011).

Relevance of behavioral and environmental factors in the prevalence of professional voice disorders

Some risk factors are determining, conditioning and influencing the laryngeal modifications induced by GERD. (Roy N. et al. 2005).

Genetic factors

Genetic involvement may exist in the development of GERD, exerting influence beyond of any familial environmental factors (Mohammed I et al, 2003).

Behavioral factors

Some behavioral factors are demonstrated to be trigger for the gastroesophageal reflux. Usually three factors could be identified: smoking, alcohol intake and...
Environmental factors associated with dysphonia in professional voice users


Environmental factors
Atmospheric temperature, humidity or inhaled substances may be involved in laryngeal symptoms associated with GERD (El-Serag et all, 2008). There were also studies about the concomitance between consumption of trigger foods (onions, citrus fruits, chocolate, spices) and GERD (Terry et all, 2000; Cobzeanu et all, 2012). Increased use of anticholinergic nitrates, oral steroids, contraceptives drugs is associated with higher prevalence of GER and dysphonia (El-Serag et al, 2008).

The diagnosis of laryngopharyngeal reflux (LPR) (the extraesophageal variant of GERD) may be made by any combination of history, physical examination and 24-hour pH probe testing (Koufman J.A., et all, 2000). Treatment for LPR includes any combination of behavioral modification, pharmacotherapy (medications), and surgery. Behavior modification includes weight reduction, avoidance of food high in fat and caffeine and elevation of the head of the bed.

Persons with GERD and LPR usually respond well to medications that reduce the acid content of the refluxed materials (H2-blockers/proton pump inhibitors).

2. Material And Methods
A number of 50 subjects (age 43 +/- 11.5 years, 26 males – 52% and 24 females - 48%) professional voice users (teachers, actors, singers, priests) with dysphonia were prospectively included between 1st January 2012 -1st October 2012 based on referral to ENT Department of University Hospital “St Spiridon” from the occupational/GP doctor.

A standardized questionnaire was delivered in order to reveal the presence of other ENT symptoms and also of gastroesophageal reflux and respiratory symptoms. The predisposing factors which may influence the appearance of dysphonia, vocal abuse during physical exercise, the presence of environmental and individual factors associated with gastroesophageal reflux were also investigated in the questionnaire.

1) Including criteria in the study were the following:
- vocal professionals (teachers, actors, singers, priests);
- dysphonia for at least 3 months (chronic dysphonia);
- absence of laryngeal benign or malignant tumors;
- no pharmaceutical treatment that could alter the esophageal motor function or the acid secretion (anticholinergics, sedatives, prostaglandins, calcium channel blockers, potassium, antibiotics, NSAIDs).

2) Patients with the following criteria were excluded:
- upper airways infections during the last month (before being included in the research study);
- prior history of anti-reflux surgery;
- All patients were examined by an ENT surgeon and included a laryngoscope examination.

In order to check the relevance of our study we used data specific parametric and non-parametric tests. We used SPSS for statistical analysis. Data are presented as Mean +/- SD and percentage. We used multivariate analysis ANOVA to investigate multiple correlations.

3. Results and Discussion
The study included 50 cases (10 actors, 40 singers, 10 teachers and 10 priests (Fig. 1) with demographic data presented in fig 2 and fig 3.

![Fig. 1. Type of professional voice users](image-url)
Environmental factors associated with dysphonia in professional voice users

Summary: AGE [year]

Komogorov-Smirnov d=.08454, p> .20; Lilliefors p> .20

Expected Normal

<table>
<thead>
<tr>
<th>X &lt;= Category Boundary</th>
<th>No. of obs.</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td>15</td>
</tr>
<tr>
<td>6</td>
<td>16</td>
</tr>
<tr>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>10</td>
<td>3</td>
</tr>
</tbody>
</table>

Summary Statistics: age [year]
Valid N=50
Mean= 43.18
Confidence -95%= 39.912460
Confidence +95%= 46.447540
Median= 43.5
Minimum= 17
Maximum= 64
Lower Quartile= 36
Upper Quartile= 51
Std.Dev.= 11.497453
Standard Error= 1.625985

Fig. 2. Distribution of age

Fig. 3. Distribution of gender

Patient’s ENT, digestive and respiratory symptomatology is presented in Table 1 and fig 4. Patients included in the study presented more often heartburn (70%) or regurgitation (24%) suggesting that GERD is more often present in patients with dysphonia than in the general population. Also, almost all (90%) of patients with dysphonia had respiratory symptoms (irritating cough). Our results are consistent with recent data, however showing a higher association between dysphonia, GERD and respiratory symptoms.
Table 1. Distribution of cases according to symptoms

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Number of cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GERD</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heartburn</td>
<td>35</td>
<td>70%</td>
</tr>
<tr>
<td>Regurgitation</td>
<td>12</td>
<td>24%</td>
</tr>
<tr>
<td><strong>ENT Symptoms</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Foreign body sensation</td>
<td>15</td>
<td>30%</td>
</tr>
<tr>
<td>Hoarseness</td>
<td>50</td>
<td>100%</td>
</tr>
<tr>
<td>Fonasteny</td>
<td>17</td>
<td>34%</td>
</tr>
<tr>
<td><strong>RESPIRATORY Symptoms</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Irritating cough</td>
<td>45</td>
<td>90%</td>
</tr>
<tr>
<td><strong>Total cases</strong></td>
<td><strong>50</strong></td>
<td></td>
</tr>
</tbody>
</table>

Results on the laryngoscopy examination are presented in table 2 and fig 5. As it is showed in the table 2, congestion of vocal cords and edema of posterior comissure was the most prevalent lesion (66%). Reincke edema (16%), leukoplakia (8%) interarytenoid pachydermy (6%) and granuloma (4%) was often frequent present.

Age may influence the type of laryngeal lesions present in these patients according to data presented in fig. 6.

Table 2. Laryngeal lesions

<table>
<thead>
<tr>
<th>Lesions</th>
<th>Number of cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edema post, comissure + congestion vocal cords</td>
<td>33</td>
<td>66%</td>
</tr>
<tr>
<td>Granuloma</td>
<td>2</td>
<td>4%</td>
</tr>
<tr>
<td>Reinke Edema</td>
<td>8</td>
<td>16%</td>
</tr>
<tr>
<td>Pachyderminteraritonoidalia</td>
<td>3</td>
<td>6%</td>
</tr>
<tr>
<td>Leukoplakia</td>
<td>4</td>
<td>8%</td>
</tr>
<tr>
<td><strong>Total cases</strong></td>
<td><strong>50</strong></td>
<td></td>
</tr>
</tbody>
</table>

Fig. 4. Distribution of cases according to symptoms
As showed in table 3 multivariate analysis of risk factors vs laryngeal lesions showed a positive association between smoking, alcohol and age with the presence of laryngeal symptoms.

**Multivariate analysis of risk factors versus laryngeal lesion**

**Table 3. Multivariate analysis of risk factors versus laryngeal lesion**

<table>
<thead>
<tr>
<th>Multiple correlations</th>
<th>Estimated value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple correlation coefficient</td>
<td>0.56598</td>
</tr>
<tr>
<td>Multiple $R^2$</td>
<td>0.3203334</td>
</tr>
<tr>
<td>$F$</td>
<td>11.044100</td>
</tr>
<tr>
<td>$p$ (95%CI)</td>
<td>0.0410636</td>
</tr>
<tr>
<td>Std.Err. of Estimate</td>
<td>1.336667</td>
</tr>
</tbody>
</table>
Environmental factors associated with dysphonia in professional voice users

### Partial correlation laryngeal lesions

<table>
<thead>
<tr>
<th></th>
<th>Coefficient correlation (Beta)</th>
<th>Std.Err. (Beta)</th>
<th>B</th>
<th>Std.Err. B</th>
<th>t(135)</th>
<th>P 95% interval confidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>-0.049032</td>
<td>1.437483</td>
<td>-0.0049032</td>
<td>1.437483</td>
<td>-0.034109</td>
<td>0.972948</td>
</tr>
<tr>
<td>Smoking</td>
<td>2.292841</td>
<td>0.171074</td>
<td>0.583952</td>
<td>0.004904</td>
<td>3.711780</td>
<td>0.009414</td>
</tr>
<tr>
<td>Alcohol</td>
<td>2.141565</td>
<td>0.148643</td>
<td>0.431650</td>
<td>0.017328</td>
<td>2.952378</td>
<td>0.034622</td>
</tr>
<tr>
<td>Age</td>
<td>1.145309</td>
<td>0.208269</td>
<td>0.358741</td>
<td>0.008419</td>
<td>2.397699</td>
<td>0.048912</td>
</tr>
<tr>
<td>Coffee</td>
<td>-0.139261</td>
<td>0.233156</td>
<td>-0.003662</td>
<td>0.006131</td>
<td>-0.597287</td>
<td>0.553448</td>
</tr>
<tr>
<td>Gender</td>
<td>0.083683</td>
<td>0.160985</td>
<td>-0.222238</td>
<td>0.427533</td>
<td>0.519815</td>
<td>0.605858</td>
</tr>
<tr>
<td>Spices</td>
<td>-0.094598</td>
<td>0.241612</td>
<td>-0.002881</td>
<td>0.007359</td>
<td>-0.391530</td>
<td>0.697339</td>
</tr>
</tbody>
</table>

### Table 4. Estimated parameters in the assessment report on matters chance of contributing factors laryngeal lesion

<table>
<thead>
<tr>
<th>Larynx lesions</th>
<th>Param.β</th>
<th>Std.Err</th>
<th>-95.00% Cnf.Lmt</th>
<th>+95.00% Cnf.Lmt</th>
<th>Beta (B)</th>
<th>St.Err.β</th>
<th>-95.00% Cnf.Lmt</th>
<th>+95.00% Cnf.Lmt</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>-0.049032</td>
<td>1.437483</td>
<td>-2.94799</td>
<td>2.849930</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>0.583952</td>
<td>0.004904</td>
<td>0.10150</td>
<td>0.618285</td>
<td>2.292841</td>
<td>0.171074</td>
<td>1.052163</td>
<td>3.637845</td>
</tr>
<tr>
<td>Alcohol</td>
<td>0.431650</td>
<td>0.017328</td>
<td>0.10184</td>
<td>0.651447</td>
<td>2.141565</td>
<td>0.148643</td>
<td>1.158203</td>
<td>3.441333</td>
</tr>
<tr>
<td>Age</td>
<td>0.358741</td>
<td>0.008419</td>
<td>0.01211</td>
<td>0.522853</td>
<td>1.145309</td>
<td>0.208269</td>
<td>1.274706</td>
<td>3.565324</td>
</tr>
<tr>
<td>Coffee</td>
<td>-0.003662</td>
<td>0.006131</td>
<td>-0.01603</td>
<td>0.008702</td>
<td>-0.139261</td>
<td>0.233156</td>
<td>-0.609464</td>
<td>0.330943</td>
</tr>
<tr>
<td>Gender</td>
<td>0.222238</td>
<td>0.427533</td>
<td>-0.63997</td>
<td>1.084442</td>
<td>0.083683</td>
<td>0.160985</td>
<td>-0.240975</td>
<td>0.408341</td>
</tr>
<tr>
<td>Spices</td>
<td>-0.002881</td>
<td>0.007359</td>
<td>-0.001772</td>
<td>0.001195</td>
<td>-0.094598</td>
<td>0.241612</td>
<td>-0.581856</td>
<td>0.392659</td>
</tr>
</tbody>
</table>

5. Conclusions
Professional voice users with dysphonia often may present gastroesophageal reflux symptoms and also respiratory complains. A correct diagnostic and therapeutic attitude in these patients involves a multidisciplinary team (including otolaryngologist, gastroenterologist and pneumologist).

This study demonstrates the connection between GERD and secondary laryngitis on one hand, and the generating environmental and biologic factors on the other hand. Thus, unappropiate feeding habits (spicy food, alcohol intake, coffee consumption) and other behavioral factors (smoking) are resulting in GERD with heartburn and regurgitation. Moreover, these modifications are statistic significant correlated with the laryngeal lesions that finally will lead to hoarseness, foreign body sensation and globus histicus.

All of the investigated groups (actors, priests, singers, teachers) due to the specificity of their profession (intense voice use, physical effort during speech in some cases) and the association with different behavioral and environmental factors, presented a high rate of GERD related inflammatory laryngeal lesions.

The positive diagnostic requires modern and accurate investigations: flexible endoscopic laryngoscopy, pH monitoring, esophageal impedance study, upper gastrointestinal endoscopy (UGIE). The laryngoscopy even is an operator dependent investigation, is the first investigation used for LPR diagnosis.

The edema and erythema of the vocal folds, the edema of the interarytenoid area are the most frequent laryngeal changes that demonstrate, with statistical significance, that the gastro-esophageal reflux is involved in the laryngeal pathology.

Pyrosis (heartburn) is highly specific for gastroesophageal reflux. In the absence of symptoms, upper gastrointestinal endoscopy may reveal esophagitis as a complication of GERD. In the absence of esophagitis pH-impedance has clear indication and it is considered to be gold standard for the diagnostic of GERD.

References
Voineag M., (2011), Diagnosis and treatment of dysphonias caused by the gastroesophageal reflux disease (the case of vocal professionals), PhD Thesis.

The research was partially supported by “Gr. T. Popa” University of Medicine and Pharmacy of Iasi, Internal Grant - 2011.
The implications of gastroesophageal reflux in ENT inflammatory pathology with involvement related to voice quality of professional singers

M.D. Cobzeanu, D. Rusu*, V. Drug**, Al. Ciochină***, M. Moscalu**** and V. Munteanu*****


Summary

This study was determined by the increasing incidence of voice changes at professional singers of Opera and at Academy of Music students from Iaşi. There were associated with inflammatory digestive and upper respiratory symptomatology. A multidisciplinary complex analyse was made on 30 professional singers in comparison with a subgroup of 15 subjects from other fields that need to solicit voice. The contribution of laryngologists, gastroenterologists, psychiatrists and musicians permitted us to perform this study. The following aspects have been observed: occupation, age, the male to female ratio; type of disphonia and involved diseases; method of voice investigation (fibroscopy, videoostroboscopy, pH manometry, electroglottography, psychiatric evaluation, radiology); therapeutic approach of disphonia associated with gastroesophageal reflux, inflammatory upper airway disorders, external factors. The performed study permitted the drawing of some important conclusions in order to obtain superior vocal performances at the analyzed cases.

Key words: gastroesophageal reflux, laryngitis, voice disorders.
Introduction

The increasing incidence of disphonias with different causes in the professional vocalists determines changes in the voice performances [1,2,3]. Many voice disorders are often multifactorial and may be both functional and organic. Gastroesophageal reflux as well as ENT infection diseases are involved [6,7].

Material and Method

The authors made a comparative prospective study between a lot of 30 patients (group A) consisting of professional vocalists with dysphonia and a lot of 15 patients (group B) from other fields (teachers, actors, priests) with the same symptomatology. The influence of different external and internal factors (ENT inflammatory diseases, gastroesophageal reflux) on the vocal performances was evaluated (Figure 1).

The multidisciplinary assessment teams were consisted of laryngologists, speech language pathologists, gastroenterologists, psychiatrists, musicians.

The followed patients were grouped according to: activity, age, male and female incidence; stage of vocal performances; causes of dysphonia; para-clinic exams used in assessment of voice disorders; therapeutic modalities.

The diagnostic protocol included: anamnisis of superior aerodigestive tract disorders associated with dysphonia; digestive endoscopy which permitted to show hypopharyngeal, esophageal, gastroduodenal lesions and to take a gastric biopsy for gastritis HPP(+) diagnosis; ambulatory esophageal pH manometry; microlaryngoscopy and videostroboscopy used for the recognition of laryngeal lesions, associated with radiologic and bacteriologic exams.

![Figure 1. Mean age according to patient's sex](image-url)
Results

The lot A of 30 patients including professional vocalists consisted of 21 women and 9 men between 21 and 55 years old (Figure 2, Table 1). The fiberoptic endoscopy, indirect laryngoscopy and microlaryngoscopy showed interaritenoidian and vocal cords edema and hyperemia at 23 patients, vocal nodules at 3 patients, Reinke’s edema at 3 patients and vocal polyp in 1 case. The symptoms included hoarseness and different stages of dysphonia in 28 cases, chronic throat clearing and heartburn in 21 cases, deglutition disorders in 15 cases, globus pharyngeus in 9 cases, cough in 12 cases. In these cases, the digestive symptomatology (heartburns, globus pharyngeus, deglutition disorders) required esophagoduodenoscopy (EDS). The gastroesophageal reflux was associated with 19 patients, confirmed by pH metry (Figure 3).
Table 1. Patients distribution sex according to mean age

<table>
<thead>
<tr>
<th></th>
<th>95% +95% Std.Dev Std.Err Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>38.70 30.43 46.97 11.57 3.66</td>
<td>21.00</td>
</tr>
<tr>
<td>Female</td>
<td>41.40 35.27 47.53 8.57 2.71</td>
<td>29.00</td>
</tr>
<tr>
<td>All Grps</td>
<td>40.05 35.37 44.73 10.00 2.24</td>
<td>21.00</td>
</tr>
</tbody>
</table>

The lot B consisting of 15 patients with different professions which required vocal effort (teachers, priests) presented dysphonia associated or not with digestive symptoms. Laryngoscopy and fibroscopy showed lesions of chronic laryngitis in 12 cases, vocal nodules in 2 cases and laryngeal polyp in 1 case. Esophagoduodenoscopy revealed esophagitis in 3 cases, gastritis HP(+) in 3 cases, confirmed by biopsy. PH metry was performed at patients with symptoms according to Johnson and De Meesters criteria. Gastroesophageal reflux was confirmed in 9 cases. At 12 patients with gastroesophageal reflux and laryngeal lesions, electroglottography confirmed motility disorders and muscle tension dysphonias [4] (Table 2).

The applied treatment of voice disorders at the professional vocalists was necessary to solve the gastroesophageal reflux and chronic laryngitis determined by associated pharyngolaryngeal reflux. The treatment consisted of diet, rest voice, drugs. The treatment of reflux esophagitis requires Omeprazol 40 mg bid, more than two weeks after disappearance of gastroesophageal reflux symptoms. Afterwards, the patient took Omeprazol 20 mg/day "on demande". Association of gastritis HP(+) required Amoxicilin 2 g/day, Claritromicină 1 g/day, Metronidazol 1 g/day.

Discussion

The studied patients presented a suggestive anamnasis for irritative laryngitis and associated dispeptic syndrom.

Clinical assessment was followed by paralineic exams:

Table 2. The association risk of HP(+) is 2.67 greater at professional vocalists than the risk of other professions which require vocal effort.

<table>
<thead>
<tr>
<th>Point</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odds-based</td>
<td></td>
</tr>
<tr>
<td>Odds Ratio (cross product OR)</td>
<td>2.67</td>
</tr>
<tr>
<td>Risk-based</td>
<td></td>
</tr>
<tr>
<td>Risk Ratio (RR)</td>
<td>2.0</td>
</tr>
</tbody>
</table>
microlaryngo-scopy, electroglottography, esophagoduodenoscopy and pH manometry which provide information about gastroesophageal reflux associated with different types of chronic laryngitis involved in voice disorders at professional vocalists.

The diet and voice rest followed by progressive renewal of voice activity provide superior vocal performances [5].

The interdisciplinary approach (otolaryngologists, speech language pathologists, gastroenterologists, voice coach) is very important and permitted to obtain superior therapeutic results in dysphonia.

Conclusions

1. Dysphonia at the professional vocalists and other categories of patients who require vocal effort is a multifactorial disorder. Gastroesophageal reflux is often causally associated with chronic laryngitis.

2. The assessment of voice disorders requires laryngoscopy, videostroboscopy, fibroscopy including esophagoduodenoscopy, pH manometry associated with biopsy of gastric mucosa in gastritis HP(+).

3. The laryngopharyngeal reflux involved in chronic laryngitis and dysphonia has similar characteristics with gastroesophageal reflux.

4. One of the most important factors in management of voice disorders at the professional vocalists is the preventive treatment consisting of diet, voice rest associated with medical treatment.

References


Foreign bodies

**International grant - researcher** (Team member) - Susy safe project, Phase 1, 2 – European project on Foreign Body Injuries in the Aero–Digestive tract in Children 2005-2008.

**ISI articles**

   

   

   

   

   
Food foreign body injuries

Arjan B. (Sebastian) van As*, Abdullah M. Yusof, Alastair J.W. Millar
the Susy Safe Working Group¹

Trauma Unit, University of Cape Town, Red Cross War Memorial Children’s Hospital, Rondebosch, 7701 Cape Town, South Africa

ABSTRACT

Rationale and aim: The purpose of this study is to acquire a better understanding of Food Foreign Bodies (FFB) injuries in children characterizing the risk of complications and prolonged hospitalization due to food items according to patients’ characteristics, circumstances of the accident, Foreign Body (FB) features and FB location, as emerging from the SUSY Safe Web-Registry.

Methods: The present study uses data provided by the SUSY Safe Project, a DFJ SANCO co-funded project started in February 2005, which was aimed at establishing an international registry of cases of Foreign Bodies (FB) injuries in children aged 0–14 years. The analysis was carried out on injuries due to a food item.

FB location was reported according to ICD9-CM code: ears (ICD931), nose (ICD932), pharynx and larynx (ICD933) trachea, bronchi and lungs (ICD934), mouth, esophagus and stomach (ICD935).

Age and gender injury distributions were assessed. Data regarding adult supervision and activity before injury were also evaluated. FBs which most frequently cause complications were identified. The association between children age, adult presence, object characteristics and hospitalization/complications was computed using unweighted odds ratios and the related 95% confidence intervals.

Results: 16,878 FB injuries occurred in children aged 0–14 years have been recorded in the SUSY Safe databases. FB type was specified in 10,564 cases; among them 2,744 (26%) were due to a food item. FB site was recorded in 1,344 cases: FB was located in the ears in 99 patients, while 1,140 occurred in the upper and lower respiratory tract; finally, 105 food items were removed from mouth, esophagus and stomach. Complications occurred in 176 cases and the most documented was pulmonary or bronchial infections (23%); followed emphysema or atelectasis and by and asthma (7%). Bones were the commonest retrieved FB encountered in this study, while nuts seem to be the FB most frequently associated to complications.

Conclusions: On the basis of this study we make a strong recommendation that parents should be adequately educated and provide age-appropriate food to their children and be present in order to supervise them during eating especially during a critical period ranging from 2 to 3 years of age.

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1. Introduction

Foreign body injuries are very common in children being still an important cause of childhood morbidity and mortality [1], in fact, through play, experimentation and daily activities, children are likely to place foreign bodies into their ears, nose or mouth [2]. While the placement or presence of foreign bodies in the ear canal and their subsequent removal can be a source of significant morbidity but rarely constitutes a life-threatening event [3], the inhalation/aspiration of foreign bodies (FB) into the upper airways can be a very serious event, sometimes resulting in fatal outcome [4].

Even if the spectrum of foreign bodies varies from country to country, depending on the diet and customs of the population, the most common FB causing injuries are small food items [5]. Particularly, case reports, cases series and data coming from death certificates testify that nuts and seeds could represent a serious threat being not only the most documented foreign body, but also frequently involved in cases presenting complications and requiring hospitalization [6].

The purpose of this study is to acquire a better understanding of Food Foreign Bodies (FFB) injuries in children characterizing the risk of complications and prolonged hospitalization due to food...
items according to patients’ characteristics, circumstances of the accident, FB features and FB location, as emerging from the SUSY Safe Web-Registry.

2. Methods

2.1. Data collection

The present study uses data provided by the SUSY Safe Project, a DG SANCO co-funded project started in February 2005, which was aimed at establishing an international registry of cases of Foreign Bodies (FB) injuries in children aged 0–14 years. At the present, the project is collecting data among 60 institutions, located in 26 countries. Details on injuries are entered in the SUSY Safe Web-Registry [7] through a standardized case report form, that includes information regarding: children age and gender, features of the object, circumstances of injury (presence of parents, activity) and hospitalization’s details (duration, complications and removal details). Cases are prospectively collected using the Susy Safe system from 06/2005; moreover, also information regarding past consecutive cases available in each centre adhering to the project have been entered in the Susy Safe Registry.

2.2. Statistical analysis

The analysis was carried out on injuries due to a food item.

FB location was reported according to ICD9-CM code [8]: ears (ICD931), nose (ICD932), pharynx and larynx (ICD933) trachea, bronchi and lungs (ICD934), mouth, esophagus and stomach (ICD935).

Age and gender injury distributions were assessed. Data regarding adult supervision and activity before injury were also evaluated.

According to the Rimmell’s classification [5], FB was characterized by size, shape and consistency. Descriptive statistics (absolute number or median, 1 and III quartile according to the categorical or continuous variable, respectively) were calculated for each considered food item characteristics; FB features distribution by children class age and site of obstruction were assessed.

Removal techniques were described according to FB location.

Two different outcomes were considered: hospitalization and complication. Hospitalization has been defined whether the child was admitted in the hospital for at least 1 day. Complications included all the pathological conditions due to delayed diagnosis or to the attempts at removing the FB.

FBs which most frequently caused complications were identified. The association between children age, adult presence, object characteristics and outcomes was computed using unweighted odds ratios and the related 95% confidence intervals.

Analyses were performed using Design and Hmisc libraries from R version 2.8 [9].

Table 1

<table>
<thead>
<tr>
<th>FB description</th>
<th>N</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone</td>
<td>885</td>
<td>32%</td>
</tr>
<tr>
<td>Nut</td>
<td>613</td>
<td>22%</td>
</tr>
<tr>
<td>Other food</td>
<td>563</td>
<td>21%</td>
</tr>
<tr>
<td>Seed and grain</td>
<td>430</td>
<td>16%</td>
</tr>
<tr>
<td>Bean and pea</td>
<td>142</td>
<td>5%</td>
</tr>
<tr>
<td>Sweet</td>
<td>91</td>
<td>3%</td>
</tr>
<tr>
<td>Fruit stone</td>
<td>20</td>
<td>1%</td>
</tr>
<tr>
<td>Total</td>
<td>2744</td>
<td></td>
</tr>
</tbody>
</table>

3. Results

A total of 16,878 FB injuries occurred in children aged 0–4 years have been recorded in the SUSY SAFE databases. FB type was specified in 10,64 cases; among them 2744 (26%) were due to a food item. Details regarding retrieved FBs are given in Table 1.

FB site is known in 1344 cases: FB was located in the ears in 99 patients, while 1140 occurred in the upper and lower respiratory tract; finally, 105 food items have been removed from mouth, esophagus and stomach. In Table 2 the total amount of food related injuries, the number of complicated injuries and the number of injuries in which hospitalization is needed are reported for each site.

Data regarding age was available in 1362 FB cases. Distribution of incidence of analyzed injuries by age class is shown in Fig. 1. More than half of observed injuries involved patients 1–years old. 58% of patients were males, while 42% were females. When injury happened, 85% of children were eating while 12% were playing. Almost 40% (1090) of injuries happened under adults’ supervision.

FB characteristics by age and by location are described respectively in Tables 3 and 4.

When FB are located in pharynx and larynx, or in trachea, bronchi and lungs, or in mouth, esophagus and stomach the most documented removal technique is endoscopy (accounting respectively for the 93%, 96% and 78% of cases) while in a large amount of cases (70%) other unspecified techniques were adopted in order to remove FB located in ears or nose. Surgery was needed in the extraction of 3% of FB in the ears and 1% of nasol FB.

Looking to the outcomes, 847 (31%) children needed hospitalization; among them, 349 (45%) were discharged after 24 h whereas 169 (22%) required hospitalization more than 3 days.

Complications occurred in 176 cases and the most documented were pulmonary or bronchial infections (23%) followed by emphysema or atelectasis and by and asthma (7%). Food items which most frequently caused complications are listed in Table 5.

In order to verify the association among children age, adult supervision, object characteristics and outcomes, odds ratios of complications and hospitalization, with 95% confidence intervals, are presented in Table 6.

Table 2

<table>
<thead>
<tr>
<th>Location</th>
<th>Food related injuries</th>
<th>Complications</th>
<th>Hospitalization</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Ear</td>
<td>7% (99)</td>
<td>8% (10)</td>
<td>5% (56)</td>
</tr>
<tr>
<td>Nose</td>
<td>19% (253)</td>
<td>14% (17)</td>
<td>16% (169)</td>
</tr>
<tr>
<td>Pharynx and larynx</td>
<td>16% (220)</td>
<td>10% (12)</td>
<td>16% (165)</td>
</tr>
<tr>
<td>Trachea, bronchi and lungs</td>
<td>50% (667)</td>
<td>62% (74)</td>
<td>57% (583)</td>
</tr>
<tr>
<td>Mouth, esophagus and stomach</td>
<td>8% (105)</td>
<td>6% (7)</td>
<td>5% (54)</td>
</tr>
<tr>
<td>Total</td>
<td>1344</td>
<td>124</td>
<td>1032</td>
</tr>
</tbody>
</table>

Table 3

<table>
<thead>
<tr>
<th>Location</th>
<th>Food related injuries</th>
<th>Complications</th>
<th>Hospitalization</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Ear</td>
<td>1% (6)</td>
<td>15% (59)</td>
<td>5% (56)</td>
</tr>
<tr>
<td>Nose</td>
<td>45% (175)</td>
<td>2% (8)</td>
<td>57% (583)</td>
</tr>
<tr>
<td>Pharynx and larynx</td>
<td>34% (133)</td>
<td>3% (13)</td>
<td>16% (165)</td>
</tr>
<tr>
<td>Trachea, bronchi and lungs</td>
<td>2% (8)</td>
<td>45% (175)</td>
<td>57% (583)</td>
</tr>
<tr>
<td>Mouth, esophagus and stomach</td>
<td>3% (13)</td>
<td>16% (165)</td>
<td>57% (583)</td>
</tr>
<tr>
<td>Total</td>
<td>15% (59)</td>
<td>57% (583)</td>
<td>85% (636)</td>
</tr>
</tbody>
</table>

Table 4

<table>
<thead>
<tr>
<th>Location</th>
<th>Food related injuries</th>
<th>Complications</th>
<th>Hospitalization</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Ear</td>
<td>5% (28)</td>
<td>2% (14)</td>
<td>15% (84)</td>
</tr>
<tr>
<td>Nose</td>
<td>16% (90)</td>
<td>3% (17)</td>
<td>45% (255)</td>
</tr>
<tr>
<td>Pharynx and larynx</td>
<td>10% (56)</td>
<td>5% (28)</td>
<td>34% (184)</td>
</tr>
<tr>
<td>Trachea, bronchi and lungs</td>
<td>4% (22)</td>
<td>2% (14)</td>
<td>34% (184)</td>
</tr>
<tr>
<td>Mouth, esophagus and stomach</td>
<td>4% (22)</td>
<td>2% (14)</td>
<td>34% (184)</td>
</tr>
<tr>
<td>Total</td>
<td>34% (184)</td>
<td>2% (17)</td>
<td>34% (184)</td>
</tr>
</tbody>
</table>
Fig. 1. Distribution of incidence (%) of FB injuries by age class. Over the bars, 95% confidence intervals are plotted.

Table 3
Food items characteristics by age. Data are first quartile/median/third quartile for continuous variables and percentages (absolute numbers) for categorical variables. N is the number of valid cases for each given variable.

<table>
<thead>
<tr>
<th>Foreign body characteristics</th>
<th>N</th>
<th>Age class</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>&lt;1 year (N=99)</td>
</tr>
<tr>
<td>Volume (mm³)</td>
<td>1362</td>
<td>1/1/1</td>
</tr>
<tr>
<td>Shape</td>
<td>994</td>
<td>33% (28)</td>
</tr>
<tr>
<td>Spherical</td>
<td></td>
<td>27% (23)</td>
</tr>
<tr>
<td>3D</td>
<td></td>
<td>7% (6)</td>
</tr>
<tr>
<td>2D</td>
<td></td>
<td>2% (2)</td>
</tr>
<tr>
<td>2Dcircle</td>
<td></td>
<td>31% (26)</td>
</tr>
<tr>
<td>other</td>
<td>368</td>
<td>1/1.33/6.5</td>
</tr>
<tr>
<td>Ellipticity*</td>
<td>1055</td>
<td>15% (13)</td>
</tr>
<tr>
<td>Consistency</td>
<td></td>
<td>24% (21)</td>
</tr>
<tr>
<td>Conforming</td>
<td></td>
<td>24% (21)</td>
</tr>
<tr>
<td>Semi-rigid</td>
<td></td>
<td>30% (26)</td>
</tr>
<tr>
<td>Rigid</td>
<td></td>
<td>32% (28)</td>
</tr>
<tr>
<td>Do not know</td>
<td></td>
<td>3% (2)</td>
</tr>
</tbody>
</table>

* Ratio between the maximum and the minimum size reported.

4. Discussion

In scientific literature food particles are described as the items most frequently involved in FB injuries, being indicated in a number of case series as responsible of the major part of events [5]. Starting from data collected by the Susy Safe Register, it appears that food particles are responsible of not more than 26% of injuries due to insertion/aspiration/inhalation/ingestion of FBs. However, this result can be easily explained by the fact that the Susy Safe Project was originally designed in order to establish a surveillance registry of non-food FB injuries, while only recently information regarding FFB have been collected included in the registry.

Children are prone to aspirate/inhale FBs for several reasons including behavioral and anatomic aspects such as the tendency to explore their surrounding using the mouths and to talk and run around while chewing, anatomical characteristics (the incomplete dentition with presence of incisors to tear foods but lack of cuspids necessary to grind food into a smooth bolus) and physiological features including immature swallowing coordination, poor chewing capacity and higher respiratory rates compared with adults: once an object or food particle is in a child’s mouth, it can lodge within the respiratory tract, be ingested in the gastrointestinal tract or end up in the nasopharynx [10].

According to the European experience, tracheobronchial foreign bodies seem to cause complications more frequently than FB located in any other site. The FB location in tracheobronchial tree has in fact a range of possible outcomes, including recurrent pulmonary diseases. Confirming the occurrence of aspiration is important in patient management in order to take steps to prevent recurrence [11–13].
Table 4
Food items characteristics by FB location. Data are first quartile/median/third quartile for continuous variables and percentages (absolute numbers) for categorical variables. N is the number of valid cases for each given variable.

<table>
<thead>
<tr>
<th>Foreign body characteristics</th>
<th>Foreign body location</th>
<th>N</th>
<th>Ear (N=218)</th>
<th>Nose (N=625)</th>
<th>Pharynx and larynx (N=855)</th>
<th>Trachea, bronchi and lungs (N=906)</th>
<th>Mouth, esophagus and stomach (N=120)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td></td>
<td>2744</td>
<td>1/1/1</td>
<td>1/1/1</td>
<td>1/1/1</td>
<td>1/1/1</td>
<td>1/1/1</td>
</tr>
<tr>
<td>Shape</td>
<td></td>
<td>1475</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spherical</td>
<td></td>
<td>59%</td>
<td>52% (103)</td>
<td>3% (16)</td>
<td>36% (215)</td>
<td>24% (15)</td>
<td></td>
</tr>
<tr>
<td>3D</td>
<td></td>
<td>20%</td>
<td>30% (60)</td>
<td>50% (269)</td>
<td>30% (180)</td>
<td>46% (29)</td>
<td></td>
</tr>
<tr>
<td>2D</td>
<td></td>
<td>6%</td>
<td>2% (4)</td>
<td>30% (193)</td>
<td>6% (34)</td>
<td>8% (5)</td>
<td></td>
</tr>
<tr>
<td>2D circle</td>
<td></td>
<td>3%</td>
<td>6% (11)</td>
<td>0% (1)</td>
<td>15% (5)</td>
<td>6% (3)</td>
<td></td>
</tr>
<tr>
<td>other</td>
<td></td>
<td>12%</td>
<td>11% (22)</td>
<td>12% (64)</td>
<td>27% (160)</td>
<td>17% (11)</td>
<td></td>
</tr>
<tr>
<td>Ellipticity*</td>
<td></td>
<td>384</td>
<td>1.00/1.00/1.33</td>
<td>1.00/0.00/2.00</td>
<td>2.00/14.25/30.00</td>
<td>1.00/1.67/4.00</td>
<td>1.21/1.43/8.25</td>
</tr>
<tr>
<td>Consistency</td>
<td></td>
<td>2283</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conforming</td>
<td></td>
<td>40%</td>
<td>45% (250)</td>
<td>25% (197)</td>
<td>4% (31)</td>
<td>16% (12)</td>
<td></td>
</tr>
<tr>
<td>Rigid</td>
<td></td>
<td>42%</td>
<td>37% (201)</td>
<td>46% (351)</td>
<td>41% (283)</td>
<td>42% (31)</td>
<td></td>
</tr>
<tr>
<td>Semirigid</td>
<td></td>
<td>15%</td>
<td>14% (78)</td>
<td>11% (84)</td>
<td>27% (190)</td>
<td>31% (23)</td>
<td></td>
</tr>
<tr>
<td>Do not know</td>
<td></td>
<td>3%</td>
<td>4% (21)</td>
<td>18% (138)</td>
<td>27% (188)</td>
<td>11% (8)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>176</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Ratio between the maximum and the minimum size reported.

In children ingesting a large foreign body it is often impacted in the upper esophagus at the level of cricoid cartilage, which is the narrowest part of the esophagus. The most common area of impaction however is the midesophagus where the esophagus is crossed by the aortic arch and left main bronchus [14]. Food bolus impaction is common with meat, fish bones and chicken bone [15–17]. If this type of food particle is impacted in the esophagus, the symptoms may range from foreign body sensation, chest pain, odynophagia, and vomiting as well as respiratory symptoms. A food bolus impaction should not be allowed to remain in the esophagus beyond 24 h from presentation [15]. Endoscopic retrieval is mandatory. If the food bolus passes the stomach, the potential impediment sites include the pylorus, the ioececal valve and the anus. The risk of perforation is however less than one percent [18].

Finally, small children also have a tendency to put things into the nose [19] and ear [20.21]. They are typically brought by their parents to emergency units after the parents noticed the presence of foreign body in these body orifices. Some may not be noticed until persistent symptoms present. Nasal and middle ear canal obstruction by a foreign body can cause severe irritation in the children. Obstruction of the nasal passage may lead to rhinosinusitis which may be recurrent and is often manifested by a purulent nasal discharge. Unilateral symptoms and signs in a child suggest an object impacted in the nasal fossa usually introduced through the ipsilateral nostril [22]. Unnoticed foreign body in the ear canal can also lead to chronic otitis media [3].

In our experiences bones were the commonest retrieved FFB encountered in this study, while nuts seem to be the FFB most frequently associated to complications. Particularly fish bones are dangerous because they possess the potential hazard of

Table 5
Description of FB which caused complications.

<table>
<thead>
<tr>
<th>FB description</th>
<th>N</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nut</td>
<td>74</td>
<td>42%</td>
</tr>
<tr>
<td>Other food</td>
<td>43</td>
<td>24%</td>
</tr>
<tr>
<td>Seed and grain</td>
<td>35</td>
<td>20%</td>
</tr>
<tr>
<td>Bone</td>
<td>12</td>
<td>7%</td>
</tr>
<tr>
<td>Bean and pea</td>
<td>6</td>
<td>3%</td>
</tr>
<tr>
<td>Sweet</td>
<td>4</td>
<td>2%</td>
</tr>
<tr>
<td>Fruit stone</td>
<td>2</td>
<td>1%</td>
</tr>
<tr>
<td>Total</td>
<td>176</td>
<td></td>
</tr>
</tbody>
</table>

Table 6
Odds ratio of complications and of hospitalization with the 95% confidence intervals are presented. P values are also presented. N number of valid cases for each given variable. Ref, reference category.

<table>
<thead>
<tr>
<th>Variables</th>
<th>N</th>
<th>Hospitalization</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes (N=847)</td>
<td>No (N=664)</td>
<td>OR (95%CI)</td>
</tr>
<tr>
<td>Age class</td>
<td>1362</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1 year</td>
<td>111 (81)</td>
<td>24% (9)</td>
<td>0.021</td>
</tr>
<tr>
<td>1-2 years</td>
<td>655 (488)</td>
<td>32% (126)</td>
<td>0.43 (0.21; 0.88)</td>
</tr>
<tr>
<td>&gt;3 years</td>
<td>255 (187)</td>
<td>65% (256)</td>
<td>0.08 (0.04; 0.17)</td>
</tr>
<tr>
<td>Adult supervision</td>
<td>1381</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adult present</td>
<td>75% (393)</td>
<td>71% (256)</td>
<td>1.26 (0.93; 1.70)</td>
</tr>
<tr>
<td>Volume</td>
<td>2744</td>
<td>1/1/1</td>
<td>1.05 (0.94; 1.18)</td>
</tr>
<tr>
<td>Shape</td>
<td>1475</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spherical</td>
<td>36% (235)</td>
<td>26% (136)</td>
<td>Ref</td>
</tr>
<tr>
<td>3D</td>
<td>27% (176)</td>
<td>20% (106)</td>
<td>0.96 (0.70; 1.32)</td>
</tr>
<tr>
<td>2D</td>
<td>7% (46)</td>
<td>36% (191)</td>
<td>0.14 (0.09;0.20)</td>
</tr>
<tr>
<td>2D circle</td>
<td>15% (6)</td>
<td>3% (16)</td>
<td>0.22 (0.08; 0.57)</td>
</tr>
<tr>
<td>Other</td>
<td>20% (190)</td>
<td>14% (76)</td>
<td>1.45 (1.03; 2.03)</td>
</tr>
<tr>
<td>Ellipticity</td>
<td>384</td>
<td>1.00/1.50/3.75</td>
<td>0.89 (0.82; 0.96)</td>
</tr>
<tr>
<td>Consistency</td>
<td>2283</td>
<td>1.00/1.50/3.43</td>
<td>1.00/1.50/3.43</td>
</tr>
</tbody>
</table>

Ref, reference category.
perforating the bowel, mandating surgical exploration [23]. On the other hand, when located in the respiratory airways, nuts represent a serious threat: in fact, swallowing with time and irritating the bronchial mucosa, they lead to an intense, local, chemical inflammatory reaction, early obstruct the tracheobronchial tree and make bronchoscopic identification and removal more difficult [6].

Traditionally, injuries have been regarded as unavoidable accidents and only recently have they been recognized as being eligible for preventive efforts. In order to prevent injuries, supervision of children is very important in all aspects of their lives, even during eating. Particularly, children should eat appropriate types of food according to their age. As reported by Burney Yeo in British Medical Journal in 1889 [24], food other than milk may be introduced into the infant’s diet, but in a wise manner. Solid food should never be given before the fourth month, and it is better not to provide these feeds until after the seventh or eighth month, when the teeth and salivary glands have begun to develop. Between the tenth and twelfth months, breast feeding may be gradually suspended but milk should still form the staple feed up to the age of eighteen months. At this age a little meat may be wisely introduced in the solid form, to furnish some employment to the masticating organs [24].

Parents need to be informed about children’s physiological and anatomic features and about their nutritional requirements; moreover, parents need to be educated to provide appropriate food to children in order to avoid injury; therefore, since education plays a key role in injury prevention, counseling about safe behaviors should be included in all visits to pediatricians in order to make parents conscious of risk associated with eating some foods and enable them to select a safe environment for their children.

Appendix A. The Susy Safe Working Group

Coordination group
Prof Dario Gregori, University of Padova, Italy, Principal Investigator
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Dr. Francesco Maria Passali, ENT Department, Catholic University
“The Sacred Heart” of Rome, Italy

Japan
Eng. Yoshihumi Nishida, National Institute of Advanced Industrial Science and Technology (AIST), Japan

Kazakhstan
Dr. Gainel Usatalyev, Kazakhstan School of Public Health, Kazakhstan

Mexico
Dr. Ricardo De Hoyos, San Jose-Tec de Monterrey Hospital, Mexico

Nigeria
Dr. Foluwaseyo Emmanuel Ologe, University of Ilorin Teaching Hospital, Nigeria

Pakistan
Dr. Muazzam Nasrullah, Services Hospital, Paediatric Ward, Pakistan

Panama
Dr. Amarilis Melendez, Santo Tomas Hospital, Panama

Poland
Dr. Mieczyslaw Chmielik, Medical University of Warsaw, Poland

Portugal
Dr. Teresa Belchior, Deco Proteste, Portugal

Romania
Dr. Mihail Dan Cobzeanu, Sf. Spiridon Hospital, Romania
Dr. Dan Cristian Gheorghe, Maria Sklodowska Curie Hospital, Romania
Dr. Adelia Iorgulescu, Grigore Alexandrescu Pediatric Hospital, Romania
Dr. Caius-Codrut, Sarofeleanu SF. Maria Hospital, Romania
Dr. Miorita Toader, Grigore Alexandrescu Pediatric Hospital, Romania

Slovak Republic
Dr. Jana Barkociová, Children University Hospital, Slovak Republic
Dr. Beata Havelkova, Public Health Authority of the Slovak Republic, Slovak Republic

Slovenia
Dr. Miha Zargi, University Medical Centre, Slovenia

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Prof AB (Sebastian) van As, Red Cross War Memorial Children’s Hospital and Childsafe, South Africa

Spain
Dr. Felix Pumarola, Vall d’Hebron University Hospital, Spain
Dr. Lorenzo Rubio, Ruber International Hospital, Spain

Sweden
Dr. Pontus S-tiera, Huddinge University Hospital, Sweden

Taiwan
Dr. Wei-chung Hsu, National Taiwan University Hospital, Taiwan

Thailand
Dr. Sakda Arj-Ong, Ramathibodi Hospital, Thailand
Dr. Chulathida Chomchai, Siriraj Hospital, Thailand

The Netherlands
Dr. Lennaert Hoep, VU Medical Center, The Netherlands

Dr. Rico Rinkel, VU Medical Center, The Netherlands

Turkey
Dr. Erdinc Aydin Baskent, University Ankara Hospital, Turkey
Dr. Volkan Sarper Eriksik, Bebect Uz Children Hospital, Turkey
Dr. Metin Onerci, Hacettepe University, Turkey

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Dr. Christopher Raine, Bradford Royal Infirmary, United Kingdom

References
The Susy Safe project overview after the first four years of activity

The Susy Safe Working Group 1,*

ABSTRACT

Objectives: to collect relevant, up-to-date, representative, accurate, systematic information, related to foreign bodies (FB) injuries.

Methods: The “Susy Safe” registry, a DG SANCO co-funded project gathering data on choking in all EU Countries and beyond, was established in order to create surveillance systems for suffocation injuries able to provide a risk-analysis profile for each of the products causing the injury. Main findings after 4 years of activities are resumed here.

Results: 16,878 FB injuries occurred in children aged 0–14 years have been recorded in the SUSY SAFE databases; 8046 cases have been reported from countries outside EU. Almost one quart of the cases involving very young children (less than one year of age) presented a FB located in bronchial tract, thus representing a major threat to their health. Esophageal foreign bodies are still characterizing injuries occurred to children younger than one year, in older children the most common locations are the ears and the nose. FB type was specified in 10,564 cases. Food objects represented the 26% of the cases, whereas non-food objects were the remaining 74%. Among food objects, the most common were bones, nuts and seed, whereas for the non-food objects pearls, balls and marbles were observed most commonly (29%). Coins were involved in 15% of the non-food injuries and toys represented the 4% of the cases.

Conclusions: this data collection system should be taken into consideration for the calculation of the risk of injuries in order to provide the EU Commission with all the relevant estimates on FB injuries.

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1. Introduction

Suffocation due to foreign bodies (FBs) is a leading cause of death in children aged 0–3 and it is common also in older ages, up to 14 years old. Based on the RPA report [1] the estimated number of incidents per year in children aged 0–14 is in European Union (EU) of about 50,000, 10% of which are fatal. In the RPA report [1] about 10,000 accidents are estimated to involve inorganic objects, in general industrial products, mostly plastic and metal parts, coins, and toys [2]. Out of the estimated 2000 incidents per year involving toys, the fatalities are around 20. Based on official records, the cost in terms of life loss due to suffocation in general has been estimated, for the EU community, as about 5 billion euros per year, only because of injuries due to industrial products [3].

The need for a multinational pan-European study derived by the lack of comparable data on the choking risk prevalence in European countries has been recently pointed out in few papers [4–6]. In fact, most of the epidemiologic evidence on foreign bodies (FBs) in children comes from single-center retrospective studies, covering a time range of about 3–10 years [7–13] in the past. Very recently, attempts have been made to start a systematic collection of FBs in view of using them to characterize the risk of choking in terms of size, shape and consistency of the FB [14]. Also several review papers discussed more clinical aspects of the FB injuries, like clinical diagnosis and management of the injured child [15]. Country specific experiences have also been presented in the literature, with a wide although not systematic spread and geographical coverage [16–19]. In particular, very small attention has been paid to this subject in Europe, which was, till few years ago, lagging behind the North-American experience, often based on large databases and data collection repositories. Even if not too many papers have been published on the argument based on European data [4,20–22], still very few attempts have been made to synthesize the epidemiological data as arising from the literature.

Difficulties are arising from the relative rarity of the phenomenon, in particular in EU and USA, after the adoption of severe rules for toy packaging and distribution. Actually the effect of regulatory acts had the effect of step-down the trend in choking injuries. Actual estimates are indicating mortality for suffocation (all causes) in EU exceeding nearly a death per 100,000 children. The heterogeneity among countries is very high, making the comparison among countries very difficult.
From the methodological point of view, basically three approaches were actually adopted for these purposes: (i) official data re-analysis, mostly based on discharge records of official death certificates, and published official statistical data, (ii) clinical registries, most often single center-based \cite{15,23}, and (iii) foreign body collections, with the specific aim of describing the shape and the material of the object causing the injury \cite{14}. Unfortunately, all these methods are revealing as largely inadequate to address the epidemiological characterization of the phenomenon in the sense described above, because of the relatively scarce and geographically limited area of the clinical registry, the poor clinical information of the official data and the limited spectrum of perspectives of the object collections.

In addition to this scientific scenario, also from the political point of view things changed in EU. Indeed, over the last years, the focus in the European Commission has moved toward what is sometimes called “science-based policy making” and better regulation. As a consequence, increasing pressure has been put on the scientific community, not necessarily because it is essential to justify decisions, legislations, or activities, but because in order to do so it is extremely important to have a sound knowledge, a sound basis in terms of information for every area that needs to be investigated, in terms of Commission work but naturally also in terms of Consumer Safety. Now that more formal recognition has been given in the new Consumer Policy Strategy for the years 2007–2013, it is important to remark the importance of data collection at an EU level. So, it is considered as an absolute priority the creation of a harmonized system for collecting such data to improve the evidence base for the assessment of risks related to Product and Service Safety \cite{24}. Therefore, the key objective of the European Commission is to ensure that relevant, up-to-date, representative, accurate, systematic information, related to accidents and injuries for consumer products or related to consumer products and any provision of consumer service are available to the Commission and other relevant bodies when decisions need to be taken.

To overcome such scientific issues and to address such political needs with respect to foreign bodies’ injuries in children, a large, multi-center registry has been established in Europe: the Susy Safe project.

2. The Susy Safe registry

The surveillance registry for injuries due to non-food foreign bodies’ ingestion, the “Susy Safe” registry, gathering data on choking in all EU Countries and beyond, was established in order to:

1. provide a risk-analysis profile for each of the products causing the injury with the aim at:
   a. creating a surveillance systems for suffocation injuries caused to young consumers by inappropriate product design or packaging;
   b. helping guaranteeing the safety of consumers, indicating products whose risk profile is clearly not compatible with a safe fruition of the product itself;
   c. providing the EU Commission with comparative data on risk/benefit of each of the products causing the injuries, in order to weight acceptable risks versus the foreseen economic impact of recalling the product involved from the market;

2. providing an evaluation of how socio-economic disparities among EU citizens may affect the likelihood of being injured by FB ingestion, with the aim of implementing specific educational activities on safe behavior and active parental guard with regards to the specific products causing the injury;

3. involving, as appropriate, Consumer Associations and/or National Market Surveillance Authorities in data collection and proper education of consumers, allowing a precise estimate of the risk profiles for those products which are actually causing the injury, but, because of the low impact in terms of child health (self resolved FB ingestions) are usually under reported and not known in the official clinical discharge data.

Thus, the project used the previous experience gained with the European Survey of Foreign Body Injuries (ESFB) \cite{25} as a starting point, with the aim of applying that methodology to creation of a surveillance registry in EU and EFTA countries, with the joint effort of statisticians, public health expert, otoroynolaryngologists, consumers and educational professionals.

The objectives envisaged by the project were planned to be met in particular by:

1. establishing an ad-hoc WEB server for collection of data in a centralized manner, in order to allow:
   a. constant quality control on data collection and completeness;
   b. easy and cost-effective access (via low-band internet connection) to data collection activities for public and private institutions willing to share their data with the project, with the aim of lowering as much as possible any barriers to participation to the project;

2. setting up an ad-hoc risk analysis engine (running on the WEB server) with the aim of obtaining an updated estimate of risk profiles for each of the objects causing the injuries, effectively as new data become available;

3. translating risk-analysis and statistical concepts into accessible information for EU citizens, involving EU consumer’s associations in the process of safe product consumption, also in the view of lowering the effects of the possible socio-economic disparities involved in the injuries.

3. Data collection

16,878 FB injuries occurred in children aged 0–14 years have been recorded in the SUSY SAFE databases; 8046 cases have been reported from countries outside EU. Details regarding the patients’ distribution by country are reported in Table 1.

<table>
<thead>
<tr>
<th>Countries</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>EU Countries</td>
<td>8832</td>
</tr>
<tr>
<td>Austria</td>
<td>12</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>607</td>
</tr>
<tr>
<td>Cyprus</td>
<td>99</td>
</tr>
<tr>
<td>Denmark</td>
<td>70</td>
</tr>
<tr>
<td>Finland</td>
<td>421</td>
</tr>
<tr>
<td>France</td>
<td>122</td>
</tr>
<tr>
<td>Germany</td>
<td>157</td>
</tr>
<tr>
<td>Greece</td>
<td>88</td>
</tr>
<tr>
<td>Italy</td>
<td>5241</td>
</tr>
<tr>
<td>Poland</td>
<td>45</td>
</tr>
<tr>
<td>Romania</td>
<td>753</td>
</tr>
<tr>
<td>Slovak Republic</td>
<td>241</td>
</tr>
<tr>
<td>Slovenia</td>
<td>105</td>
</tr>
<tr>
<td>Spain</td>
<td>149</td>
</tr>
<tr>
<td>Sweden</td>
<td>236</td>
</tr>
<tr>
<td>The Netherlands</td>
<td>77</td>
</tr>
<tr>
<td>UK</td>
<td>409</td>
</tr>
<tr>
<td>Non EU Countries</td>
<td>8046</td>
</tr>
<tr>
<td>Argentina</td>
<td>2461</td>
</tr>
<tr>
<td>Croatia</td>
<td>19</td>
</tr>
<tr>
<td>FYROM</td>
<td>63</td>
</tr>
<tr>
<td>Pakistan</td>
<td>13</td>
</tr>
<tr>
<td>South Africa</td>
<td>5240</td>
</tr>
<tr>
<td>Turkey</td>
<td>250</td>
</tr>
</tbody>
</table>

Total 16,878
The registry collected 1727 prospective cases and 15,151 retrospective cases. Retrospective cases are past consecutive cases available in each center registry and shared with Susy Safe. Data collection for retrospective cases followed the same procedure as for the prospective cases. All cases, in fact, irrespectively from their retrospective or prospective nature have been entered in the registry using the Susy Safe Case Report Form (CRF), thus ensuring the same quality, at least from the data entry point of view, for all cases reported in the system. For the purposes of providing a picture of the overall data quality, three definitions have been adopted: (i) low quality data: few basic data available (e.g., gender and age), (ii) medium quality data: basic data on FB characteristics and procedures are available (FB type, type of procedure) and (iii) high quality: detailed data on at least one FB characteristic are available (shape, size, circumstances of the injury).

Sixty percent of the prospective cases have a level of quality high enough (medium or high) to meet the requirements of the risk analyses system (see below), and, although this percentage lowers down to 36% for retrospective cases, still this remains a very good achievement (Fig. 1).

4. Main findings

The children age distribution is shown in Fig. 2: 55% of the cases are males, and about 38% of them are younger than three years.

This percentage rises to 43% for females (Table 2). Forty-seven children were reported with mental of physical impairment.

FB location was reported according to ICD9-CM code: ears (ICD931), nose (ICD932), pharynx and larynx (ICD933), trachea, bronchi and lungs (ICD934), mouth, esophagus and stomach (ICD935).

Distribution of cases by location and by gender is shown in Fig. 3: while FBs in the ears were more common in females, all other sites were more common for males than for females.

FB type was specified in 10,564 cases; the retrieved FB description is given in Table 4. Food objects represented the 26% of the cases, whereas non-food objects were the remaining 74%. Among food objects, the most common were bones, nuts and seed, whereas for the non-food objects pearls, balls and marbles were observed most commonly (29%). Coins were involved in 15% of the non-food injuries and toys represented the 4% of the cases.
Tables 5 and 6 show the distribution of the cases according to the shape and consistency stratified by foreign body type. Spherical objects represent the 36% of the cases; the 76% of the retrieved FBs were rigid.

Looking to FB volume, food objects had a median volume of 31.4 mm³, with a maximum observed volume of 4710 mm³; bones tended to have higher volumes than nuts and beans. Non food objects had a median volume of 41.9 mm³, with an upper 95th percentile of 470.1 and 99th percentile of 1045 mm³ (Table 7). The maximum volume observed was of 2093 mm³. To allow a comparison with commonly used objects, a 5 eurocent coin has a volume of 483 mm³, a flat battery of 943 mm³. Accessorize had a greater volume among various foreign body types (Table 8).

An important tool has been introduced both in USA and in Europe to foster safety of toys avoiding the contact of small parts with children [26]. Indeed, toys with small parts cannot be sold to children younger than three years old without specific warnings. Small parts are defined as those object components fitting in the so-called “small part cylinder” (Fig. 4). Regarding the “small-part cylinder”, overall 617 objects collected in the Susy Safe registry and looking at the longer axis’ length, did not fit in the cylinder: out of them, 85 were spherical and none were non food objects. Looking at the overall volume, no one object had a volume greater than volume A.

In order to understand the impact of spherical objects to the risk of injuries, the “ellipticity” measure has been computed, which is nothing but the ratio of the longer and the shorter axis of the object, thus being equal to one for spherical objects. Toys were mostly spherical, at most with a very small ellipticity ratio of 2. The description of FB ellipticity by age of the child is given in Table 9. Looking at the consequences of the injury, the Susy Safe registry adopted the DTI definition [27] of severe injury, as that requiring at least one day of hospitalization. In addition, we considered also the occurrence of complications, as reported by the physician.

Table 4
Description of the FB which caused the incident.

<table>
<thead>
<tr>
<th>FB description</th>
<th>N</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearl, ball and marble</td>
<td>1698</td>
<td>16%</td>
</tr>
<tr>
<td>Coin</td>
<td>1534</td>
<td>15%</td>
</tr>
<tr>
<td>Bone</td>
<td>885</td>
<td>8%</td>
</tr>
<tr>
<td>Other non-food</td>
<td>639</td>
<td>6%</td>
</tr>
<tr>
<td>Nut</td>
<td>613</td>
<td>6%</td>
</tr>
<tr>
<td>Other food</td>
<td>563</td>
<td>5%</td>
</tr>
<tr>
<td>Pin and needle</td>
<td>506</td>
<td>5%</td>
</tr>
<tr>
<td>Toy</td>
<td>441</td>
<td>4%</td>
</tr>
<tr>
<td>Seed and grain</td>
<td>430</td>
<td>4%</td>
</tr>
<tr>
<td>Pebble</td>
<td>424</td>
<td>4%</td>
</tr>
<tr>
<td>Stationery</td>
<td>422</td>
<td>4%</td>
</tr>
<tr>
<td>Paper</td>
<td>365</td>
<td>3%</td>
</tr>
<tr>
<td>Plastic</td>
<td>304</td>
<td>3%</td>
</tr>
<tr>
<td>Jewellery</td>
<td>215</td>
<td>2%</td>
</tr>
<tr>
<td>Metal</td>
<td>183</td>
<td>2%</td>
</tr>
<tr>
<td>Battery</td>
<td>170</td>
<td>2%</td>
</tr>
<tr>
<td>Cotton</td>
<td>162</td>
<td>2%</td>
</tr>
<tr>
<td>Button</td>
<td>152</td>
<td>1%</td>
</tr>
<tr>
<td>Stick</td>
<td>150</td>
<td>1%</td>
</tr>
<tr>
<td>Bean and pea</td>
<td>142</td>
<td>1%</td>
</tr>
<tr>
<td>Sponge</td>
<td>95</td>
<td>1%</td>
</tr>
<tr>
<td>Sweet</td>
<td>91</td>
<td>1%</td>
</tr>
<tr>
<td>Arthropod</td>
<td>80</td>
<td>1%</td>
</tr>
<tr>
<td>Cap</td>
<td>70</td>
<td>1%</td>
</tr>
<tr>
<td>Other stationery</td>
<td>56</td>
<td>1%</td>
</tr>
<tr>
<td>Polystyrene</td>
<td>53</td>
<td>1%</td>
</tr>
<tr>
<td>Tinfoil and cellophone</td>
<td>42</td>
<td>0%</td>
</tr>
<tr>
<td>Accessorize</td>
<td>26</td>
<td>0%</td>
</tr>
<tr>
<td>Fruit stone</td>
<td>20</td>
<td>0%</td>
</tr>
<tr>
<td>Earplug</td>
<td>20</td>
<td>0%</td>
</tr>
<tr>
<td>Medicine</td>
<td>13</td>
<td>0%</td>
</tr>
<tr>
<td>Total</td>
<td>10,564</td>
<td></td>
</tr>
</tbody>
</table>

Table 5
Distribution of non-food objects by shape (numbers are percentages).

<table>
<thead>
<tr>
<th>FB description</th>
<th>2D/circle</th>
<th>3D/cylinder</th>
<th>Spherical</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accessorize</td>
<td>21.7</td>
<td>52.2</td>
<td>26.1</td>
<td></td>
</tr>
<tr>
<td>Arthropod</td>
<td>4.5</td>
<td>63.6</td>
<td>27.3</td>
<td>4.5</td>
</tr>
<tr>
<td>Battery</td>
<td>73.8</td>
<td>16.9</td>
<td>4.6</td>
<td>4.6</td>
</tr>
<tr>
<td>Button</td>
<td>68.4</td>
<td>10.5</td>
<td>15.8</td>
<td>5.3</td>
</tr>
<tr>
<td>Cap</td>
<td>3.6</td>
<td>92.9</td>
<td>3.6</td>
<td></td>
</tr>
<tr>
<td>Coin</td>
<td>97.9</td>
<td>0.3</td>
<td>1.7</td>
<td>12.1</td>
</tr>
<tr>
<td>Cotton</td>
<td>24.2</td>
<td>33.3</td>
<td>30.3</td>
<td>12.1</td>
</tr>
<tr>
<td>Earplug</td>
<td>24.1</td>
<td>35.4</td>
<td>26.6</td>
<td>13.9</td>
</tr>
<tr>
<td>Jewellery</td>
<td>66.7</td>
<td>33.3</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>Medicine</td>
<td>12.5</td>
<td>31.3</td>
<td>9.4</td>
<td>46.9</td>
</tr>
<tr>
<td>Metal</td>
<td>32.3</td>
<td>36.0</td>
<td>11.8</td>
<td>19.9</td>
</tr>
<tr>
<td>Other non-food</td>
<td>18.2</td>
<td>63.6</td>
<td>18.2</td>
<td></td>
</tr>
<tr>
<td>Other stationery</td>
<td>10.7</td>
<td>5.6</td>
<td>85.8</td>
<td>1.1</td>
</tr>
<tr>
<td>Paper</td>
<td>5.5</td>
<td>7.5</td>
<td>85.8</td>
<td>1.1</td>
</tr>
<tr>
<td>Pearl, ball and marble</td>
<td>4.9</td>
<td>33.1</td>
<td>50.0</td>
<td>12.0</td>
</tr>
<tr>
<td>Pebble</td>
<td>4.9</td>
<td>33.1</td>
<td>50.0</td>
<td>12.0</td>
</tr>
<tr>
<td>Pin and needle</td>
<td>16.1</td>
<td>59.8</td>
<td>2.3</td>
<td>21.8</td>
</tr>
<tr>
<td>Plastic</td>
<td>25.6</td>
<td>52.3</td>
<td>7.0</td>
<td>15.1</td>
</tr>
<tr>
<td>Polystyrene</td>
<td>4.2</td>
<td>33.3</td>
<td>45.8</td>
<td>16.7</td>
</tr>
<tr>
<td>Sponge</td>
<td>60.0</td>
<td>20.0</td>
<td>80.0</td>
<td>12.0</td>
</tr>
<tr>
<td>Stationery</td>
<td>7.6</td>
<td>75.9</td>
<td>8.9</td>
<td>7.6</td>
</tr>
<tr>
<td>Stick</td>
<td>14.3</td>
<td>57.1</td>
<td>26.8</td>
<td></td>
</tr>
<tr>
<td>Tinfoil and cellophone</td>
<td>81.3</td>
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<td>6.3</td>
<td>2.7</td>
</tr>
<tr>
<td>Toy</td>
<td>22.4</td>
<td>52.1</td>
<td>22.8</td>
<td>2.7</td>
</tr>
<tr>
<td>Total</td>
<td>29.6</td>
<td>26.7</td>
<td>35.7</td>
<td>8.0</td>
</tr>
</tbody>
</table>
Table 6
Distribution of non-food objects by consistency (numbers are percentages).

<table>
<thead>
<tr>
<th>FB description</th>
<th>Conforming</th>
<th>Rigid</th>
<th>Semi-rigid</th>
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<tbody>
<tr>
<td>Accessorize</td>
<td>12.0</td>
<td>72.0</td>
<td>16.0</td>
</tr>
<tr>
<td>Arthropod</td>
<td>20.6</td>
<td>41.2</td>
<td>38.2</td>
</tr>
<tr>
<td>Battery</td>
<td>100.0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Button</td>
<td>95.8</td>
<td>4.2</td>
<td>-</td>
</tr>
<tr>
<td>Cap</td>
<td>2.7</td>
<td>64.9</td>
<td>32.4</td>
</tr>
<tr>
<td>Coin</td>
<td>100.0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cotton</td>
<td>92.6</td>
<td>-</td>
<td>7.4</td>
</tr>
<tr>
<td>Earplug</td>
<td>16.7</td>
<td>5.6</td>
<td>77.8</td>
</tr>
<tr>
<td>Jewellery</td>
<td>97.8</td>
<td>-</td>
<td>2.2</td>
</tr>
<tr>
<td>Medicine</td>
<td>77.8</td>
<td>11.1</td>
<td>11.1</td>
</tr>
<tr>
<td>Metal</td>
<td>100.0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Other non-food</td>
<td>26.6</td>
<td>62.4</td>
<td>11.0</td>
</tr>
<tr>
<td>Other stationery</td>
<td>4.7</td>
<td>90.7</td>
<td>4.7</td>
</tr>
<tr>
<td>Paper</td>
<td>86.5</td>
<td>5.9</td>
<td>7.6</td>
</tr>
<tr>
<td>Pearl, ball and marble</td>
<td>3.4</td>
<td>89.6</td>
<td>7.0</td>
</tr>
<tr>
<td>Pebble</td>
<td>1.1</td>
<td>98.1</td>
<td>0.7</td>
</tr>
<tr>
<td>Pin and needle</td>
<td>2.7</td>
<td>97.3</td>
<td>-</td>
</tr>
<tr>
<td>Plastic</td>
<td>13.3</td>
<td>63.6</td>
<td>23.1</td>
</tr>
<tr>
<td>Polystyrene</td>
<td>34.9</td>
<td>41.9</td>
<td>23.3</td>
</tr>
<tr>
<td>Sponge</td>
<td>95.1</td>
<td>-</td>
<td>4.9</td>
</tr>
<tr>
<td>Stationery</td>
<td>18.7</td>
<td>64.0</td>
<td>17.3</td>
</tr>
<tr>
<td>Stick</td>
<td>92.9</td>
<td>-</td>
<td>7.1</td>
</tr>
<tr>
<td>Tinfoil and cellophane</td>
<td>44.1</td>
<td>2.9</td>
<td>52.9</td>
</tr>
<tr>
<td>Toy</td>
<td>13.7</td>
<td>71.1</td>
<td>15.2</td>
</tr>
<tr>
<td>Total</td>
<td>14.6</td>
<td>76.4</td>
<td>9.1</td>
</tr>
</tbody>
</table>

Some injuries occurred for what is called the “unexpected usage” or “mis-usage” of the object: this includes packaging and association with food and non-food object when combined without the necessary attention to safety issues. In the Susy Safe registry, 5 different categories of objects have been considered in view of providing the EU Commission with useful information:

a. not an industrial component;
b. a piece of an object: the FB was a broken part of the product (e.g. a broken part of a pen and the wheel of a toy car);
c. in co-presence with another object: when the objects were sold together like the cap with the pen, the marble with a board game, etc.;
d. a package or a part of a package of a product (e.g. the tinfoil containing a chocolate, a polystyrene ball, and a piece of cardboard);
e. the inedible part of food products containing inedibles (FPCI): stickers in crisps, toys in chocolate eggs, etc. Moreover we divided this category in two subcategories: the proper FPCI and the improper FPCI.

Where the association was not specified we considered the product like a single object and not an industrial component. Obviously, food and the other organics objects were treated as non industrial components. In the RPA report [28] the food products containing inedibles (FPCI) were defined as the combination of edible and inedible components, such as toys, used by food manufacturers to promote a wide range of products including sweets, crisps, yoghurt, ice cream and cereal. Several studies [29–33] were published on the risk that a child may face placing the inedible object contained in the product in or near their mouth, causing potentially ingestion, choking or suffocation. For such injuries we used the definition of “proper FPCI”. We defined the “improper FPCI” as the objects sold with food but not for a strict promoting purpose, like the candles on a cake, the drinking-straw with a juice or other non-organic decorations on the food. Overall, nine FPCI only have been observed in the Susy Safe registry, all without neither hospitalizations nor complications.

What is lacking is really proper adult supervision: according to Susy Safe data, an adult was present in 25% of the injuries, and in 40% of those involving a child younger than one year. In 87.9% of the cases the child was playing. This evidence suggests the need of fostering the attention of families toward a proper surveillance of children, in particular of younger ages.

5. Providing evidence to the EU Commission

The final aim of this data collection system was the construction of a system able to provide the EU Commission with all the relevant estimates on FB injuries. This has been accomplished via a fairly complex statistical system being developed for the purposes of the project: the so-called “Susy Safe risk engine”.

A risk engine can be thought of as a table in which one could look up the potential threat associated with any given consumer product. To perform a risk analysis, key factors affecting risk need to be identified. Factors impacting hazards usually include product design and consumer exposure [6,34–36]. Thus through the use of injury data, consideration of product characteristics and statistical tools it is possible to provide a numerical assessment of the threat of a product in terms of the probability of injury occurrence. At the end, the analysis results can be used both by consumers and manufacturers to make informed risk management decisions, in accordance with the “knowledge-based” action demanded by the EU Consumer Policy Strategy 2002–2006 [2.2.2. 3rd Comma] [37].

A risk engine is expected to produce the probability of occurrence of an injury given hazardous factors – e.g. an object that has a volume lower than a threshold value and a spherical shape – and it is expected to give insights of how the risk of injury occurrence changes when new data becomes available since product safety design, which depends also on the object dimension, shape and consistency, is subject to change over time in order to reduce or preclude further injuries.

Inside the Susy Safe project the object features taken into consideration for the calculation of the risk of injuries were size and shape of the foreign body which caused the injury [38].

Such a choice allows for evaluating the impact of dimension and shape as hazardous product characteristics in the spirit of European standard BS EN 71-1 of 1998 (Safety of Toys – Specifications for Mechanical and Physical Properties) which introduced the cylinder test to reduce the risk of choking in children. In fact, the cylinder test consists of a cylinder with an

Table 7
Distribution of volume by food object (mm³).

<table>
<thead>
<tr>
<th>FB description</th>
<th>Min</th>
<th>5%</th>
<th>25%</th>
<th>Median</th>
<th>75%</th>
<th>95%</th>
<th>99%</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bean and pea</td>
<td>15.7</td>
<td>16.3</td>
<td>26.2</td>
<td>37.7</td>
<td>94.2</td>
<td>350.4</td>
<td>–</td>
<td>452.2</td>
</tr>
<tr>
<td>Bone</td>
<td>0.2</td>
<td>0.2</td>
<td>2.7</td>
<td>14.4</td>
<td>31.4</td>
<td>628.0</td>
<td>–</td>
<td>2110.1</td>
</tr>
<tr>
<td>Fruit stone</td>
<td>9.4</td>
<td>9.4</td>
<td>37.7</td>
<td>84.8</td>
<td>352.7</td>
<td>–</td>
<td>–</td>
<td>795.5</td>
</tr>
<tr>
<td>Nut</td>
<td>6.3</td>
<td>9.4</td>
<td>25.1</td>
<td>26.2</td>
<td>51.3</td>
<td>229.0</td>
<td>–</td>
<td>471.0</td>
</tr>
<tr>
<td>Other food</td>
<td>1.0</td>
<td>3.8</td>
<td>26.2</td>
<td>42.9</td>
<td>104.7</td>
<td>1177.5</td>
<td>–</td>
<td>4710.0</td>
</tr>
<tr>
<td>Seed and grain</td>
<td>1.0</td>
<td>7.3</td>
<td>19.4</td>
<td>37.7</td>
<td>104.7</td>
<td>246.4</td>
<td>–</td>
<td>418.7</td>
</tr>
<tr>
<td>Sweet</td>
<td>4.2</td>
<td>4.2</td>
<td>14.9</td>
<td>33.0</td>
<td>134.2</td>
<td>–</td>
<td>–</td>
<td>937.8</td>
</tr>
<tr>
<td>Overall</td>
<td>0.2</td>
<td>2.5</td>
<td>16.7</td>
<td>33.5</td>
<td>83.7</td>
<td>418.7</td>
<td>2565.3</td>
<td>4710.0</td>
</tr>
</tbody>
</table>
inner diameter of 31.7 mm and truncated askew with an upper dimension of 51.7 mm and a lower dimension of 25.4 mm. Any toy entering the cylinder without pressure is considered unsuitable for children younger than 3 and is legally banned.

In order to calculate this probability we need to know the distribution of such characteristics, the coverage of the surveillance system and finally the probability of occurrence of an injury. In fact, let us consider the following equation:

\[
P(I|l_{SS}, C) = \frac{P(C|l_{SS}) \times P(I|l_{SS}) \times P(I)}{P(C)}
\]

where \(l_{SS}\) stands for an injury covered by the surveillance system, \(l\) stands for an occurred injury and \(C\) stays for the object

![Fig. 4. Characteristics of the “small parts” cylinder (measures in mm).](image)

![Fig. 5. Distribution of complications (%) requiring hospitalization by age class.](image)

### Table 8

Distribution of volume by non-food object (mm³).

<table>
<thead>
<tr>
<th>FB description</th>
<th>Min</th>
<th>5%</th>
<th>25%</th>
<th>Median</th>
<th>75%</th>
<th>95%</th>
<th>99%</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accessorize</td>
<td>20.9</td>
<td>20.9</td>
<td>38.9</td>
<td>400.1</td>
<td>1478.9</td>
<td>–</td>
<td>–</td>
<td>1657.9</td>
</tr>
<tr>
<td>Arthropod</td>
<td>8.4</td>
<td>8.4</td>
<td>15.2</td>
<td>26.2</td>
<td>37.7</td>
<td>–</td>
<td>–</td>
<td>37.7</td>
</tr>
<tr>
<td>Battery</td>
<td>3.1</td>
<td>7.9</td>
<td>19.6</td>
<td>50.2</td>
<td>78.5</td>
<td>418.7</td>
<td>–</td>
<td>418.7</td>
</tr>
<tr>
<td>Button</td>
<td>7.1</td>
<td>7.1</td>
<td>24.3</td>
<td>72.7</td>
<td>158.6</td>
<td>–</td>
<td>–</td>
<td>314.0</td>
</tr>
<tr>
<td>Cap</td>
<td>33.5</td>
<td>33.5</td>
<td>67.4</td>
<td>82.2</td>
<td>176.6</td>
<td>–</td>
<td>–</td>
<td>261.7</td>
</tr>
<tr>
<td>Coin</td>
<td>3.1</td>
<td>78.5</td>
<td>86.7</td>
<td>314.0</td>
<td>435.4</td>
<td>669.9</td>
<td>–</td>
<td>1256.0</td>
</tr>
<tr>
<td>Cotton</td>
<td>16.7</td>
<td>16.7</td>
<td>16.7</td>
<td>26.2</td>
<td>34.0</td>
<td>–</td>
<td>–</td>
<td>51.3</td>
</tr>
<tr>
<td>Earplug</td>
<td>18.8</td>
<td>18.8</td>
<td>67.0</td>
<td>104.7</td>
<td>104.7</td>
<td>–</td>
<td>–</td>
<td>104.7</td>
</tr>
<tr>
<td>Jewellery</td>
<td>1.6</td>
<td>1.7</td>
<td>29.0</td>
<td>52.3</td>
<td>268.9</td>
<td>754.9</td>
<td>–</td>
<td>785.0</td>
</tr>
<tr>
<td>Medicine</td>
<td>4.2</td>
<td>4.2</td>
<td>4.2</td>
<td>6.8</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>9.4</td>
</tr>
<tr>
<td>Metal</td>
<td>1.0</td>
<td>1.0</td>
<td>30.1</td>
<td>52.3</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>117.8</td>
</tr>
<tr>
<td>Other non-food</td>
<td>6.3</td>
<td>8.6</td>
<td>16.7</td>
<td>39.8</td>
<td>140.5</td>
<td>850.4</td>
<td>–</td>
<td>1046.7</td>
</tr>
<tr>
<td>Other stationery</td>
<td>37.7</td>
<td>37.7</td>
<td>37.7</td>
<td>84.3</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>130.8</td>
</tr>
<tr>
<td>Paper</td>
<td>14.1</td>
<td>14.1</td>
<td>14.1</td>
<td>33.5</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>94.2</td>
</tr>
<tr>
<td>Pearl, ball and marble</td>
<td>0.5</td>
<td>4.2</td>
<td>9.4</td>
<td>26.2</td>
<td>67.0</td>
<td>235.5</td>
<td>434.6</td>
<td>1496.7</td>
</tr>
<tr>
<td>Pebble</td>
<td>6.3</td>
<td>9.4</td>
<td>26.2</td>
<td>37.7</td>
<td>67.0</td>
<td>130.2</td>
<td>–</td>
<td>235.5</td>
</tr>
<tr>
<td>Pin and needle</td>
<td>1.6</td>
<td>1.6</td>
<td>3.5</td>
<td>12.6</td>
<td>51.8</td>
<td>–</td>
<td>–</td>
<td>314.0</td>
</tr>
<tr>
<td>Plastic</td>
<td>2.1</td>
<td>2.1</td>
<td>18.3</td>
<td>62.8</td>
<td>240.3</td>
<td>–</td>
<td>–</td>
<td>1046.7</td>
</tr>
<tr>
<td>Polystyrene</td>
<td>1.0</td>
<td>1.0</td>
<td>4.2</td>
<td>9.4</td>
<td>37.7</td>
<td>–</td>
<td>–</td>
<td>837.3</td>
</tr>
<tr>
<td>Sponge</td>
<td>4.2</td>
<td>4.2</td>
<td>19.9</td>
<td>85.8</td>
<td>141.6</td>
<td>–</td>
<td>–</td>
<td>153.9</td>
</tr>
<tr>
<td>Stationery</td>
<td>1.6</td>
<td>3.5</td>
<td>23.6</td>
<td>55.0</td>
<td>94.2</td>
<td>355.9</td>
<td>–</td>
<td>418.7</td>
</tr>
<tr>
<td>Stick</td>
<td>31.4</td>
<td>31.4</td>
<td>31.4</td>
<td>172.7</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>314.0</td>
</tr>
<tr>
<td>Tinfoil and cellophone</td>
<td>16.7</td>
<td>16.7</td>
<td>19.1</td>
<td>60.2</td>
<td>94.2</td>
<td>–</td>
<td>–</td>
<td>94.2</td>
</tr>
<tr>
<td>Toy</td>
<td>1.0</td>
<td>6.3</td>
<td>26.2</td>
<td>67.0</td>
<td>104.7</td>
<td>671.6</td>
<td>2093.3</td>
<td>2093.3</td>
</tr>
<tr>
<td>Overall</td>
<td>0.5</td>
<td>4.2</td>
<td>16.7</td>
<td>47.1</td>
<td>104.7</td>
<td>486.7</td>
<td>1046.7</td>
<td>2093.3</td>
</tr>
</tbody>
</table>

### Table 9

FB ellipticity stratified by child age (numbers are percentages).

<table>
<thead>
<tr>
<th>Age class</th>
<th>Min</th>
<th>5%</th>
<th>25%</th>
<th>Median</th>
<th>75%</th>
<th>95%</th>
<th>99%</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 year</td>
<td>1.0</td>
<td>1.0</td>
<td>1.3</td>
<td>2.5</td>
<td>8.5</td>
<td>28.3</td>
<td>–</td>
<td>30.0</td>
</tr>
<tr>
<td>1–2 years</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.5</td>
<td>3.7</td>
<td>22.0</td>
<td>40.0</td>
<td>63.5</td>
</tr>
<tr>
<td>≥3 years</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>3.0</td>
<td>25.0</td>
<td>40.0</td>
<td>60.0</td>
</tr>
<tr>
<td>Total</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.2</td>
<td>3.6</td>
<td>24.0</td>
<td>40.0</td>
<td>63.5</td>
</tr>
</tbody>
</table>

![Table 10](image)

<table>
<thead>
<tr>
<th>Complication</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume (mm³)</td>
<td>16.7</td>
<td>25.1</td>
</tr>
<tr>
<td>Median</td>
<td>37.7</td>
<td>37.7</td>
</tr>
<tr>
<td>75%</td>
<td>98.9</td>
<td>78.5</td>
</tr>
<tr>
<td>Ellipticity</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>75%</td>
<td>3.5</td>
<td>2.3</td>
</tr>
</tbody>
</table>
Table 11
Percentage of complication according to shape and consistency.

<table>
<thead>
<tr>
<th>Complications (%)</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shape</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2D</td>
<td>91.4</td>
<td>8.6</td>
</tr>
<tr>
<td>2D circle</td>
<td>94.1</td>
<td>5.9</td>
</tr>
<tr>
<td>3D</td>
<td>89.1</td>
<td>10.9</td>
</tr>
<tr>
<td>Other</td>
<td>91.3</td>
<td>8.7</td>
</tr>
<tr>
<td>Spherical</td>
<td>91.2</td>
<td>8.8</td>
</tr>
<tr>
<td>Consistency</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conforming</td>
<td>84.8</td>
<td>15.2</td>
</tr>
<tr>
<td>Rigid</td>
<td>93.4</td>
<td>6.6</td>
</tr>
<tr>
<td>Semi-rigid</td>
<td>87.9</td>
<td>12.1</td>
</tr>
</tbody>
</table>

characteristics. Thus with $P(I, I_0|C)$ at the first member of equation we indicated the probability that a foreign body injury occurred and it was detected by the surveillance system given foreign body characteristics $C$. An example of the risk estimates is shown in Tables 12 and 13.

6. Final remarks

Every infant injury, every dead child, is something utterly intolerable. We should bear in mind the objective to avoid as many of these infant injuries as possible. The European Commission devotes a lot of time and work within its activities minimizing infant injuries and making objects and environments safer, so that these injuries no longer occur to such an extent. The Commission however needs secure data about injuries in order to adopt administrative or legislative measures. We will not be able to immediately adopt strict measures based only on a few injuries that occur in all large communities. The quality of legislative or administrative measures depends precisely on the amount and the reliability of data. We should always consider this when we discuss any preventive or legislative measure.

Table 12
Risk of injury.

<table>
<thead>
<tr>
<th>Foreign body type</th>
<th>Median volume (mm$^3$)</th>
<th>Median ellipticity (spherical shape = 1)</th>
<th>Risk estimate</th>
<th>95% credibility interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non food</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Battery</td>
<td>33.36</td>
<td>6</td>
<td>6.14E-05</td>
<td>1.58E-06; 6.18E-05</td>
</tr>
<tr>
<td>Coin</td>
<td>314</td>
<td>10</td>
<td>0.00019</td>
<td>5.62E-06; 0.00022</td>
</tr>
<tr>
<td>Toy</td>
<td>66.99</td>
<td>1</td>
<td>0.00016</td>
<td>5.55E-06; 0.00022</td>
</tr>
<tr>
<td>Pearl, ball and marble</td>
<td>16.75</td>
<td>1</td>
<td>0.00037</td>
<td>1.07E-06; 0.00041</td>
</tr>
<tr>
<td>Paper, tinfoil and cellophane</td>
<td>33.49</td>
<td>2</td>
<td>2.29E-06</td>
<td>1.43E-08; 2.36E-05</td>
</tr>
<tr>
<td>Button</td>
<td>67</td>
<td>5</td>
<td>3.60E-05</td>
<td>1.08E-06; 6.78E-05</td>
</tr>
<tr>
<td>Pin and needle</td>
<td>9.03</td>
<td>4.5</td>
<td>2.25E-05</td>
<td>1.01E-06; 3.56E-05</td>
</tr>
<tr>
<td>Stationery (pen cap, pencil lead)</td>
<td>6.28E+01</td>
<td>2</td>
<td>8.51E-05</td>
<td>2.33E-06; 8.71E-05</td>
</tr>
<tr>
<td>Pebble</td>
<td>37.68</td>
<td>1</td>
<td>0.00013</td>
<td>3.75E-06; 0.00017</td>
</tr>
<tr>
<td>Food</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nut</td>
<td>26.17</td>
<td>1</td>
<td>0.00012</td>
<td>8.03E-05; 0.00017</td>
</tr>
<tr>
<td>Bone</td>
<td>5.88</td>
<td>16</td>
<td>4.63E-05</td>
<td>1E-06; 6.83E-05</td>
</tr>
<tr>
<td>Seed and grain</td>
<td>36.63</td>
<td>2.5</td>
<td>7.02E-05</td>
<td>4.73E-05; 8.46E-05</td>
</tr>
<tr>
<td>Sweet</td>
<td>32.97</td>
<td>1</td>
<td>7.12E-05</td>
<td>6.20E-05; 8.32E-05</td>
</tr>
</tbody>
</table>

Table 13
Risk of severe injury (injury which required at least one day of hospitalization).

<table>
<thead>
<tr>
<th>Foreign body type</th>
<th>Median volume (mm$^3$)</th>
<th>Median ellipticity (spherical shape = 1)</th>
<th>Risk estimate</th>
<th>95% credibility interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Food</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Battery</td>
<td>33.36</td>
<td>6</td>
<td>6.14E-05</td>
<td>1.58E-06; 6.18E-05</td>
</tr>
<tr>
<td>Coin</td>
<td>314</td>
<td>20</td>
<td>2.87E-05</td>
<td>2.15E-05; 3.52E-05</td>
</tr>
<tr>
<td>Toy</td>
<td>69.86</td>
<td>1.66</td>
<td>2.93E-05</td>
<td>2.88E-05; 2.99E-05</td>
</tr>
<tr>
<td>Pearl, ball and marble</td>
<td>9.42</td>
<td>1</td>
<td>0.00018</td>
<td>1.04E-05; 0.00023</td>
</tr>
<tr>
<td>Paper, tinfoil and cellophane</td>
<td>25.12</td>
<td>1</td>
<td>5.07E-07</td>
<td>5.04E-07; 3.2E-06</td>
</tr>
<tr>
<td>Button</td>
<td>50.24</td>
<td>4</td>
<td>1.26E-05</td>
<td>1.22E-05; 1.28E-05</td>
</tr>
<tr>
<td>Pin and needle</td>
<td>20.02</td>
<td>5</td>
<td>1.56E-05</td>
<td>1.38E-05; 1.63E-05</td>
</tr>
<tr>
<td>Stationery (pen cap, pencil lead)</td>
<td>28.78</td>
<td>2.33</td>
<td>2.53E-05</td>
<td>2.20E-05; 2.59E-05</td>
</tr>
<tr>
<td>Pebble</td>
<td>28.78</td>
<td>1</td>
<td>1.72E-05</td>
<td>1.53E-05; 1.77E-05</td>
</tr>
<tr>
<td>Food</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nut</td>
<td>27.17</td>
<td>1</td>
<td>2.32E-05</td>
<td>1.45E-05; 3.32E-05</td>
</tr>
<tr>
<td>Bone</td>
<td>26.17</td>
<td>6.67</td>
<td>3.12E-05</td>
<td>4.20E-06; 3.87E-05</td>
</tr>
<tr>
<td>Seed and grain</td>
<td>33.68</td>
<td>3.33</td>
<td>2.38E-05</td>
<td>1.1E-05; 3.35E-05</td>
</tr>
<tr>
<td>Sweet</td>
<td>16.75</td>
<td>1</td>
<td>4.43E-06</td>
<td>4.25E-06; 4.57E-06</td>
</tr>
</tbody>
</table>
Appendix. The Susy Safe Working Group

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[1] RPA, Inedibles in Food Product Packaging Prepared for STOA, European Parlia-
ment, 2003.
Toys in the upper aerodigestive tract: New evidence on their risk as emerging from the Susy Safe Study

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ABSTRACT

Foreign body (FB) inhalation, aspiration or ingestion are relatively common events in children. Despite many efforts made in several countries to achieve acceptable safety levels for consumer products devoted to children, small toys or toy parts are still frequently mentioned among risky foreign bodies. The aim of the present study is to characterize the risk of complications and prolonged hospitalization due to toys inhalation, aspiration or ingestion according to age and gender of patients, FB characteristics, circumstances of the accident, as emerging from the Susy Safe Registry. The Susy Safe Registry started in the 2005 to collect data to serve as a basis for a knowledge-based consumer protection activity. It is actually one of the wider databases collecting foreign body injuries in the upper aero-digestive tract in pediatric patients. It is distinguished by a deep characterization of objects which caused the injuries and a multi-step quality control procedure which assures its reliability.

Preventive strategies imposing a regulation of industrial production, even if fundamental, are not sufficient and need to be integrated along with other intervention addressed to make aware caregivers toward a proper surveillance of children.

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1. Introduction

Aspiration, swallowing and insertion of foreign bodies (FBs) is still a leading cause of injuries in children aged 0–14, particularly in those aged from 1 to 3 years, whose consequences vary based on the object characteristics (shape, size), its anatomical location, and the patient’s age and gender [1,2].

The mechanical obstruction of the airways due to foreign body inhalation or aspiration is the primary source of fatal accidents in children younger than one year, and it represents a major cause of death in children from 1 to 4 years old [3]. Moreover, because of late diagnosis, injury may result in severe complications including asphyxia, pneumonia, atelectasis and bronchiectasis [4]. The most common complication is entrapment in the oesophagus. However, while most ingested foreign bodies pass the intestinal tract without leading to complications, some may cause gastrointestinal obstruction and possible sequelae include erosion, perforation and even mediastinitis [5].

The aim of the present study is to characterize the risk of complications and prolonged hospitalization due to inhalation, aspiration or ingestion of toys, according to children age and gender, FB characteristics, its anatomical location and circumstances of the accident, as emerging from the Susy Safe Registry.
2. Data collection

The Susy Safe Project is aimed at establishing a registry of cases of foreign bodies injuries in children age 0–14 years [6]. From 2005 to 2010 case were collected from 70 centres in 32 different countries. Details on the injuries, identified by means of the International Classification of Diseases, Ninth Revision (ICD-9) codes listed on hospital discharge records, were collected through a standardized case report form, that provides a full set of information on injuries, with specific details on age and gender of the child, location, shape, volume, consistency and ellipticity of the foreign body, behavioral aspects linked to the injury, like the supervision of the parents or the activity concomitant to the accident, any complication occurred, length of hospitalization.

3. Toys characteristics definition

According to the Rimell’s classification [7], objects which caused injuries were characterized by size, shape and consistency. If the dimensions (width, length, and height in mm) of the object were reported, the volume was calculated according to the shape of the objects itself. Such volume measures represent how much space the smallest geometrical figure containing the irregular-shaped FB takes up. Moreover, the ellipticity (the ratio between the maximum and the minimum FB size reported) was calculated.

4. Statistical analysis

The analysis was carried out on injuries caused by toys. Age and gender injury distributions were examined. Data regarding adult supervision were also evaluated.

FB location was reported according to ICD9-CM code: nose (ICD932), pharynx and larynx (ICD933), trachea, bronchi and lungs (ICD934), mouth, esophagus and stomach (ICD935).

Descriptive statistics (absolute and relative frequency or median, I and III quartile according to the categorical or continuous variable, respectively) were worked out; FB features distributions by children class age and site of obstruction were assessed.

Two different outcomes were considered: complications and hospitalizations. The presence of complications was defined as the occurrence of at least one complication, as reported by the physician, requiring or not hospitalization. The association between outcomes and children’s age, adult presence and toys characteristics was computed using unweighted odds ratios and the related 95% confidence intervals. Odds ratios not possible to be evaluated due to small cell frequency were labeled as NS (not significant). Statistical significance was defined as p-value < 0.05.

Analyses were performed using Design and Hmisc libraries from R version 2.8 [8].

A total of 16,878 FB injuries, occurred between 1980 and 2010 in children aged 0–14 years, were recorded by the Susy Safe Registry. Overall, 441 (2.6%) were due to toys and among them 355 (2.1%) occurred in the lower/upper aero-digestive tract. Distribution of incidence of toys injuries by age class is shown in Fig. 1. Overall, 256 (58%) of injured children were males, while 183 (42%) were females. Almost 61% of toys related injuries happened under adults’ supervision. Details about FB location are given in Table 1: the total amount of toys injuries, the number of complicated injuries and the number of injuries in which hospitalization is needed are reported for each site.

Toys volume, shape, ellipticity and consistency by age and by location in aero-digestive tract are described respectively in Tables 2 and 3.

Looking to the outcomes, 49 children needed hospitalization; the median in hospital stay was 1 day in absence of complications, whereas for complications, the hospitalization stay was reported in the database for only three children: two of them stayed in hospital 1 day and the other one more than 3 days; removal was performed in the great part of cases by endoscopy while one case required surgery; complications were obstructions, epistaxis, secretion, infection, pneumonia and asphyxia [1]. No deaths were observed. In order to verify the association among children age, adult supervision, object characteristics and outcomes, odds ratios of complications and hospitalization, with 95% confidence intervals, are presented in Table 4.

Table 1

<table>
<thead>
<tr>
<th>Toy related injuries</th>
<th>Complications</th>
<th>Hospitalization</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Nose</td>
<td>75% (265)</td>
<td>88% (15)</td>
</tr>
<tr>
<td>Pharynx and larynx</td>
<td>4% (13)</td>
<td>6% (1)</td>
</tr>
<tr>
<td>Trachea, bronchi and lungs</td>
<td>9% (32)</td>
<td>0% (0)</td>
</tr>
<tr>
<td>Mouth, esophagus and stomach</td>
<td>13% (45)</td>
<td>6% (1)</td>
</tr>
<tr>
<td>Total (N)</td>
<td>355</td>
<td>18</td>
</tr>
</tbody>
</table>
Table 2
Toys characteristics by age. Data are first quartile/median/third quartile for continuous variables and percentages (absolute numbers) for categorical variables. N, number of valid cases for each given variable.

<table>
<thead>
<tr>
<th>Foreign body characteristics</th>
<th>N</th>
<th>Age class</th>
<th>&lt;1 year (N=15)</th>
<th>1–2 years (N=78)</th>
<th>≥3 years (N=205)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>109</td>
<td></td>
<td>346.7/588.75/614.92</td>
<td>28.26/66.94/94.20</td>
<td>26.17/62.80/78.50</td>
</tr>
<tr>
<td>Shape</td>
<td>207</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spherical</td>
<td>0%</td>
<td></td>
<td>14% (8)</td>
<td>29% (41)</td>
<td></td>
</tr>
<tr>
<td>3D</td>
<td>75%</td>
<td></td>
<td>68% (38)</td>
<td>44% (63)</td>
<td></td>
</tr>
<tr>
<td>2D</td>
<td>12%</td>
<td></td>
<td>4% (2)</td>
<td>6% (9)</td>
<td></td>
</tr>
<tr>
<td>2D circle</td>
<td>12%</td>
<td></td>
<td>4% (2)</td>
<td>6% (9)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>6%</td>
<td></td>
<td>2% (2)</td>
<td>2% (3)</td>
<td></td>
</tr>
<tr>
<td>Ellipticity</td>
<td></td>
<td></td>
<td>3.14/3.29/3.43</td>
<td>1.05/1.60/2.88</td>
<td>1.00/1.00/1.60</td>
</tr>
<tr>
<td>Consistency</td>
<td>98</td>
<td></td>
<td></td>
<td></td>
<td>1% (0)</td>
</tr>
<tr>
<td>Conforming</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Semi-rigid</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rigid</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do not know</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3
Toys characteristics by FB location. Data are first quartile/median/third quartile for continuous variables and percentages (absolute numbers) for categorical variables. N, number of valid cases for each given variable.

<table>
<thead>
<tr>
<th>Foreign body characteristics</th>
<th>N</th>
<th>Foreign body location</th>
<th>Nose (N=157)</th>
<th>Pharynx and larynx (N=11)</th>
<th>Trachea, bronchi and lungs (N=23)</th>
<th>Mouth, esophagus and stomach (N=42)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
<td>81</td>
<td></td>
<td>29.57/66.99/104.67</td>
<td>27.08/43.96/62.80</td>
<td>78.50/94.20/333.36</td>
<td>10.99/75.95/225.69</td>
</tr>
<tr>
<td>Shape</td>
<td>164</td>
<td></td>
<td>27.08/43.96/62.80</td>
<td>78.50/94.20/333.36</td>
<td>10.99/75.95/225.69</td>
<td></td>
</tr>
<tr>
<td>Spherical</td>
<td>19%</td>
<td></td>
<td>10% (1)</td>
<td>0% (0)</td>
<td>8% (1)</td>
<td></td>
</tr>
<tr>
<td>3D</td>
<td>60%</td>
<td></td>
<td>80% (8)</td>
<td>71% (15)</td>
<td>54% (7)</td>
<td></td>
</tr>
<tr>
<td>2D</td>
<td>4%</td>
<td></td>
<td>0% (0)</td>
<td>10% (2)</td>
<td>8% (1)</td>
<td></td>
</tr>
<tr>
<td>2D circle</td>
<td></td>
<td></td>
<td>14% (3)</td>
<td></td>
<td>31% (4)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>2%</td>
<td></td>
<td>5% (1)</td>
<td>0% (0)</td>
<td>43% (6)</td>
<td></td>
</tr>
<tr>
<td>Ellipticity</td>
<td></td>
<td></td>
<td>1.00/1.00/2.00</td>
<td>1.54/2.84/8.50</td>
<td>1.86/3.23/3.33</td>
<td>1.75/3.00/4.29</td>
</tr>
<tr>
<td>Consistency</td>
<td>73</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rigid</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do not know</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 4
Odds ratio of complications and of hospitalization with the 95% confidence intervals are presented. P values are also presented. N, number of valid cases for each given variable; NS, not significant; –, not possible to be evaluated due to small cell frequency; Ref, reference category.

<table>
<thead>
<tr>
<th>Hospitalization</th>
<th>Yes (N=177)</th>
<th>No (N=49)</th>
<th>OR (95%CI)</th>
<th>p</th>
<th>Yes (N=20)</th>
<th>No (N=326)</th>
<th>OR (95%CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age class</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1 year</td>
<td>18% (8)</td>
<td>1% (2)</td>
<td>17.29 (3.48; 85.88)</td>
<td>&lt;0.001</td>
<td>11% (1)</td>
<td>4% (9)</td>
<td>2.22 (0.25;20.08)</td>
<td>0.48</td>
</tr>
<tr>
<td>1–2 years</td>
<td>20% (9)</td>
<td>27% (46)</td>
<td>0.85 (0.37; 1.93)</td>
<td>0.69</td>
<td>11% (1)</td>
<td>27% (55)</td>
<td>0.36 (0.04; 3.02)</td>
<td>0.35</td>
</tr>
<tr>
<td>≥3 years</td>
<td>62% (28)</td>
<td>72% (121)</td>
<td>Ref</td>
<td></td>
<td>78% (7)</td>
<td>69% (140)</td>
<td>Ref</td>
<td>–</td>
</tr>
<tr>
<td>Adult supervision</td>
<td>314</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adult present</td>
<td>7% (3)</td>
<td>5% (7)</td>
<td>Ref</td>
<td>–</td>
<td>100% (20)</td>
<td>0% (0)</td>
<td>NS</td>
<td>–</td>
</tr>
<tr>
<td>Volume</td>
<td>111</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nose (N=157)</td>
<td>50.77/84.78/111</td>
<td>26.17/62.80/111</td>
<td>1 (0.00;1.01)</td>
<td>0.92</td>
<td>10.21/44.49/111</td>
<td>26.17/66.99/111</td>
<td>1.00 (0.99;1.01)</td>
<td>0.88</td>
</tr>
<tr>
<td>Shape</td>
<td>219</td>
<td></td>
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<tr>
<td>Spherical</td>
<td>4% (2)</td>
<td>28% (47)</td>
<td>0.11 (0.03; 0.49)</td>
<td>0.004</td>
<td>30% (3)</td>
<td>23% (46)</td>
<td>1.17 (0.28;4.90)</td>
<td>0.95</td>
</tr>
<tr>
<td>3D</td>
<td>69% (31)</td>
<td>49% (82)</td>
<td>Ref</td>
<td>–</td>
<td>60% (6)</td>
<td>53% (108)</td>
<td>Ref</td>
<td>–</td>
</tr>
<tr>
<td>2D</td>
<td>7% (3)</td>
<td>5% (9)</td>
<td>0.88 (0.22; 3.47)</td>
<td>0.86</td>
<td>0% (0)</td>
<td>6% (12)</td>
<td>NS</td>
<td>–</td>
</tr>
<tr>
<td>2D circle</td>
<td>18% (8)</td>
<td>15% (26)</td>
<td>0.81 (0.33; 1.99)</td>
<td>0.65</td>
<td>10% (1)</td>
<td>16% (33)</td>
<td>0.55 (0.06; 4.69)</td>
<td>0.69</td>
</tr>
<tr>
<td>Other</td>
<td>8% (1)</td>
<td>3% (5)</td>
<td>0.53 (0.06; 4.71)</td>
<td>0.57</td>
<td>0% (0)</td>
<td>2% (5)</td>
<td>NS</td>
<td>–</td>
</tr>
<tr>
<td>Ellipticity</td>
<td>100 (50/1/3.25</td>
<td>1.00/1.00/1.80</td>
<td>1.00/1.50/2.05</td>
<td>1.00/1.20/2.00</td>
<td>0.92 (0.58;1.48)</td>
<td>0.74</td>
<td></td>
<td></td>
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<tr>
<td>Consistency</td>
<td>351</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conforming</td>
<td>4% (2)</td>
<td>7% (12)</td>
<td>Ref</td>
<td>–</td>
<td>40% (8)</td>
<td>12% (38)</td>
<td>Ref</td>
<td>–</td>
</tr>
<tr>
<td>Semi-rigid</td>
<td>17% (8)</td>
<td>25% (44)</td>
<td>1.09 (0.20; 5.83)</td>
<td>0.92</td>
<td>10% (2)</td>
<td>16% (50)</td>
<td>0.19 (0.04; 95)</td>
<td>0.04</td>
</tr>
<tr>
<td>Rigid</td>
<td>79% (38)</td>
<td>65% (113)</td>
<td>2.02 (0.43; 9.42)</td>
<td>0.37</td>
<td>50% (10)</td>
<td>71% (229)</td>
<td>0.21 (0.08; 0.56)</td>
<td>0.002</td>
</tr>
<tr>
<td>Do not know</td>
<td>0% (0)</td>
<td>2% (4)</td>
<td>NS</td>
<td>–</td>
<td>0% (0)</td>
<td>1% (4)</td>
<td>NS</td>
<td>–</td>
</tr>
</tbody>
</table>
6. Discussion

Aspiration and ingestion of foreign bodies are common events in children aged 0–14 years, which can have severe, even if frequently underestimated consequences [9]. Preventing them has been a concern of physicians since the first half of the twentieth century, when Chevalier Jackson collected over 3000 objects from injured children. The collection served as the basis for the creation of standards for the Small Parts Test Fixture (SPTF) within the US [1] and the utility of the SPTF to predict size of FBs associated with a high risk of choking injury has received strong support [10] leading also the EU to adopt of strict rules concerning the toys packaging and their distribution (EN 71-1: 1998 “Safety of Toys”) [11–13], which bans objects with small parts for children under three years old and requires that toys with small parts for children from 3 to 6 years must be labeled as unsuitable for children under 3 years [14,15].

The adoption of these preventive strategies mainly based on products modification by manufacturers, has resulted in a decrease of injuries due to toys [16,17] and in a decrease of children's mortality rate for choking in the last decades [7,18]. The effectiveness of regulations finalized to limit the commercialization of products for children up to three years seems to be confirmed also by our study, where more than half of injuries (69%) involved children older than three years.

In our data, the most documented incident is the insertion in the nose. Severe consequences seem to be rare, probably due the relative inert nature of the plastic material, which implies a mild tissue inflammation and allows a relatively quick response of the patient upon removal of the FB [19–21]. Objects were mainly tridimensional, even if ellipticity ratio of FBs that caused hospitalization was at most 1, indicating objects which are shaped like a sphere. The first determinant of an injury leading to complications is the conforming consistency of the object [22]. However, rigid and semi-rigid consistence was encountered most among objects involved in injury that required hospitalization, even if the excess of risk was not statistically significant.

When details regarding toys were available, the most frequently retrieved foreign bodies were part of broken toys. This lead to consider the commercialization of not safe products; or the accessibility to inappropriate toys when children are younger the 3 years; or, when children are more than 3 years old, poor parents education regarding this issue. Incorrect adult supervision is commonly encountered in the injury mechanism. In our study, in fact, an adult was present in only 6% of cases. Interestingly, adults were present for children who had complications. The attention paid to accident occasion and caregivers' behavior represents another important step in the implementation of preventive strategies, which should integrate educational campaigns especially designed for parents and caretakers along with the regulation of industrial production [23,24].

Appendix A. The Suty Safe Working Group

Coordination group
Prof. Dario Gregori, Principal Investigator, University of Padova, Italy.
Dr. Francesca Foltran, University of Padova, Italy.
Mrs. Simonetta Ballali, PROCHILD ONLUS, Italy.
Dr. Paola Berchialla, University of Torino, Italy.

Governing board
Dr. Hugo Rodriguez, Hospital De Pediatría Juan P. Garrahan, Argentina.
Dr. Paola Zaupa, Grosse schützen Kleine, Austria.
Dr. Peter Spitzer, Grosse schützen Kleine, Austria.

Dr. Costantinos Demetriades, Ministry of Commerce, Industry and Tourism, Cyprus.
Prof. Ivo Slapáčk, Masaryk University, Czech Republic.
Prof. Ljiljana Sokolova, Institute for Respiratory Diseases in Children, Fyrom.
Prof. Eleni Petridou, Athens University – Medical School – Department of Hygiene and Epidemiology, Greece.
Dr. Antonella D’Alessandro, Ministero dello Sviluppo Economico, Italy.
Prof. Manuel Antonio Caldeira Pais Clemente, Instituto Portugues de Tabacologia, Portugal.
Prof. Jana Jakubiková, Children’s University Hospital, Slovack Republic.
Prof. Sebastian Van As, Red Cross War Memorial Children’s Hospital, South Africa.
Prof. Sebastian Van As, Red Cross War Memorial Children’s Hospital, South Africa.

Quality control
Prof. Desiderio Passali, University of Siena, Italy.
Argentina
Prof. Alberto Chinsky, Children’s Hospital Gutierrez, Argentina.
Dr. Hugo Rodriguez, Children’s Hospital Juan P. Garrahan, Argentina.

Bosnia and Herzegovina
Dr. Fuad Brkic, University Clinical Center, Bosnia and Herzegovina.

Croatia
Dr. Ranko Mladina, University Hospital Salata, Croatia.

Cyprus
Dr. Olga Kalakouta, Medical and Public Health services, Ministry of Health, Cyprus.
Dr. Andreas Melis, Aretaieon hospital, Cyprus.

Czech Republic
Dr. Michaela Máchalová, Childrens University Hospital, Czech Republic.

Denmark
Dr. Per Caye-Thomasen, Gentofte University Hospital of Copenhagen, Denmark.

Egypt
Dr. Enas Elsheikh, Suez Canal University, Egypt.
Dr. Ahmed Ragab, Menoufiya University Hospital, Egypt.

Finland
Dr. Anne Pitkäranta, Helsinki University Central Hospital, Finland.

France
Dr. Philippe Contencin Necke, Enfants Malades Hospital, France.
Dr. Jocelyne Derelle, CHU Nancy, France.
Dr. Magali Duwelz, SOS Benjam – Observatoire National d’Etudes des Conduites à Risques, France.

Germany
Dr. Martine Francois, Robert Debré Hospital, France.
Dr. Stephane Pezzettigotta, Armand Trousseau Hospital, France.
Dr. Christian Righini, CHU A. Michallon, France.
Dr. Pezzettigotta Stephane, Armand Trousseau Hospital, France.

Fyrom
Dr. Jane Buzarov, Institute for Respiratory Diseases in Children, Fyrom.

Greece
Dr. Roehrich Bernhard, St. Joseph Hospital, Germany.
Dr. Volker Jahnke, Charité Campus Virchow, Germany.
Dr. Goktas Onder, Charité Campus Virchow, Germany.
Dr. Petra Zieriacks, Kinderheilkunde und Jugendmedizin, Naturheilverfahren und Akupunktur, Germany.

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Greece
Dr. Vicky Kalampoki, Athens University, Department of Hygiene and Epidemiology, Greece.
Dr. Nikola Simasko, Democritus University School of Medicine, Greece.
Dr. Charalampos Skoulakis, General Hospital of Volos, Greece.

Italy
Dr. Angelo Camaino, San Giovanni Addolorata Calvary Hospital, Italy.
Dr. Cesare Cutrone, University Hospital of Padova, Italy.
Dr. Elisa Gaudini, Ear–Nose–Throat Department, Policlinico Le Scotte, Italy.
Dr. Domenico Grasso, Burlo Garofolo Pediatric Institute, Italy.
Dr. Nicola Mansi, Santobono Pausilipon Pediatric Hospital, Italy.
Dr. Gianni Messi, Burlo Garofolo Pediatric Institute, Italy.
Dr. Claudio Orlando, Santobono Pausilipon Pediatric Hospital, Italy.
Dr. Sabino Preziosi, Elissoccorpo ospedale Ravenna, Italy.
Dr. Italo Sorrentini, G. Rummo Hospital, Italy.
Dr. Marilena Trozzi, Bambino Gesù Pediatric Hospital, Italy.
Dr. Alessandro Vigo, Sant’Anna Pediatric Hospital, Italy.
Dr. Giuseppe Villari, G. Rummo Hospital, Italy.
Dr. Giulio Cesare Passali, Ear, Nose, and Throat Clinic, University “Tor Vergata”, Rome, Italy.
Dr. Francesco Maria Passali, ENT Department, Catholic University “The Sacred Heart” of Rome, Italy.

Japan

Kazakhstan
Dr. Gайнel Ussatayeva, Kazakhstan School of Public Health, Kazakhstan.

Mexico
Dr. Ricardo De Hoyos, San Jose-Tec de Monterrey Hospital, Mexico.

Nigeria
Dr. Foluwasayo Emmanuel Ologe, University of Ilorin Teaching Hospital, Nigeria.

Pakistan
Dr. Muazzam Nasrullah, Services Hospital, Paediatric Ward, Pakistan.

Panama
Dr. Amariis Melendez, Santo Tomas Hospital, Panama.

Poland
Dr. Mieczysław Chmielik, Medical University of Warsaw, Poland.

Portugal
Dr. Teresa Belchior, Deco Proteste, Portugal.

Romania
Dr. Mihail Dan Cobzeanu, Sf. Spiridon Hospital, Romania.
Dr. Dan Cristian Gheorghe, Maria Sklodowska Curie Hospital, Romania.
Dr. Adelaida Iorgulescu, Grigore Alexandrescu Pediatric Hospital, Romania.
Dr. Caius-Codrut, Sarafoleanu SF, Maria Hospital, Romania.
Dr. Miorita Toader, Grigore Alexandrescu Pediatric Hospital, Romania.

Slovak Republic
Dr. Jana Barkociová, Children University Hospital, Slovak Republic.
Dr. Beata Havelkova, Public Health Authority of the Slovak Republic, Slovak Republic.

Slovenia
Dr. Miha Zargi, University Medical Centre, Slovenia.

Spain
Dr. Felix Pumarola, Vall d’Hebron University Hospital, Spain.
Dr. Lorenzo Rubio, Riber International Hospital, Spain.

Sweden
Dr. Pontus Stierna, Huddinge University Hospital, Sweden.

Taiwan
Dr. Wei-chung Hsu, National Taiwan University Hospital, Taiwan.

Thailand
Dr. Sakda Arj-Ong, Ramathibodi Hospital, Thailand.
Dr. Chulathida Chomchai, Siriraj Hospital, Thailand.

The Netherlands
Dr. Lennaert Hoep, VU Medical Center, The Netherlands.
Dr. Rico Rinkel, VU Medical Center, The Netherlands.

Turkey
Dr. Erdinc Aydin Baskent, University Ankara Hospital, Turkey.
Dr. Volkan Sarper Eriki, Behcet Uz Children Hospital, Turkey.
Dr. Metin Onerci, Hacettepe University, Turkey.

United Kingdom
Dr. John Graham, Royal Free Hampstead NHS Trust, United Kingdom.
Dr. Sadie Khwaja, Royal Manchester Children’s Hospital, United Kingdom.
Dr. Christopher Raine, Bradford Royal Infirmary, United Kingdom.

References


My scientific activity took form by writing 152 scientific papers (author and co-author) that were published in full in national and international journals, as follows: 10 in ISI journals, 11 proceeding ISI, 32 in Pubmed, Index Copernicus and Med Line, 7 in CNSIS journals and 92 in national and international congress books. 

I sustained over 100 oral presentations at national and international ENT congresses and have also actively participated at organizing different ENT events with international participation (national congresses, conferences and symposiums).

I have organized and I have been:

- President of the National Congress of ENT and Cervico-Facial Surgery with international participation, 22-25 September 2010, Iasi, Romania.
- President of the 2nd Congress of the Romanian Society of Rhinolgy with international participation, September 2013, Piatra Neamt, Romania
- Course coordinator – Modern diagnosis and treatment methods in the neoplasm of the superior aero-digestive tract, Iasi, 2008.
- Course coordinator – Diagnosis and treatment methods for ENT neoplasms – Iasi, 2011.

I have moderated and have been speaker at over 25 round tables at national and international congresses.

Throughout my entire research career, I have been actively implicated in 5 grants, for one of which I was project manager:


5. **Researcher** (Team member) in international grant - Susy safe project, Phase 1, 2 – European project on Foreign Body Injuries in the Aero–Digestive tract in Children 2005-2008.

Also, I was **member** in 3 projects won in competitions:

1. **POSDRU/87/1.3/S/622085** – Centre for specialists and resources in oral rehabilitation, 2011 – 2013, co-financed by the Social European Fund, through POSDRU 2007-2013, Project ID: 62208.

2. Transnational partnership for more attractive practical studies for construction students, ID 412286, project co-financed by the Social European Fund through **POSDRU 2007-2013** – Invest in humans.


**National memberships:**

- 1999 - Member of the National Society of the Oncological Surgeons.
- 2011 - Member of Rhinologic Romanian Society
- 2013 – 2015 - President of the Romanian Rhinologic Society

**International memberships:**

- 1996 - Regular Member of B.U.O.N.
- 1996 – Corresponding Member of American Academy of Otorhinolaryngology Head and Neck Surgery.
- 1999 - Member of Francophone Society d'ORL et de Chirurgie Cervico-Faciale.
- 2001 - Member of European Academy of Facial Plastic Surgery, The Joseph Society.

Writing board memberships:

- 2011 – Member of the editorial board of the Romanian Journal of Rhinology (index Copernicus)

**3. Medical activity**

I have never forgotten the essence of my work, always trying to assure the best treatment for my patients. To do this, I had to implement new diagnosis and surgical techniques in our ENT clinic in order to make an early diagnosis and to give a better treatment. So, I introduced the endoscopic techniques that allowed minimally invasive surgery and a more accurate diagnosis process.
PART 1.(b.ii)
Development of my academic career

My objectives for the future development of my academic career are:
- Axiological orientation of the educational process.
- Anticipation of the educational objectives
- Evaluation of the efficiency of the education process in order to improve this process.
To achieve these objectives I plan to:
- improve the teaching methods with the direct implication of the student and by allowing a national and international informational exchange
- enroll the resident doctors and young specialists in the research activities of the clinic
- intensify the collaboration efforts between different ENT departments from Romania and from other countries in order to implement new surgical and research methods
- improve the learning experience through the E-learning platform
- organize courses for continuous medical education for resident doctors and young ENT specialists.

Development of the research activity
Research development focuses, as up until now, on attending national and international scientific events, on establishing new scientific collaborations with other specialists and on developing new methods and techniques.
In order to substantially increase the impact of my scientific papers I intend to do the following:
- Publish at least one article per year in Thomson Reuters indexed journals
- Publish at least two articles per year in journals that are not Thomson Reuters indexed, but which are recognised by CNATDCU
- Attend different conferences, especially international, at least 2 per year, which will help in sharing the results of my work with other colleagues and will raise the prestige of our department and of our university.
- Participate in national and international research networks.
- Publish ENT books at CNSIS or CNATCDU affiliated of international publishing houses.
- Obtain the certificate of empowerment in the near future.
- Continue the current research directions in oncology, gastro-esophageal and hypofaringo-laryngeal reflux

Proposals for the research activity:
- Coordination and management of the research activity of the ENT department in order to favor the participation in different grants and in different national and international multicentric studies.
- Coordination and publishing of the results of the studies, both by preliminary presentations at the main national and international congresses and by original articles in the main information flux
- Conceiving and presenting the thesis for the certificate of empowerment in order to become a PhD supervisor
- Encouraging the gifted young researchers to take up doctoral studies and help then become doctors in medicine
- Obtaining financing by participating at national and international research competitions that will motivate the your researchers.
I also plan to submit a research project for PN-II-PT-PCCA in order to continue the research started in the internal grant of UMF Gr.T.Popă Iași:

INVESTIGATION AND PERSONALIZED ANALYSIS OF HEALTH LEVEL ASSOCIATED WITH METHODS OF TREATMENT, RECUPERATION AND RE-EDUCATION IN THE DYSPHONIAE INDUCED AT THE PROFESSIONS WITH INTENSE USER VOICE (DISFONOTEST)

FUNDING APPLICATION FOR JOINT APPLIED RESEARCH PROJECTS

0. SUMMARY OF THE PROPOSAL

1. TECHNICAL AND SCIENTIFIC DESCRIPTION OF THE PROJECT
   1.1. The project topic and its practical relevance
   1.2. Project contribution beyond the state of the art
   1.3. Project objectives and outcomes
   1.4. Original and innovative contributions of the project

2. IMPACT AND DISSEMINATION OF THE PROJECT RESULTS
   2.1. Possible applications with market potential

3. CONSORTIUM STRUCTURE
   3.1. Project director
   3.2. Consortium structure

4. PROJECT MANAGEMENT

5. REFERENCES
SUMMARY OF THE PROPOSAL

The aim of this project is to assess the social impact of dysphonia appearance on a large group of the population (those who use their voice very intense) and reduce as much as possible its negative effects. The voice quality of lyrical performers, announcers and actors, and the other professions that use intense their voice (teachers, theologians, judges, civil servants) is an important condition for the normal course of their profession. The project aims to characterize ENT specific disorders and to associate them with the digestive pathology and other risk factors involved in their genesis, to show the significance of the influence of biological and psycho-social environment on the occurrence and development of dysphonias in professions with intensive vocal demands, the acquisition of an accurate database on larynx diseases, the introduction of this topic within the national policy for prevention and recovery of various dysphonia etiologies, early diagnosis and reduction in number of illnesses related to associated larynx disorders in professions with intensive vocal demands and the elaboration of a strategy on the recovery and reeducation with social and economic effectiveness, including the periodical monitoring of the vocal cords recovery level.

The novelty, interdisciplinary aspect and complexity of the proposed solutions are given by the fact that this is one of the first national and European research in this regard because:

1) It develops a database for the clinical course of dysphonia belonging to various professions included in the study groups; the exact definition of the stage of disease and association with other risk factors (smoking, exposure to emissions / radiation, the use of sprays and incentive / calmative voice solutions etc.)

2) The proposed applications are more substantial, also due to the tests on the health level in a wider concept, associated with prevention in professions with intensive vocal demands and high risks for ENT and digestive disorders. The size of activities is correctly adjusted to the intended purpose and they include: a) The elaboration and validation of a complex questionnaire on dysphonia evolution; b) The elaboration of the database on the incidence and clinical evolution of dysphonias;

3) The development of a new innovative methodology on dysphonia evolution testing, with the diagnosis using the esophageal impedance;

4) The development of a new innovative methodology on dysphonia evolution testing using the electro-acoustic method;

5) The elaboration and validation of professional dysphonia diagnosis and recovery protocol. There is an immediate possibility of transferring data to potential beneficiaries—Specialty clinics in Europe, but also to SMEs manufacturing high-tech DISFONO-meters. There have been provided clear protection measures for intellectual property, and a wide dissemination area, including patents, web site, ISI publications and books, brokerage actions for industry, colloquia and round tables. The project may generate clear social effects on the population health, but also significant economic effects, by a possible future reduction and recovery up to 60% of various dysphonia etiologies and the provision of preventive measures for professions with intensive vocal demands. The team members with great expertise in interdisciplinary research activity are young, but it is also forecasted the involvement in the research activity of 11 young specialists.
THE PROJECT TOPIC AND ITS PRACTICAL RELEVANCE

THE SITUATION AT THE NATIONAL AND INTERNATIONAL LEVEL CONSIDERING THE DOMAIN AND THE THEME PROPOSED

The voice quality of lyrical interpreters and actors as well as that of other professions which intensively make use of voice (teaching staff, theologians, magistrates, etc.) represents a sine qua non condition for exercising the profession. This can be deteriorated (dysphonia) due to some ENT diseases, sometimes being associated with certain digestive diseases. Pharyngolaryngeal reflux boosted by GERD can affect any professional category, and the usual first symptoms of reflux laryngitis include the appearance of hoarseness and fonastenia.

The most frequent ENT diseases, which can determine dysphonias, i.e. acute or chronic laryngitis, can have as a starting factor the Gastro esophageal reflux disease. Therefore it is estimated that approximately 4-10% from the patients who came to ENT have a symptomatology induced by the reflux (1).

Dysphonia is the medical term for disorders of the voice: an impairment in the ability to produce voice sounds using the vocal organs from ORL field. The dysphonic voice can be hoarse or excessively breathy, harsh, or rough. Dysphonia has both organic or functional causes due to impairment of any one of the vocal organs. [Definition - Wikipedia].

According to actual international studies on the impact of Dysphonia on social life, it can create severe damages such a disabling communication due to voice condition. There are a lot of mechanisms which are involved in disphonia such traumas, inflammations, tumours, allergy, vocal effort, gastroesophageal and pharyngolaryngeal reflux. These factors produce laryngeal lesions with voice disorders.

The Gastroesophageal reflux disease represents a widespread illness among the general population. Up to almost 15-20% from the people present at least weekly one symptomatology specific to the Gastro esophageal reflux (2).

Among the patients with laryngitis and dysphonia, the reflux symptomatology is especially frequent. Thus 73% from these patients have GERD symptoms, and 50% of them present a pathological pH measurement tract (3, 4), which represents much more than the frequency of the reflux symptomatology in the general population. On the other hand, a recent study, conducted among the patients suffering from Gastro esophageal reflux disease, showed a 10, 4% prevalence of the symptomatology suggestive for concomitant laryngeal diseases (5).

Furthermore, proof sustaining the implication of the pathological Gastro esophageal reflux in the appearance of laryngitis at certain patients, is also offered by the therapeutical test, that is the improvement of the ENT symptomatology after having been administered Omeprazol (specific GERD treatment). The treatment in these patients also improves the laryngoscopical aspect and objective voice parameters (6).

One special particularity is represented by the voice modifications at the persons who have a profession that requires an extra vocal effort, either teachers, actors, priests or even professional singers (7, 8). The stroboscope-laryngoscopical evaluation (9) of teachers who teach singing has emphasized that the laryngeal reflux is very frequently met in their case.
It has also been shown that there is a rising frequency of dysphonia and of the laryngeal-pharyngeal reflux, too, among the teaching staff. An emphasis of the Gastro esophageal reflux has been emphasized in professional singers, while singing, because of the sudden rising of the intraperitoneal pressure.

The starting point in the diagnosis is the association of ENT symptomatology with the symptomatology causing the Gastro esophageal reflux disease, of which pyrosis has a high specificity, together with regurgitation, esophageal pain or dysphagia. Belasfschy and his collaborators elaborated and validated a questionnaire which includes nine parameters, questionnaire which many researchers have began to use for diagnosis. This score was subsequently checked by Oelscher, who considered it useful for diagnosis. The laryngoscopical examination permits the emphasizing of some suggestive aspects for the laryngeal-pharyngeal reflux, i.e. the association of one series of injuries, as for example: edema, erosions, the erythema of the median wall of the arytenoids. Still the laryngoscopical emphasizing of the erythema weakly correlates with the presence of a laryngeal-pharyngeal reflux.

Dysphonia can affect children as well as adults, can be either sudden or gradual in its onset, is not curable simply by ‘trying harder’, and needs to be handled by voice specialists who are fully aware of the research and current treatment regimes.

It can be said that voice disorders can seriously affect social and professional life of an important segment of the population in Romania.

For a long time the esophageal pH-measurement has been considered the “golden standard” of the Gastro esophageal reflux disease diagnosis and it is still of the day. In order to emphasize a reflux possibly implicated in the appearance of ENT pathology, it is required an ambulatory monitoring of the pH, with the multiple pH electrons, located in the proximal esophagus and, if possible, in the hypopharynx, too. The correlation between the reflux episodes (which have a limited time duration) and the ENT symptomatology is much more difficult to establish because of the chronic, persistent character of the ENT symptomatology opposite to the correlation with the esophageal symptomatology (pyrosis or pain).

Another method somehow empirical but simple for diagnosis is represented by the therapeutical test which consists in the administration of a proton pump inhibitor for 4-5 weeks.

At this moment the study of esophageal impedance is considered the best method for the diagnosis of the Gastro esophageal reflux disease, because it emphasizes both the liquid reflux (acid and non-acid) and the gaseous reflux.

The administration of a double dose of the proton pump inhibitor (40mg/day) can clearly improve the ENT symptomatology, induced by an acid reflux. In the absence of a significant improvement, the therapeutical possibilities include the endoscopic or surgical treatment of the reflux disease.

In the following bibliography there is information which, using another methodology on a limited group of subjects, suggests an implication of the Gastro esophageal reflux in the genesis of the inflammatory laryngeal diseases, involved in the appearance of dysphonia. Our study will use a top interdisciplinary methodology, applied on a large number of subjects who suffer from dysphonia, all for the use of optimizing the vocal performances.

In 2002, Belasfschy and Co. elaborated and validated a nine parameters questionnaire that was...
subsequently checked by Oelscher s.a. The laryngoscopic investigation allows the outline of suggestive aspects of injuries like: edem, erosions, medial arytenoid wall erythema. A research conducted in 2004 in USA among GERD patients showed a 10.4% prevalence of the symptoms of associated laryngeal diseases. The reflux treatment in these patients also improves the laryngoscopic aspect and the objective parameters of the voice. The strobos-video-laryngoscopic examination of music teachers in 2002 in SUA and in 2003, in Iasi, outlined that they are often suffering from laryngeal reflux, also when they sing, due to the sudden increase of intra-abdominal pressure. The starting point in the diagnosis is the association of laryngeal symptoms with the GERD symptoms, among which the pyrosis has a high specificity, being accompanied by regurgitation, esophageal pain or dysphagia.

To outline the potential involvement of a reflux, an ambulatory pH-monitoring is required, using multiple pH electrodes in the proximal esophagus and, if possible, in hypopharynx. It is very difficult to make the correlation between the reflux episodes (limited in time) and the symptomology, due to the chronicity and persistency of laryngeal symptomology, compared to the correlation with esophageal symptomology (pyrosis or pain). Another empirical but simple diagnosis method consists in the administration of a proton pump inhibitor for 4-5 weeks. Presently, the research on esophageal impedance is considered to be the best method for the diagnosis of gastro-esophageal reflux disease, because it also highlights the liquid reflux (acid and non acid) and the gas reflux. In the absence of a significant improvement, the therapeutical possibilities for reflux diseases include the endoscopic treatment or surgery. A great interest in this field is noticed abroad, but there is no correlated analysis as the one proposed in the hereby project, the best known teams being the following: in USA: Prof. Reza Shaker, Medical College of Wisconsin Dysphagia Institute, Milwaukee, Wisconsin USA; Joel Richter, MF Vaezi, Center for Swallowing and Esophageal Disorders, Department of Gastroenterology and Hepatology, Cleveland Clinic Foundation, Cleveland, Ohio; and in Europe: G Gasbarrini, Catholic University of the Sacred Hear, Rome, Italy. In Romania, the first steps in this field were made in Bucharest (ENT Clinic – Coltea Hospital: Prof. Dr. Cr. R. Popescu [48, 58], “D. Hociota” Phono-audiology Center: Prof. Dr. R. Calarasu [68, 69], Gastroenterology Clinic within Fundeni Hospital: Prof. Dr. M. Diculescu [59, 60, 65, 66]), Cluj (ENT Clinic, Prof. Dr. M. Cosgarea [70, 71, 72], 3rd Medical Clinic: Prof. O. Pascu [73, 74, 75]) Timisoara (ENT Clinic, Prof. Dr. S. Cotulbea [76, 77, 78], Gastroenterology Clinic: Prof. I. Sporea [73]), Craiova (Gastroenterology Clinic Prof. Dr. T. Ciurea) and, more advanced, in Iasi (ORL Clinic, Prof. Dr. V. Costinescu [90], and the Gastroenterology and Hepatology Institute, Prof. C. Stanciu [73]) materialized in scientific articles. With regard to the development of pulse-electroacoustic methods for the versatile analysis of sound signals in broad band frequency, the TUIasi has international priorities since 2001, materialized in cooperations with internationally acknowledged universities. Original techniques of vocal signals analysis (techniques previously completed by H. N. Teodorescu) will extend to the objectivation of both the vocal performances and to the ENT paraclinical evaluation.

The collective body from the Theoretical Informatics Institute has international priorities in what regards the processing and analysis of the vocal signal (especially non-linear methods) and the objective quantification of vocal performances. The protocols and the analysis methods previously established by Professor H. N. Teodorescu will be specifically applied to this research theme.
Beneficiaries: the voice is one of the main factors of the communicative life, a most important method of self expression which individuals have in society. Dysphonia patients among the professional soloists (opera, lyrical choirs), actors (dramatic and musical theatre), priests, teachers, magistrates and other professions which require intensive use of voice will benefit of the potential results of this study. The target population (dysphonia subjects) represents more than 500,000 in Romania only. The Ph.D. candidates included in the project will contribute to its development, benefiting at the same time from the obtained results to complete Ph.D. theses.

The project end-products
The project aims at the elaboration of the first national protocol on professional dysphonia prevention, identification at an early stage, non-invasive diagnosis and efficient recovery.

Expected results
- Knowledge of the causes/prevention/assessment at early stage of occupational dysphonia.
- 15% improvement over the next 5 years of the number of cases of occupational dysphonia at national level. The Target Population (dysphonia subjects) represents more than 500,000 only in Romania.
- Efficient Rehabilitation and socio-professional reflow of affected by occupational dysphonia subjects.

State of the art and bottlenecks
Gastroesophageal reflux disease (GERD) afflicts more than 100 million US adults, significantly impacts quality of life, and imposes more than $9 billion per year in total cost on the US healthcare system. Gastro-oesophageal reflux disease (GERD) is also one of the commonest diseases of European populations, affecting 20 to 30% of adults. GERD is multifaceted and the classical oesophageal symptoms such as heartburn and regurgitation often overlap with atypical symptoms that impact upon the respiratory system and airways [11, 20]. This is referred to as extra-oesophageal reflux disease (EERD), or laryngopharyngeal reflux (LPR), which manifests as chronic cough, laryngitis, hoarseness, voice disorders and asthma.

The quality of the voice of professionals requiring an intensive use of voice (teachers, priests, magistrates, radio/TV speakers, lyric actors) is one of the first conditions for performing one of these professions. The voice may be altered (namely ‘dysphonia’) by certain laryngeal disorders, which might be anatomic anomalies (2.43%), pure professional fatigue (14.78%) but, most frequently associated with secondary clinical symptoms (82.79% !!), as for example the gastro-esophageal reflux disease [23, 24, 25, 28, 31]. The clinical association of dysphonia with GERD is a new breakthrough in medicine, and in the present gold standard investigation in the disphonia being impedance, pH-metric, videofibroscopy which permit acid and non acid reflux diagnosis and larynx lesions [14, 15, 30, 38, 39, 41]. It was clinically proved that the reflux symptoms are very frequent in patients with laryngitis and dysphonia, and thus 73% of them present GERD symptoms and 50% present pathologic pH measurements - significantly more than the reflux symptoms frequency at population in general, showing thus the need for an integrative approach of these two
biological systems in the case of dysphonia. Reflux measurement employing ambulatory pH and/or impedance monitoring as alternative diagnostic tests for GERD have acceptable sensitivity (77%–100%) and specificity (85%–100%) in patients with endoscopically proven esophagitis. However, they are less sensitive (0%–71%) in endoscopy negative disease, which represents a majority of patients with dysphonia, for whom the test is currently recommended.

Thus, the actual medical diagnosis of dysphonia is uncertain, at a late phase – when secondary clinical symptoms are present and most alterations may remain irreversible, very costly and invasive.

There is no protocol on professional dysphonia prevention, identification at an early stage, non-invasive diagnosis and efficient recovery.

**Project contribution:**
A professional interdisciplinary protocol on professional dysphonia prevention (a), identification at an early stage (b), non-invasive diagnosis (c) and efficient professional reintegration, with long term survey of treatment and recovering effects (d).

a) The project will bring a significant contribution to the knowledge by analysing the integrative biological systems of human beings, by clarifying the significance of professional dysphonia, by the association of the digestive pathology (particularly of the gastroesophageal reflux), larynx disorders (of any cause) and impact of some risk factors (smoking, exposure to pollutants / radiation, the use of incentive / calmative voice sprays and solutions etc), causing the alteration of the speaking and singing voice in professions with intensive vocal demands.

b) The project will bring a significant contribution to the knowledge, by analysing the voice functional alterations within the professional dysphonia disorders by an original electroacoustic method [84, 86, 87, 88, 89]. Dysphonia is caused by the interruption of the ability of the vocal folds to vibrate normally during respiration. It is most often observed in the production of vowel sounds. Weakness of the larynx can lead to irregular movement in one or both sides of the glottis, and this irregular motion is heard as roughness with a unique frequency spectra that can evolve in time, or under certain stress, or clinical conditions as described above. It is expected that even minor alterations to be identified at an early stage due to this non-invasive method, leading to efficient, quick and low cost recovery. At this stage, the elaboration of a highly accurate database on the patient’s ‘individual dysphonic pattern’ is foreseen.

c) The project will bring a significant contribution to the knowledge, by promoting the electroacoustic method with advanced software support (in term of expert system) in the complementary / non-invasive functional testing for medical purpose. The creation of a DISFONO-meter prototype for medical use is foreseen, to be used in association with actual methods for both digestive pathology and larynx anatomic disorders evaluation.

d) The project will bring a significant contribution to the knowledge, by using the expert system for efficient recovery, with long term survey of treatment, recovering and social-
reintegration effects. The strategy will be complex, by outlining first of all the specific clinical effects and by helping in the elaboration of the optimal medical recovery. The second stage is related to reeducation strategies, for socio-professional reintegration of subjects. The software system is accessible on-line, via the development of certain remote investigation and self-evaluation modules, for re-testing and recovery purpose. The system will also include the necessary modules for preventive or periodical investigation of individuals with risk of professional dysphonia disorders and will statistically quantify the psychological-social-economical effects.

**PROJECT OBJECTIVES AND OUTCOMES**

**Objectives**

1) The elaboration and validation of a complex questionnaire on the dysphonia socio-professional evolution, by the association of professional stress with clinical investigations; The involvement of a large number of target groups of subjects of various age and professions; The validation of the sampling method and of the social and professional relevance of the research.

2) The elaboration of a database on the incidence and clinical evolution of dysphonias. To obtain access effectiveness. To show the necessity of periodical tests for professions with intensive vocal demands.

3) To develop an innovative testing methodology on dysphonia evolution, with the diagnosis of the gastro-esophageal reflux based on esophageal impedance. The complex and multidisciplinary research on dysphonia and the completion of a database with the parameters resulted by using the esophageal impedance.

4) The development of an innovative testing methodology on dysphonia evolution based on the electroacoustic method and the creation of a DISFONO-meter prototype. The elaboration of a highly accurate database on the patient’s ‘individual dysphonic pattern’; The exact definition of the disease stage and of the association of the digestive pathology and ENT disorders in the study of laryngeal disorders, correlated or not with other hazards (smoke/smoking, alcohol, exposure to ozone or electromagnetic radiation).

5) The elaboration and validation of professional dysphonia diagnosis and recovery protocol; The elaboration of a recovery and reeducation strategy with social and economic effectiveness, including the periodical monitoring of the voice recovery level, and of ENT trauma reversibility; The development of certain remote investigation and self-evaluation modules, for re-testing and recovery purpose.

**Scientific and technical barriers**

There are some technical problems in gastro esophageal investigations caused by patient cooperation, as much of these investigations are perform in the ambulatory system. Many voice users don’t want to have a good cooperation and recognition of their professional voice disorders. They are afraid to loose their job. Many patients are going at the beginning to the family doctor so they will come to late to ENT specialists.
Outcomes and comparative contribution

The project aims to improve the quality of life of the target group, extending the social impact on the entire population due to the nature of their job. First of all we need to identify the target groups of the research. For this a complex questionnaire will be developed. A large number of relevant subjects with different ages, professions and clinical aspects will be involved. After that a preliminary structure of the database will be developed by statistical validating of sampling mode and socio-professional relevance of the study. The next step is the development of a strategy for rapid identification and periodic preventive test for patients with intense vocal demand professions and the development and validation of a diagnostic protocol of occupational dysphonia and vocal performance based on dedicated electroacoustic measurements. Integrating and correlating of the measurements results with the database of social incidence of dysphonia will be effectuated. Testing will be performed by a complex system that will allow automatic measurements, corrections in real time, the statistical analysis of tolerance and automatic calibration, the outline of the specific voice pattern, the linear and non-linear analysis of parameters (including impedance methods – Thiele parameters and transformed Fourier - FFT), the selection of critical parameters ('threshold' system), data saving in post-processing system (for off-line analysis, type PULSE Steady State Response Analysis (SSR) or Time Selective Response Analysis (TSR)).

Comparative personalized analysis of recorded human voice and definition of a new concept of 'individual dysphonia pattern' of the patient is based on electroacoustic signal processing. Development of specific mathematical models for signals analysis associated with spectral images obtained by electroacoustic measurement will be performed. The expert system for elaboration of individualized / personalized strategy of identification, recovery and rehabilitation of occupational dysphonia at subjects with different ages, professions and clinical aspects will be developed. A study of voice analysis techniques in order to develop strategies for early detection of occupational dysphonia will be performed. Will be made a correlation between electroacoustic method and investigation and current clinical casuistry for the development of new complex equipment for specialized electroacoustic measurement for occupational dysphonia.

The main achievement of the proposed research is development and technical testing of prototype: DISFONO-meter and development of the preventive ('remote') testing strategy at professions with intense voice stress, by implementing of an online self-assessment of patients’ individual vocal performances, e-medicine model.
ORIGINAl AND INNOVATIVE CONTRIBUTIONS OF THE PROJECT

The project aims at the elaboration of the first national protocol on professional dysphonia diagnosis and recovery, applicable both to professions with intensive vocal demands and to population in general, opening thus the perspective on a multidisciplinary approach. The research shall include a new method for the gastro-esophageal reflux diagnosis using gastroesophageal tests (esophageal impedance, Bilitec method and Ph metric) that shall be applied to this population group (professional), all methods that shall also be introduced in the GER diagnosis for the first time at national level for this kind of voice users. Compared to the research conducted so far, the project novelty consists in the involvement of a large number of target groups of subjects of different age and with different professions (from Canto students—with their voice in formation, to subjects with experience in various professions, to whom a prolonged exposure to potential hazards to voice alteration may result in a voice quality deterioration accompanied by major professional effects). The project contribution also consists in its original approach of the personalized comparative analysis of the human voice (based on medical functional investigations, and on spectral modeling using specialized software), together with the subjective voice analysis (conducted by persons with expertise and certified competences in voice performance assessment), in order to develop innovative testing models and methodologies, and to elaborate a highly accurate database. The testing procedure includes the development of equipment and software for specialized electroacoustic measurements, the definition of identifying and customizing models and procedures - individual voice electroacoustic pattern, associated with metrological statistics elements, followed by the identification of the links with the clinical case history, the investigation and validation of the health condition and of the recovery and reeducation strategy in an expert system, with collateral development of some investigation and self-valuation modules for individuals at distance, e-health system, for preventive or periodical tests. There shall be elaborated an innovative versatile analysis platform for sound signals in broad band frequency. The collected sounds like: vocal energy and attenuation, own band frequency, harmonic distortion, intermodular distortion, phase difference and directivity lead to the definition of several spectograms unique in the broad band frequency that we named: the ‘individual dysphonic pattern’ of the patient.
A major advantage of the system consists in the possibility to make, a-priori, the optimal choice of the measurement sensitivity and accuracy, and the correlation between measurement data and the type of precinct, the orientation of the sound signal, the environment factors (temperature, humidity etc.). Using special filters, with 3D orientation that are accurate even under noise circumstances, the responses in frequency may be selective. The complex system that we have envisaged and named: ‘DISFONO-meter’, allows automatic measurements, corrections in real time, the statistical analysis of tolerance and automatic calibration, the outline of the specific pattern, the linear and non-linear analysis of parameters (including impedance methods – Thiele parameters and transformed Fourier - FFT), the selection of critical parameters (‘threshold’ system), data saving in post-processing system (for off-line analysis, type PULSE Steady State Response Analysis (SSR) or Time Selective Response Analysis (TSR)), the identification of critical elements and of expert system based diagnosis and subsequently, the interconnection and implementation in a remote individual valuation system with intelligent sensors (e-health type). The intelligent transducers and their location and action comply with Bruel and Kjaer methods in 2012, fig.1. The signal analysis in 3D real
A system is presented in fig.2. Fig.3 presents an overview on: the panel for measurement data analysis and the preview of the patient’s image of the ‘individual dysphonic pattern’ type, with the identification of critic clinical parameters.

Another genuine contribution is: the elaboration of a preventive testing strategy (‘remote’) for professions with intensive vocal demands, and the correlation with other hazards, respectively, a recovery and reeducation strategy with social and economic effectiveness, including the periodical monitoring of the voice recovery level, an aspect that has never been approached by science.

The dissemination will be focus both on nation and large European actions. The dissemination & communication strategy is divided into 5 main steps:

**POSSIBLE APPLICATIONS WITH MARKET POTENTIAL**

The main purpose is the decrease of the dysphonia frequency in the groups with intense vocal usage. It will be established a diagnosis protocol and the improvement of the dysphonias applicable both to the professions with intense vocal stress and to the general population. The target population (dysphonia subjects) represents more than 500,000 in Romania only.

The project may generate clear social effects on the population health, but also significant economic effects, by a possible future reduction and recovery up to 60% of various dysphonia etiologies and the provision of preventive measures for professions with intensive vocal demands.

At least 5000 medical units at European level may benefit on the new technology and equipment, named herein as ‘DISFONO-meter’. The inclusion of on-line facilities for ‘DISFONO-meter’ in terms of e-medical operations, may extend the on-line use of the systems towards millions of patients, with all Internet traffic benefits of such systems and related software for the IT market.

Users: Data obtained is relevant and useful to the academic education in the field of Arts and Engineering, for the optimization of the voice training and of the medical personnel that keeps under observation persons whose professions require an intensive use their voice. The institutional users are mainly the public health units (including Labor health) under the Ministry of Public Health and the Health Insurance Agency. The database and the on-line system are instruments necessary to the assessment of the statistical evolution of the population health. Beneficiaries: The patients suffering from dysphonia among professional singers (opera, lyrical choirs), actors (drama, musicals), priests, teachers, magistrates and other professions with high demands on vocal cords. The target population (subjects suffering
from dysphonias, including other etiologies) represents over 350,000 persons in Romania. The preliminary study on the returns for one DISFONO-meter showed that the net profit of a prototype of approx. 42,600 Euro (production costs) is of approx. 2600 Euro/month, resulted from the preventive test fee for professions at risk in Romania.

**Marketing**

An Exploitation Plan based on the Cooperation Agreement was already discussed by all the Partnership members. All commercialization opportunities will be considered. Business options range from exclusive and non-exclusive licences, research exploitation agreements, or contracts through joint ventures (with direct participation of EC companies). The distribution channels will be maintained active by: Information: gathering and distributing marketing research / Promotion: developing and communicating offers / Contact: communicating with prospective buyers, including fairs, expositions etc./ Matching: fitting the offer to the buyer's needs – taking account of all open bids / Negotiation: reaching agreement on price and terms / Physical distribution: assuring transporting and storing the goods / Financing: getting and using funds to cover the costs of channel work / Risk taking: assuming the risks of the channel work.

Ways of distribution - Online - Set up of a web page with information, video sample files, sample data, and how to order etc. May let be ordered also a promotional CD

**ESTIMATED IMPROVEMENTS IN THE QUALITY OF LIFE, WITH RESPECT TO CURRENT PERFORMANCE OF PRODUCTS, TECHNOLOGIES AND/OR SERVICES**

**THE SOCIAL impact of the project**

Identification and prevention from ENT and digestive (RGE) diseases and improvement of the population health. Improvement of voice performances of patients from fields of activity with high demands on the vocal cords, reducing thus the temporary incapacity of working. Permanent professional training of various specialists involved in dysphonia treatments based on information generated by the developed project will lead to the improvement of the quality and effectiveness of the rehabilitation services.

**The target population** (dysphonia subjects) represents more than 500,000 in Romania only.

**THE ECONOMIC Impact of the project** – Romania shall be included in the circuit of countries with a sustainable interest in the preventive periodical testing for professions with high demands on vocal cords, with long term advantages for CNASS. The prospective reduction by 60% of the no. of cases of professional disease, and the increase with the same percentage of the level of recovery from dysphonia. Target group: 350,000 persons in Romania. Expansion of the IT database used in the health, cultural and technical field, if we consider a possible transfer of outcomes to other medical services in the country. The homologation and implementation throughout the country of new health assessment and testing methods (see also the economic chapter). The development of commercial software (including e-health systems) to establish sets of objective features by using the computerized analysis of voice sounds in dysphonia diagnosis and reeducation.
The project will have a significant contribution in establishing the important association of the digestive pathology (especially that of the Gastro esophageal reflux) in the laryngeal diseases which determine the deterioration of the speaking and singing voice in the case of the professionals. The project may generate clear social effects on the population health, but also significant economic effects, by a possible future reduction and recovery up to 60% of various dysphonia etiologies and the provision of preventive measures for professions with intensive vocal demands.

The project also contributes to the original inclusion of the objective comparative analysis of the voice (medical surveys, computerized analysis of the vocal performance), and also of the subjective analysis of the voice (the analysis is accomplished by experienced persons with tested competence in the analysis of vocal performance). The results of this project may be clearly included in the national politics of preventing and improving the different etiology dysphoniae, i.e. towards reducing the costs with health and social care and improving the prevention actions for certain professional exposures.

At least 5000 medical units at European level may benefit on the new technology and equipment, named herein as ‘DISFONO-meter’. The inclusion of on-line facilities for ‘DISFONO-meter’ in terms of e-medical operations, may expend the on-line use of the systems towards millions of patients, will all Internet traffic benefits of such systems and related software for the IT market.

**Impact ON THE ENVIRONMENT** - The highlight and elaboration of a strategy on the reduction of risk factors (smoke, ozone or electromagnetic radiation), that are also pollution factors.

**PROJECT DIRECTOR**
Cobzeanu Mihail Dan, 24.12.1955, Professor at ENT Department University of Medicine and Pharmacy "Grigore T. Popa" of Iasi
- *professional experience in the topic of the project:*

**CONSORTIUM STRUCTURE**

**CO - University of Medicine and Pharmacy "Grigore T. Popa" of Iasi** – Role: Assessment of dysphonia and GERD prevalence in vocal professionals; Elaboration and validation of a complex questionnaire on dysphonia evolution; Elaboration of the database on the incidence and clinical evolution of dysphonias; Support the development of a innovative methodology on dysphonia evolution testing, with the diagnosis of gastro-esophageal reflux disease using the esophageal impedance and electro-acoustic method - high-tech DISFONO-meters; Elaboration and validation of professional dysphonia diagnosis and recovery protocol, based both on DISFONO-meter and the evolution of ‘individual dysphonic pattern’.

**P1 – Technical University “Gheorghe Asachi” of Iasi** - TUIasi. Role: Support elaboration of the database on the incidence and clinical evolution of dysphonias; R&D of a innovative methodology on dysphonia evolution testing using the esophageal impedance and electro-
acoustic method - high-tech DISFONO-meters; Equipment development and optimisation vs.application.Industrial scale-up of technology.Design, test and prototyping of DISFONO-meter. Technical studies; Different dissemination actions.

**P2 - UAIC - Role:** IT development and data processing; Support the elaboration and validation of a complex questionnaire on dysphonia evolution; Elaboration of the database on the incidence and clinical evolution of dysphonias; Support the development of an innovative methodology on dysphonia evolution testing using the accurate database on the ‘individual dysphonic pattern’ of a patient; Support design and test of DISFONO-meter; Web page design and maintenance.

**P3 - Intelectro - Role:** The main role in the project is as software tool developer and R&D activities regarding the statistical analysis of signals; Data acquisition, processing, testing and validations of signals related to the evolution of ‘individual dysphonic pattern’ of each patient; R&D on tools for speech recognition technology and applications; Support the elaboration and validation of professional dysphonia diagnosis and recovery protocol, based both on ‘individual dysphonic pattern’. Support design and test of DISFONO-meter and development of related e-health type instruments.

The general expertise within the proposed consortium consists mainly in the project synergy of a complete chain of product development from simple questionnaire and database to integrated design and direct application in health and safety at work, supported by feasibility studies.
Through the proposed partnership it is intended to assuming a long-term commitment, able to ensure the stability and improve of the act of scientific research and the integration of research results into research strategies of partners, approach to develop the innovation capacity and increasing of research impact in the economical and social environment.

The project is able to generate long-term effects for the benefit of the target group, directed to:

- human resources development research by helping researchers in the period after completion of the project and strengthen their route segment of training;
- strengthen the scientific potential of the partners through the exchange of best practices to offer researchers involved in the project various skills;
- strengthen institutional potential of the partners through the managerial know-how transfer in that domain;
- Acquiring attribute "excellence" of scientific research, by addressing certain key criteria: interdisciplinarity, international dimension, quality, market utility, supporting sustainable development and environmental protection.

Through this project, the institutions involved forming a solid partnership to ensure the best combination of their technological skills to achieve the proposed activities and to provide ways of exploiting the results.

The partnership has brought together a multidisciplinary scientific team. Partners' ability to achieve complete tasks in the context of the project is supported by their scientific expertise in different fields. Partnership exploit the existing know-how about the nano-conductive materials, polymer adhesive matrix, joints modeling as thermo-electric-rheological process in

**PROJECT MANAGEMENT**

Project management is one matrix type. Each partner will have a specific research organization scheme coordinated by an individual management team that is project oriented. Each partner will nominate its project director, responsible for planning and monitoring (ongoing control of activities / planning periods, checking monitoring documents, planning and organizing workshops with the team, etc.), helped by a financial executive (preparing payment documents / schedule, settlement of stages / activities, financial reports) and a technical-scientific executive (scientific and technical reports, consulting for difficult problems, checking evaluation reports, supervising of technical-scientific meetings of our team which can be research, design team etc.). Internal communication between functional and management levels is ensured by attributing, knowing and respecting the hierarchical structure and the given tasks by the entire staff that is leading, verifying and respectively executing the project imposed activities through the Gantt and WPs descriptions. Management objectives are communicated and processed at all levels of organization described in the scheme. The general management of the project will be achieved by:
Management scheme of the project

Project working team
- Research team
- Design team
- Execution team

Subcontractors 1, 2, 3

Project director

Third parts: Beneficiaries, OSIM etc.

TCPA 1, 2, 3

Research team
- Design team
- Execution team

Representative
- Planification-monitoring
- Financial executive
- Technical-scientific executive

Working team for activity 1, 2, ...

Table: Project management scheme

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<thead>
<tr>
<th>Activity</th>
<th>1st Year</th>
<th>2nd Year</th>
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WPs and Activities

WP4: Research on personalized analysis of the cause of dysphagia
- Th4.1: Design and implement a computerized software system for the monitoring and prevention of dysphagia.
- Th4.2: An analysis of the treatment of dysphagia by different research teams providing specialized software.
- Th4.3: Development of methods for the identification of dysphagia by different research teams.
- Th4.4: Development of methods for the monitoring and prevention of dysphagia.

WP5: Development and validation of specific software for monitoring and monitoring of dysphagia.
- Th5.1: Development of methods for the identification of dysphagia.
- Th5.2: Development of methods for the monitoring and prevention of dysphagia.
- Th5.3: Development of methods for the monitoring and prevention of dysphagia.

<table>
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<tr>
<th>Activity</th>
<th>Description</th>
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<tr>
<td>Th4.1</td>
<td>Design and implement a computerized software system for the monitoring and prevention of dysphagia.</td>
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<td>Th4.2</td>
<td>An analysis of the treatment of dysphagia by different research teams providing specialized software.</td>
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<tr>
<td>Th4.3</td>
<td>Development of methods for the identification of dysphagia by different research teams.</td>
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<td>Th4.4</td>
<td>Development of methods for the monitoring and prevention of dysphagia.</td>
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<tr>
<td>Th5.1</td>
<td>Development of methods for the identification of dysphagia.</td>
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<tr>
<td>Th5.2</td>
<td>Development of methods for the monitoring and prevention of dysphagia.</td>
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<tr>
<td>Th5.3</td>
<td>Development of methods for the monitoring and prevention of dysphagia.</td>
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WP7: Development of a specialized software system for the monitoring and monitoring of dysphagia.
- Th7.1: Development of a specialized software system for the monitoring and monitoring of dysphagia. |
Mixing educational and researching activities
Adjusting the study plans in order to be consistent with the needs and possibilities
Career development of young researchers by introducing new fields of activity.
Skill improvement by continuous medical learning.
The results of the studies will be found in articles and books that I will publish within the research projects that I will coordinate. These projects will encourage young PhD’s and master students to participate in research activities and to present their results at different conferences.
I will gather books, magazines and articles in electronic format in order to set up a mini electronic library for our ENT department that will be useful for anyone willing to obtain an up-to-date information in the field of ENT.

Development of my medical (professional) activity
I will introduce in my department new methods of endoscopical approach in order to solve rhinologic and part of hypopharingeal and laryngeal pathologies.
Also I’ll go for training in the important ENT European departments, to learn new surgical methods for to be applied after that in my department.
I also try to obtain new instruments like CO2 laser, videoendoscopy in order to diagnose and solve easier our patients.
PART 1.(b.iii)
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