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Assessment of asymptomatic coronary artery disease in aeronautical personnel

Anghel M1, Macri M1, Greere V2

National Institute of Aeronautical and Space Medicine, Bucharest, Romania
Army Cardiovascular Disease Center, Bucharest, Romania

Abstract. Coronary artery disease (CAD) will always be a major concern for aeromedical disposition and aircrew standards, being one of the most frequent causes of loss or restriction of license for all categories of civilian and military flying. We have studied a group of 712 subjects, aged 30-55, representing the military and civilian aeronautical personnel, medically examined periodically at the National Institute of Aerospace Medicine, Bucharest, Romania, in 2004. These subjects were usually evaluated by clinical exam, laboratory tests, resting ECG, and chest X-ray. We have selected the subjects with persistent ECG abnormalities (possible ischemic changes) or associated cardiac risk factors. The study group was further evaluated for asymptomatic CAD by exercise treadmill testing, echocardiography, ambulatory ECG monitoring and coronary angiography. We studied the independent risk factors associated with asymptomatic CAD using multiple logistic regression analysis (SPSS v.10). In more than 50% of subjects, asymptomatic coronary artery disease has been associated with at least two risk factors, more or less reversible. Exercise treadmill testing, echocardiography and/or ambulatory ECG monitoring had positive results in less than one third of the studied group. The majority of subjects investigated by coronary angiography had normal results. 1. Asymptomatic coronary artery disease has a prevalence of 5.75% in aeronautical personnel. 2. The majority of the studied subjects associate more cardiovascular risk factors. 3. The specific professional stress is significantly associated with asymptomatic CAD. 4. The centerpiece of long-term risk reduction is modification of lifestyle habits with physical activity, weight control, smoking cessation, and proper diet.

Key words: aeronautical personnel, asymptomatic coronary artery disease.

Correspondence to: Mirela Anghel, M.D., e-mail: mirela@chisel.ro
Results

The gender-dependent structure of the studied lot showed a male predominance (91.3%). The mean age of subjects was 46.2 ± 5.3. The studied lot structure according to professional activity was as follows (Table 1).

Table 1. The group structure according to professional activity

<table>
<thead>
<tr>
<th>Professional activity</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supersonic pilots</td>
<td>12.5</td>
</tr>
<tr>
<td>Subsonic pilots</td>
<td>15.6</td>
</tr>
<tr>
<td>Helicopter pilots</td>
<td>18.7</td>
</tr>
<tr>
<td>Commercial pilots</td>
<td>28.1</td>
</tr>
<tr>
<td>Ground aeronautical personnel</td>
<td>25.0</td>
</tr>
</tbody>
</table>

The age-dependent prevalence of resting ECG abnormalities (possible ischemic changes) in aeronautical personnel was higher in the age group 46-55 (Table 2).

Table 2. The age-dependent prevalence of resting ECG abnormalities (possible ischemic changes)

<table>
<thead>
<tr>
<th>Age group</th>
<th>Resting ECG abnormalities (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-35</td>
<td>11.2</td>
</tr>
<tr>
<td>36-45</td>
<td>28.5</td>
</tr>
<tr>
<td>46-55</td>
<td>33.2</td>
</tr>
</tbody>
</table>

In univariate analysis, the following risk factors were significantly associated with asymptomatic coronary artery disease in the studied subjects (Table 3).

Table 3. The risk factors significantly associated with asymptomatic coronary artery disease

<table>
<thead>
<tr>
<th>Risk factor correlated with CAD</th>
<th>r</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.291</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Gender – male</td>
<td>0.418</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Family history of premature CAD</td>
<td>0.447</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.236</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Smoking</td>
<td>0.224</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>0.583</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Impaired glucose tolerance / diabetes mellitus</td>
<td>0.370</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Obesity</td>
<td>0.312</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Professional stress</td>
<td>0.437</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

In more than 50% of subjects, asymptomatic coronary artery disease has been associated with at least two risk factors, more or less reversible. A critical point is that any single risk factor can lead to premature CAD if left untreated. This means each major risk factor deserves intervention in the clinical setting, regardless of short-term absolute risk. Preventive efforts should target each major risk factor. In multiple linear regression analysis (Backward, Stepwise, Forward), after adjustment for possible confounders (such as age, sex, BMI, smoking), the following parameters were found to be significant independent determinants of asymptomatic coronary artery disease (Table 4).

Table 4. Independent determinants of asymptomatic coronary artery disease

<table>
<thead>
<tr>
<th>Independent determinant of asymptomatic CAD</th>
<th>β</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyslipidemia</td>
<td>0.352</td>
<td>0.001</td>
</tr>
<tr>
<td>Impaired glucose tolerance/Diabetes mellitus</td>
<td>0.284</td>
<td>0.017</td>
</tr>
<tr>
<td>Professional stress</td>
<td>0.201</td>
<td>0.032</td>
</tr>
</tbody>
</table>

The results of the echocardiography, exercise treadmill testing, and ambulatory ECG monitoring have shown the following results in the studied group (Table 5).

Table 5. Positive results of the non-invasive diagnostic methods of asymptomatic CAD

<table>
<thead>
<tr>
<th>Diagnostic method of asymptomatic CAD</th>
<th>Positive results (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Echocardiography</td>
<td>15.3</td>
</tr>
<tr>
<td>Exercise treadmill testing</td>
<td>24.1</td>
</tr>
<tr>
<td>Ambulatory ECG monitoring</td>
<td>11.4</td>
</tr>
</tbody>
</table>

The results of the angiographically-investigated subjects have shown the normal results in 81.2% of subjects (Table 6).

Table 6. The results of coronary angiography in the studied group

<table>
<thead>
<tr>
<th>Angiographic subset</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>81.2%</td>
</tr>
<tr>
<td>Minimal CAD</td>
<td>17.6%</td>
</tr>
<tr>
<td>Significant CAD</td>
<td>1.2%</td>
</tr>
</tbody>
</table>

Finally, asymptomatic CAD has been diagnosed in 5.7% of all studied subjects. Majority of these subjects were enrolled in a prophylactic and curative therapy program resulting in a good short-term prognosis. The centerpiece of this program was modification of lifestyle habits with physical activity, weight control, smoking cessation, and proper diet. We will continue this study in a long-term follow-up of aeronautical personnel.

Discussion

Nonspecific ST-T wave changes were observed in 21.1% of studied subjects. These ECG changes can be a real dilemma. On the one hand, they do have some predictive value for underlying disease, especially if new compared with prior tracings. On the other hand, they are very nonspecific and the likelihood of significant disease in an otherwise healthy, active, and asymptomatic aviator is low. If the changes persist on a repeat, fasting ECG and are new compared with prior tracings, then screening for CAD may be warranted for the older male aviator (e.g., age over 35 years). Younger men with high-risk profiles may also be considered for screening. Graded exercise testing and echocardiography are then recommended. These tests were positive in 29.3% in the studied subjects older than 35 with ST-T wave changes and in 11.6% of younger subjects with high-risk profiles. Finally, only 5.7% of all studied subjects were diagnosed with asymptomatic CAD.

Our results underline that general screening for CAD is usually not recommended on the aviator population as a whole without some form of risk stratification, such as standard cardiac risk factors or resting ECG abnormalities [6,7].

Current recommendations are that exercise treadmill testing is a Class IIb indication in asymptomatic men older than 40 years and women older than 50 years who are involved in occupations, such as aviation, in which impairment might affect public safety. Evidence-based data shows that exercise testing is a worthwhile tool to predict future risk of CAD death, especially in asymptomatic subjects with more cardiac risk factors [3]. Treadmill testing offers the ability to identify...
unknown disease, but fewer false-positive tests are generated when its use is limited to higher risk subsets. We noticed false-positive tests in 18.8% of the selected studied subjects. Coronary angiography revealed significant CAD in 1.2% of subjects. It predicts intermediate and long-term outcome of CAD. Several studies have shown that the extent of anatomic CAD is a strong predictor of survival and other clinical events [5]. Current recommendations of many aviation regulatory agencies consider this and allow varying degree of CAD to maintain license, although license is often restricted.

**Aeromedical disposition**

Aeromedically, CAD is a leading cause of disqualification or denial of licensure in both civilian and military aviators. Waiver recommendations may be made for fliers with minimal CAD (MCAD) defined as lesions on angiography resulting in maximum stenosis less than 50% of any coronary artery. Given the low event rate in aviators with minimal CAD, the USAF has for years allowed such aviators to continue to fly, but has restricted them to low-performance, multipilot aircraft, if they are also asymptomatic and have had no prior cardiac events. They are excluded from high-performance aircraft because the effects of high +Gz forces on minimal lesions are unknown [8]. Periodic noninvasive evaluation is recommended, annually for military aviators [9]. The rate of progression of minimal CAD to significant CAD is unknown [10]. Pending more reliable noninvasive methods to detect asymptomatic progression and better data in aviator populations with minimal CAD will exist; periodic repeat coronary angiography (3- to 5- year intervals) is a consideration, at least for military aviators.

Any evidence of significant CAD (stenosis greater than 50%) is typically excluded from military aviation duties, with or without revascularization. Without revascularization, return to limited commercial flying might be considered for single vessel, moderate disease (maximum lesion 50% to 70%). If so, the aviator should be asymptomatic and without evidence of ischemia when off antianginal medications, and overall LV function should be normal without significant regional wall motion abnormalities. Noninvasive reevaluation should be performed at least annually. Periodical repeated coronary angiography is a consideration, at least for commercial aviation [11].

**Conclusions**

1. Asymptomatic coronary artery disease has a prevalence of 5.7% in aeronautical personnel.
2. The majority of the studied subjects associate more cardiovascular risk factors.
3. The specific professional stress is significantly associated with asymptomatic CAD.
4. A critical point is that any single risk factor can lead to premature CAD if left untreated. Preventive efforts should target each major risk factor.
5. The centerpiece of long-term risk reduction is modification of lifestyle habits with physical activity, weight control, smoking cessation, and proper diet.

**References**

Original Article

The gunshot injuries in emergency surgery

Kalemoglu M, Yildirim I, Keskin O, Eryilmaz M, Ersanli D

Gulhane Military Medical Academy, Haydarpasa Training Hospital, Department of Emergency Medicine, Istanbul, Turkey

Abstract. This study aims to define the pattern of gunshot injury in the Gulhane Military Medicine Academy Haydarpasa Training Hospital between March 2001 and March 2004. The history was recorded for each patient presenting at the hospital with gunshot injuries from the clash. Each was examined and followed up through subsequent treatment in the wards and clinics. The study included 203 patients. The male-to-female ratio was 24 to 1. The mean age was 29.2±10.9 years, and the mortality rate was 8.3%. There were 154 warriors and 49 noncombatants. Government workers and students made up most of the noncombatants (42.5%), whereas military personnel constituted the vast majority of the warriors (23.3%). Injury to the lower limbs was the most commonly seen injury (54.6%). Sustained fractures and femoral fractures were the most common fracture (n=110, 54.1%). Head and colonic injuries were the greatest cause of mortality. Abdominal penetrating gunshot wounds consist of the small bowel (58.3%), the colon (46.8%), and the liver (21.8%). The average hospitalization period was 14.5±1.4 days. The gunshot injuries constitute the group of trauma, which are the high morbidity and mortality rates.

Key words: emergency, department, surgery, gunshot injuries, gunshot wound, high-velocity guns

Gunshot injuries are on the increase throughout the world. Although they are more common in the developed countries of Europe and North America as a whole, probably because handguns are easily accessible, civilian gunshot injuries are approaching an epidemic level in some other parts of the world [1-3]. Civilian gunshot injuries usually are caused by low-velocity bullets and result in low morbidity and mortality, as compared with injuries from high-velocity missiles. However, recently, high-velocity weapons are used increasingly, causing more complicated injuries that task the experience of the attending surgeon.

This study aims to define the pattern of gunshot injury in the Gulhane Military Medicine Academy Haydarpasa Training Hospital between March 2001 and March 2004.

Materials and methods

The histories of the patients were recorded and the following information was obtained from either the patients or those who had brought them to the hospitals: age, gender, the type of injury, the treatment, hospitalization duration, and mortality rate. Each was examined and followed up through subsequent treatment in the wards and clinics. The types of guns used were assessed according to the severity of the injury on clinical examination and the type of missiles seen on the radiographs.

High-velocity guns such as rifles have a muzzle velocity greater than 600 m/second. In contrast, low-velocity guns have a muzzle velocity less than 600 m/second and cause limited tissue damage. Associated fractures usually are not comminuted [4]. Dane guns are locally made shotguns filled with metallic pellets. They are classified as low-velocity weapons, although at very short ranges, they can inflict severe injuries.

Analysis was by determination of the mean ± standard deviation using the EPI-info analysis software, whereas diagrammatic presentation was by the use of tables.

Results

The patients included 195 men and 8 women, and the male-to-female ratio was 24 to 1. Among these patients, 49 (24.1%) were noncombatants, and the remainders were warriors. The most reason of gun shot wound in military personnel is weapon accidental. The ages ranged from 10 to 65 years (mean, 29.2 ± 10.9 years). The most commonly injured ranged in age from 21 to 30 years.

Of the 15 patients (7.6%) with peripheral nerve injuries, 5 had sustained injuries to the sciatic nerve, 4 to the brachial plexus, 3 to the ulna nerve, and 2 to the mandibular nerve. Vascular injuries were seen in seven patients (3.2%); five

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with femoral artery injury and two with brachial artery injury. No cases of tetanus or gas gangrene were recorded.

Table 2. Anatomic sites of fractures

<table>
<thead>
<tr>
<th>Sites</th>
<th>No. of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femur</td>
<td>31</td>
<td>28</td>
</tr>
<tr>
<td>Tibia and Fibula</td>
<td>23</td>
<td>22</td>
</tr>
<tr>
<td>Humerus</td>
<td>17</td>
<td>15</td>
</tr>
<tr>
<td>Skull (and facial skeleton)</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>Hand bones</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Radius and ulna</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>Foot bones</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>110</td>
<td>100</td>
</tr>
</tbody>
</table>

(No patient sustained multiple fractures)

There were 60 cases of abdominal injuries: 58 involving intraperitoneal penetration and 2 involving pellets lodged in the subcutaneous tissue. All of the 58 patients with penetrating abdominal injuries presented with abdominal pain. This pain was severe and generalized for 56 patients, whereas for the remaining 2 patients, it was localized to the left iliac region and the left hypochondrium, the site at which the pellets had penetrated. Peritonitis was noted for 56 patients, and 39 patients presented with shock. Evisceration of the abdominal viscera occurred in 12 patients. The two patients with subcutaneous pellets were managed with wound debridement. The remaining 58 patients had intraperitoneal injuries. 55 of which underwent exploratory laparotomy and 3 of which were non operative treatment. Six patients sustained splenic injuries that underwent splenectomy. Three patients had injury to the liver who had stopped bleeding during the observing time without laparotomy.

Chest injuries were found in 23 patients, and 11 of these patients had other systemic injuries as well. Five who had only subcutaneously lodged pellets were treated nonoperatively. Hemopneumothorax was found in 15 patients, which was managed with underwater seal chest tube drainage, antibiotics, analgesics, and tetanus immunoprophylaxis. Two patients were found with injuries in the pre-cardiac region. Both died a few minutes after arrival in the accident and emergency unit.

Injuries to the upper extremities were sustained by 77 patients. Among these patients, 23 had subcutaneous pellets and 34 had open fractures (16 humeral fractures, 11 radial and ulna fractures, and 7 carpal or metacarpal fractures). Another 15 of these patients sustained avulsion injuries of the soft tissues. All the patients with subcutaneous pellets were given antibiotics, tetanus immunoprophylaxis, and analgesics. The patients with open fractures had their wounds debrided and immobilized with external fixators, plaster of paris, and in the cases of fractures, Kirchner wires.

A total of 130 injuries were seen among the 111 patients with lower limb injuries. The fractures included 31 femoral fractures, 23 tibia and fibula fractures, and 11 tarsal metatarsal fractures. Four patients sustained injuries to the knee joint. Most of the patients with open femoral fractures had wound debridement and immobilization with skeletal traction. Later, 11 of them underwent open reduction and internal fixation with intramedullary nails or plates and screws.

Eleven patients had gunshot injuries to the head. Five of these patients, whose Glasgow Coma Score at presentation were less than 5, died within 24 hours of admission.

The duration of hospitalization ranged from 1 to 25 days (mean, 14.5±1.4 days). Of the 203 patients, 17 (8.4) died during hospitalization. Six of these patients had colonic and penetrating cranio-cerebral injuries, respectively, whereas three of the patients had both injuries. Two patients had duodenal and pericardial injuries, respectively.

Conclusions

Some of these shoot high-velocity missiles that cause severe injuries with high mortality and morbidity. Predominantly young active men are involved [3-5].

In this study, 54% of the patients sustained injuries suggestive of low-velocity weapons, whereas the remaining 45.4% had injuries suggestive of high-velocity weapons. This is at variance with the findings of Katchy et al. and Therese et al [5,6], who reported a low incidence (7.7%) of high-velocity weapons in a study. Similar studies from other parts of the world also have shown an equally low incidence of high-velocity weapons [4,7-9].

Antony et al reported that Seventy-four patients presented to St Vincent’s Hospital with 103 GSW (Gun Shot Wound) [10]. The age was 31 ± 11 years. Sixty-seven patients were male. Eleven patients died. The length of hospital stay was 18 ± 9 days. Our results are similar to this literature. According to USA Emergency Department, in six months there are total 1345 GSW [11]. The ratio of age (mean age 27 years) and gender (1139 - 85% male) are similar to our results.

This study showed that mostly the lower extremities were affected. This is similar to findings of Ofiaeli [3], who attributed this phenomenon to the intent to demobilize victims by gunshot injuries. For the current study, a more likely explanation is that because most of the injuries to other body regions were immediately fatal, the patients who sustained these injuries were never brought to the hospital. On the other hand, limb injuries hardly ever are immediately fatal, a fact supported by this study. Dodge et al. [10] saw trunk, head, and neck injuries more commonly than injury to the extremities, whereas Feidler et al. [1], James et al. [12], and James and Giesecke [13] observed that the abdomen is the most common single body region injured, closely followed by the lower and the upper limbs.

Femoral fractures were the most common among the 110 patients (28%) who sustained fractures. Most of these fractures were treated with early wound debridement. Stabilizations were performed using plaster of paris casts, external fixators, or tractions followed by serial wound dressing.

Abdominal injuries were sustained by 58 patients (29.7%). The surgical management of small intestinal gunshot injury has not changed, and it poses no major problem. However, the management of colonic injuries poses challenges to surgeons throughout the world because of concern about infections after primary repairs. It has long been believed that the safest practice is to divert the fecal stream and anticipate a delayed colostomy closure [14,15].
Most of the patients with chest injury underwent hemopneumothorax and were managed with underwater seal chest tube drainage and antibiotics with excellent results. This agrees with the reports of other workers [15,16]. According to the report of Hirshberg and et al., cardiac and spinal cord injuries were seen 8% and 29% respectively [15,17]. These results are similar to ours. Their mortality rate was 24%.

The current study had a mortality rate of 8.4%, which is slightly higher than the rate quoted by Katchy et al. [5]. The highest mortality was recorded among patients with intestinal and cranio-cerebral injuries. Although limb injuries were not associated with any mortality, they were associated with serious morbidity.

In conclusion, this study affirmed the changing pattern of injuries. It is associated with high morbidity and mortality. The highest rate of morbidity was among patients with limb injuries, whereas the highest rate of mortality was among patients with intestinal and cranio-cerebral injuries. There is a great need to improve the hospital facilities in the current setting to be able to care for these kinds of emergencies. The military hospitals should be prepared to manage these injuries.

References

The prevalence of hypertension and associated risk factors in aeronautical personnel

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Abstract. Hypertension (HT) is one of the most important risk factors for cardiovascular diseases. This risk is significantly increased in the presence of additional risk factors: stress, smoking, obesity, diabetes, and hyperlipemia. Because of this HT will always be a major concern for aeromedical disposition and aircrew standards. A prospective study of the aeronautical personnel, periodically examined at the N.I.A.M., has been conducted in 2004. The hypertensive subjects have been diagnosed using the JNC 7 criteria. These subjects have been studied by clinical exam, laboratory tests, ECG, chest X-ray, ophthalmologic exam and echocardiography, during twelve months. At follow-up, a fasting blood sample was analyzed for total cholesterol, LDL, HDL, triglycerides, glucose. The stress status was evaluated by psychological examination. We studied the independent risk factors associated with HT using multiple logistic regression analysis (SPSS v.10). HT had a significant prevalence in the aeronautical personnel (19.8%). The majority of patients had primary HT. Almost half of the studied subjects had the risk group B. More than 60% of subjects had one or more associated risk factors. One third of all hypertensive subjects had white coat HT having at least one major risk factor. In multiple linear regression analysis total cholesterol, triglycerides/HDL ratio, fasting plasma glucose and professional stress were found to be significant independent determinants of HT. This study reveals a significant prevalence and an early onset of HT in the aeronautical personnel. An important etiologic factor is the specific professional stress and lifestyle. The majority of the studied subjects associated more cardiovascular risk factors. One year after the diagnosis of WCH, these subjects had an unfavorable metabolic risk profile. A well-monitored program of specific therapeutic measures to reduce cardiovascular morbidity and mortality is developing.

Key words: aeronautical personnel, hypertension, prevalence, cardiovascular risk factors

Essential, uncomplicated hypertension (HT) is not uncommon in young and middle-aged aircrew. HT is one of the most important risk factors of cardiovascular diseases (CVD). The JNC 7 Report underlines that the relationship between blood pressure (BP) and CVD risk is continuous, consistent and independent of other risk factors. Cardiovascular damage begins at 115/75 mmHg, and the higher the BP value, the greater the chance of myocardial infarction, heart failure, stroke and kidney disease. In persons over 40 years, the risk of CVD doubles with each increment of 20/10 mmHg. Individuals with a systolic BP of 120 to 139 mmHg or a diastolic BP of 80 to 89 mmHg should be considered as prehypertensive and require health - promoting lifestyle modifications to prevent CVD [1].

The risk of CVD is significantly increased in the presence of additional risk factors: stress, smoking, obesity, diabetes, and hyperlipemia [2].

Because of all these, HT will always be a major concern for aeromedical disposition and aircrew standards [3,4].

Materials and methods

We have studied a lot of 1650 subjects, aged between 25 and 55, selected from the military and civilian aeronautical personnel, medically examined periodically in 2004 at the National Institute of Aerospace Medicine, Bucharest, Romania. We selected both subjects with a new HT diagnosis and subjects with a previous HT diagnosis. The hypertensive subjects have been diagnosed using the JNC 7 criteria (Table 1).

Table 1. Classification of blood pressure (mmHg) for adults (JNC 7)

<table>
<thead>
<tr>
<th>Blood pressure</th>
<th>Systolic</th>
<th>Diastolic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt; 120</td>
<td>&lt; 80</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>120 – 139</td>
<td>80 – 89</td>
</tr>
<tr>
<td>Stage 1 hypertension</td>
<td>140 – 159</td>
<td>90 – 99</td>
</tr>
<tr>
<td>Stage 2 hypertension</td>
<td>≥ 160</td>
<td>≥ 100</td>
</tr>
</tbody>
</table>

The studied subjects were evaluated by clinical exam, laboratory tests, ECG, chest X-ray, ophthalmologic exam and echocardiography, during one year (prospective study). At follow-up, a fasting blood sample was analyzed for total cholesterol, LDL, HDL, triglycerides, glucose. The stress status was evaluated by psychological examination. We studied the independent risk factors associated with HT using multiple logistic regression analysis (SPSS v.10).

Results

The gender - depending structure of the studied lot showed a male predominance (78.3%) (Figure 1). The mean age of subjects was 43.4 ± 7.48.

Figure 1. The gender - depending structure of the studied lot
The studied lot structure according to professional activity was as follows (Table 2).

Table 2. The lot structure according to professional activity

<table>
<thead>
<tr>
<th>Professional activity</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aircrew aeronautical personnel</td>
<td>72.8</td>
</tr>
<tr>
<td>Ground aeronautical personnel</td>
<td>27.2</td>
</tr>
</tbody>
</table>

The age-depending overall prevalence of HT was significant - 19.8% (Figure 2). Although the prevalence had a higher value in the age group 45-55, it had an early onset in the studied subjects. Most of the studied subjects had primary HT (99.4%).

Identification of the risk factors and the risk group for each hypertensive subject is very important because the aeromedical certification is evaluated in the context of cardiovascular risk factors, target organ damage and associated clinical conditions [6,7].

In more than 60% of subjects, HT has been associated with one or several risk factors, more or less reversible (Table 3). The mean values of cholesterol/HDL ratio, LDL/HDL ratio and triglycerides/HDL ratio were significantly higher in hypertensive patients than the same parameters in subjects without HT (HT vs. control was 7.4 vs. 6.3 for cholesterol/HDL (p<0.01) and 4.3 vs. 3.7 for LDL/HDL (p<0.01)).

Table 3. Cardiovascular risk factors in the studied hypertensive subjects

<table>
<thead>
<tr>
<th>Cardiovascular risk factor</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>78.3</td>
</tr>
<tr>
<td>Family history of premature cardiovascular disease</td>
<td>62.4</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>72.8</td>
</tr>
<tr>
<td>Obesity</td>
<td>41.5</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>64.3</td>
</tr>
<tr>
<td>Diabetes mellitus/Altered glucose tolerance</td>
<td>18.2</td>
</tr>
<tr>
<td>Professional stress</td>
<td>77.3</td>
</tr>
</tbody>
</table>

ECG results have revealed nonspecific ST-T wave changes in 16.6% out of all hypertensive patients. Further investigations have shown asymptomatic CAD in 8.4% of patients, most of them having more associated cardiovascular risk factors. Due to technical reasons, not all these subjects could have been evaluated angiographically.

White coat (isolated office) hypertension (WCH) is a frequent condition in the aeronautical personnel, studies revealing that up to 30% of subjects first time diagnosed with HT stage 1 have normal BP values in the ambulatory BP monitoring. The clinical studies have demonstrated that this HT category has higher cardiac risk than normal BP subjects; in isolated office HT have been shown ventricular functional, arterial compliance and elasticity abnormalities similar to those present in persistent HT [8].

The results of this study have revealed that 31.4% out of all hypertensive patients had isolated office HT and the majority of these subjects (74.5%) were aged 25-35 (Figure 4).

The subjects with white-coat HT had no target organ damage, but the majority (88.3%) had at least one major cardiovascular risk factor (Figure 5).
One year after the diagnosis of WCH, these subjects had an unfavorable metabolic risk profile compared to normotensives. In univariate analysis, the following parameters were significantly associated with HT (Table 4).

<table>
<thead>
<tr>
<th>Parameter correlated with hypertension</th>
<th>r</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.394</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>BMI</td>
<td>0.403</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Smoking status</td>
<td>0.442</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>0.587</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>0.521</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Cholesterol / HDL</td>
<td>0.318</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>LDL / HDL</td>
<td>0.224</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Fasting plasma glucose</td>
<td>0.536</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Professional stress</td>
<td>0.436</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

In multiple linear regression analysis (Backward, Stepwise, Forward), after adjustment for possible confounders (such as age, sex, BMI, smoking), the following parameters were found to be significant independent determinants of HT, both in established HT and WCH lot (Table 5).

### Table 5. Independent determinants of hypertension

<table>
<thead>
<tr>
<th>Independent determinants of hypertension</th>
<th>β</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol</td>
<td>0.387</td>
<td>= 0.001</td>
</tr>
<tr>
<td>Triglycerides / HDL</td>
<td>0.252</td>
<td>= 0.005</td>
</tr>
<tr>
<td>Fasting plasma glucose</td>
<td>0.198</td>
<td>= 0.018</td>
</tr>
<tr>
<td>Professional stress</td>
<td>0.157</td>
<td>= 0.029</td>
</tr>
</tbody>
</table>

**Conclusions**

Hypertension has a significant prevalence (19.8%) and an early onset in the Romanian aeronautical personnel. The specific professional stress is significantly associated with HT. The majority of the studied hypertensive subjects associate more independent cardiovascular risk factors. One year after the diagnosis of WCH, these subjects had an unfavorable metabolic risk profile compared to normotensives. The periodical medical evaluation of aeronautical personnel is very important in early diagnosis of HT, before complications start developing. A well-monitored program of specific therapeutic measures is being developed, to reduce cardiovascular morbidity and mortality.

**References**

Scientific Review

New perspectives in urologic laparoscopy

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Abstract. Laparoscopic urologic surgery has increasingly become accepted as an alternative to open urological surgical techniques. Laparoscopy offers significant advantages over conventional open surgery. Robotic systems have been developed to assist percutaneous renal access, transperineal prostate biopsy, radio active seed delivery into prostate and TURP. Substantial progress is made in developing first-generation telesurgical systems that allow telementoring and limited active surgical assistance over great distances. Laparoscopic radical prostatectomy is perfect example of most advanced laparoscopic procedure in the field of urology. Advances in technology, instrumentations, technique and deployment of these skills have changed complete management of patients in this era. Our therapy should give harm to the patients from minimal to not at all. Hence, let us continue to move with the development in the third millennium, to provide for those who seek our consultation and our skill with a resolution of their maladies in the most humane, least disruptive manner.

Key words: laparoscopic urologic surgery, robotics, telemedicine, radical prostatectomy

During the last 25 years, probably urology was the surgical specialty branch that presented the most extraordinary technological development. The evolution has ranged from open surgery to minimally invasive surgery at dawn of the third millennium. The development has ranged from techniques to technology.

Laparoscopic urologic surgery has increasingly become accepted as an alternative to open urological surgical techniques. Recent advances in laparoscopic surgery are largely attributable to technological improvements. Advances in imaging technologies, virtual reality and telemedicine have allowed a broadening of laparoscopic applications, improved training, decreased morbidity, increased urologist acceptance and patients' interest.

Laparoscopy

Laparoscopy offers significant advantages over conventional open surgery [1]. Although initially slow to pick up, urologists now rely on them to perform an ever-increasing variety of procedures. It includes adrenalectomy, adrenal cyst excision, all kinds of nephrectomy, nephroureterectomy, treatment of stone disease, orchiopexy and orchidectomy, prostatectomy, pyeloplasty, ureteroneocystostomy, renal biopsy, urethreopexy, varicocelectomy, cystectomy and lymphadenectomy [2-7]. The major difficulty to widespread application of laparoscopy in urology has been the complexity and technical demands of urological procedures [3]. The low volume of laparoscopic urologic cases makes it difficult for surgeons to progress beyond the steep portion of this learning curve and may place patients at unacceptable risk. In the 1970's Cortessi et al in Italy first introduced laparoscopy into urology with his report of Laparoscopic exploration for the cryptorchid testicle [4]. It took almost 20 years when Schuessler et al. performed first laparoscopic pelvic lymphadenectomy in a patient with prostate cancer. The first laparoscopic nephrectomy was performed by Clayman et al. [5] whereas the credit for development of retroperitoneal space by balloon goes to Gaur.

Despite substantial progress in retroperitoneoscopy it is still considered significantly more challenging as disorientation can plague the inexperienced surgeon. With increasing experience, skill, and improved instrumentation, laparoscopy is continuing to move further into surgical domain of urology [7]. The recent developments of newer techniques like donor nephrectomy [8], laparoscopic radical prostatectomy by Guilloneau and Vallancien [9], and robotic anatomical radical prostatectomy by Menon et al. [10], have changed entire scenario and bar has been set further high to any other specialty to match the development in the field of urology. Another perfect example of ablative and reconstructive procedures beside radical prostatectomy is radical cystectomy and ileal conduit diversion [11].

Thus, laparoscopy has succeeded in providing surgical cure and less morbidity to the patients. However, laparoscopy, in order to spread more, needs better and more training courses and improved instrumentation, such as hand assistance [12].

Robotics

There is fundamental question to be asked to a technologically advanced society, which is: "Once a machine has been designed to perform a task, should man be removed from the equation?" The painful and unequivocal answer to this question is a mournful but unwavering "Perhaps yes in the long future". And so robotics is coming to an operating room to assist and to replace to an extent. Surgical robots were initially used in neurosurgery and orthopedics and have since been applied to urologic surgery. Robotic systems have
been developed to assist percutaneous renal access, transperineal prostate biopsy, radio active seed delivery into prostate and TURP [2]. In a study, use of AESOP to hold camera during laparoscopy has been found to be steadier and more effective than their human counterpart [13]. The next logical step was to implement active robotic instruments that can be controlled remotely. Laparoscopic instruments are well suited for automation given their inherent simplicity and limited degrees of freedom. ZEUS has been used to perform lymphadenectomy [14]. The versatile da VINCI system has been used to perform robotic radical prostatectomy [10,15]. To operate this robotic system the surgeon manipulates controls at a work station known as console that are directly used to a surgical robot at the operating table. These are going to be modified soon for complex robotic telesurgery.

**Telesurgery**

It is a new exciting branch of medicine incorporating the integration of multimedia, telecommunications and robotic technologies to provide surgical care at a distance. It has potential to reach to surgeon in any part of the world. Laparoscopic surgery is well suited for this purpose. Urological laparoscopic procedures are complex and learning curve is steep as there is no easy learning procedure like laparoscopic cholecystectomy, hence advanced laparoscopic skills and familiarity with laparoscopic anatomy related to urological organs for both accesses transperitoneal and retroperitoneal are essential. The steep learning curve translates into long operative times and an unacceptably high rate of complication for inexperienced laparoscopic surgeons. Through telesurgical mentoring, less experienced surgeons with basic laparoscopic skills could receive training in advanced technique from a world expert without the need for travel. The first telesurgical urologic procedure a percutaneous renal access was carried out between Baltimore and Rome in 1998 using surgical robot PAKY (Percutaneous Access to the Kidney) [16].

Substantial progress is made in developing first-generation telesurgical systems that allow telementoring and limited active surgical assistance over great distances; however, several significant technical and legal barriers must be surmounted before telesurgery can be widely accepted and incorporated into general urologic practice.

**Robotic surgery for prostate cancer**

Laparoscopic radical prostatectomy is perfect example of most advanced laparoscopic procedure in the field of urology. In a world of rapid innovation, at the dawn of the third millennium, radical prostatectomy has changed hands from laparoscopic surgeon to robotic assisted surgeon. As we all know the laparoscopic technique has provided 4 degree of movements, lack of tactile feedback, and one need to realize unique anatomical perspective, hand to eye dissociation and to operate without 3 dimensional orientations, needless to say all this led to steep learning curve, beside the cost.

To overcome these drawbacks, robotic assistance is turning out to be a big help as it has certain unique qualities, i.e. six degrees of movements like human hand, filter the tremor and provide stability beside superior visualization due to three chips camera one for each eye along with 3-D environment for better depth perception. This method has few drawbacks like lack of touch sensation, hand to eye dissociation and of course the cost factor at this stage. In robotic assisted anatomical radical prostatectomy (RAP), although it takes longer time than open surgery it has advantages of less blood loss, less pain, less analgesia and shorter hospital stay. It is also appreciated that there is no difference in terms of oncological completeness and surgical outcome in terms of providing excellent anastomosis and preservation of neurovascular bundle as in open surgery, along with superb cosmetic results. Thus, RAP has made its way in the management of localized carcinoma of the prostate, as robot facilitate the execution of complex surgical maneuvers particularly during dissection of neurovascular bundle and anastomosis, which are often considered as difficult steps. Besides it opens new ways for telementoring and telerobotic surgery. It is also likely to reduce learning curve with telesurgery in remote areas.

**Conclusions**

Advances in technology, instrumentations, technique and deployment of these skills have changed complete management of patients in this era. Our therapy should give harm to the patients from minimal to not at all. Hence, let us continue to move with the development in the third millennium, to provide for those who seek our consultation and our skill with a resolution of their maladies in the most humane, least disruptive manner.

**References**

Scientific Review

Medical aspects of decontamination as an element of the defense against nuclear, chemical and biological agents

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National Medical Coordination Center², Ministry of Health, Sofia, Bulgaria

Abstract. The article systematizes the main principles in the organization and some medical aspects of the decontamination for defense against nuclear, chemical and biological agents. Literature data were used about approaches connected with various activities for elimination and securing objects, treated with nuclear, chemical and biological agents. The experience of military medical experts from the participation of Bulgarian contingents in ISAF was also taken in account.

Key words: decontamination, weapons for mass destruction, casualties

Use of weapons for mass destruction (WMD) most often includes dissemination of pathogens into the environment. In this respect, contamination after the use of nuclear, chemical, and biological (NCB) weapons is defined as the deposition of radioactive materials, microorganisms, chemicals and toxic substances in the water, air, soil, body surfaces and other objects at levels that make impossible their use without health hazards. At present, there are many methods and means available for mass decontamination of large areas or for specific contaminated objects.

Decontamination is the process of removal or minimization to safe levels of the deposited NCB agents and the subsequent elimination (reduction) of the risk and rendering the objects safe. Decontamination blocks the routes for penetration of harmful agents into the organism. Therefore, the decontamination measures are an essential component in the overall disease prevention strategy after an application of WMD and in this connection, the Army Medical Service bears significant responsibility.

These issues are also timely because of the potential danger for NCB agent use by terrorist groups.

Types of agents

Each group of WMD includes two or more subgroups of harmful 'noxious'. Biological weapons include bacteria in spore and vegetative stages; also viruses and toxins. Chemical agents are divided in phosphoroorganic (nerve agents), blistering (vesicants), choking, systemic, etc [1]. Nuclear agents are the radioactive products obtained in nuclear explosions and radioactive waste.

A great variety and diversity of active warfare agents is found. From a practical point of view, most important are those agent properties that influence their persistence. For the survival of microorganisms in the environment, their structural, biochemical, and ecological properties are of primary importance; for the chemical agents, the dissemination and deposition on the body are influenced by chemical and physicochemical properties; for the radioactive substances, most important are their physical properties.

A great variety of objects can be contaminated; therefore they may need appropriate treatment. Among them, the most conspicuous is the group of victims of NCB attack, who need to be accepted for treatment. Therefore, there are numerous conditions and medical branches that should be taken into account during the time of implementation of decontamination procedures.

Classification

In order to systematize the knowledge in this field, several classifications have been worked out for the purposes of practical decontamination. The main classification has as a criterion the type of contaminant. According to the type, the action is divided in chemical decontamination, biological decontamination (corresponding to disinfection, respective to sterilization) and radiological decontamination. This classification is used by all bodies that have responsibility for decontamination. It gives the landmarks for choice of methods and means and therefore it is considered to be of methodological character. However, the direct application of means for decontamination can be carried out only after identification of the 'noxious'. Therefore, in some cases (e.g., early stages of NCB action, before identification), the classification according to the above criterion may not be applicable.

In a situation of WMD use and mass influx of victims in treatment facilities, the medical service should organize the decontamination according to a classification which includes as categories the composition and objects to be decontaminated.
• **Personal decontamination** – decontamination of oneself or mutual decontamination

• **Casualty decontamination** – decontamination of casualties

• **Personnel decontamination** – decontamination of non-casualties

• **Mechanical (object) decontamination** – decontamination of equipment, provisions and environment [2,3].

**Methods and means of decontamination**

The mechanical and physical methods apply mostly for radiological decontamination and include removal of clothes off the body and washing with a water spray. This method achieves up to 95% efficiency.

The above two methods are important for chemical and biological decontamination, but their primary use is for the chemical agents. With respect to the phosphoroorganic and blistering chemical warfare agents (CWA) there are chemical substances used for decontamination, but there is no universal decontaminant found so far for this group. The criteria for the ideal decontaminant are at least 12, and most problems for the studied substances are connected to skin irritation, toxicity, ineffectiveness, or high cost [2]. Without disregard to the biomedical aspects of the problem, from a military medical point of view, the financial criterion is very important, because the issue is mass decontamination and maintenance (updating) of adequate stockpile.

**Recommended characteristics of skin decontaminants**

<table>
<thead>
<tr>
<th>Characteristics</th>
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<tbody>
<tr>
<td>Neutralizes all chemical and biological agents</td>
</tr>
<tr>
<td>Non-toxic and non-corrosive</td>
</tr>
<tr>
<td>Applied easily by hand</td>
</tr>
<tr>
<td>Readily available</td>
</tr>
<tr>
<td>Acts rapidly</td>
</tr>
<tr>
<td>Produces no toxic end products</td>
</tr>
<tr>
<td>Stable in long-term storage</td>
</tr>
<tr>
<td>Affordable</td>
</tr>
<tr>
<td>Does not enhance percutaneous agent adsorption</td>
</tr>
<tr>
<td>Nonirritating</td>
</tr>
<tr>
<td>Hypoallergenic</td>
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<tr>
<td>Easily disposed of</td>
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</table>

The main decontamination preparation, used at present in the army is calcium hypochlorite in solutions of 0.5% for exposed body areas (without wounds) and 5% for objects, clothes, etc. For chemical agents, its action causes neutralization (destruction) of phosphorus group (PG) containing agents or oxidation of sulfhydriile group containing agents, e.g. Vx gases. However 15 – 20 minutes of contact time is necessary for this chemical reaction [4,5]. With the biological agents, this substance achieves bactericidal and virocidal effects, while sporicidal effects are uncertain in normal concentrations. After identification of microorganisms, the possible choice of disinfectants is wider. Adsorbents are also used as means for decontamination. They are suitable for radiological, and, to a lesser extent, for chemical decontamination. In the US army, this is the personal decontamination kit M291. The numerous efforts to find universal decontaminant have not met with a complete success so far.

**Aims and priorities in decontamination of combined casualties**

From a military medical point of view, the decontamination efforts in cases that combine action of conventional weapons and WMD are directed primarily towards evacuation and hospitalization of casualties. This is the second of the categories, listed above. For the other three groups, the responsibilities lie mainly with the command of the army divisions, while the direct implementation is a responsibility of the divisions for NCB defense. The rest of the present report concerns the general principles and characteristics of decontamination that is carried out by the army medical service.

The main aims of decontamination are the following:

1. Removal of the active agent from skin and clothing of casualties thereby reducing its action on the human organism.

2. Preventing the secondary exposure of rescue teams and medical personnel

3. Ensuring the casualties’ psychological stability [6].

All these aims contribute to reducing the possibility for dissemination of the agent outside the limited area. Special attention should be given to the decontamination approaches in the medical service facilities and in the inflow of patients to the treatment centers. All casualties arriving from the incident zone are considered as contaminated regardless of issuance of certificates at previous stages. At the same time, the main principle for mass treatment of casualties remains in force: “more care for more patients” [7].

In Role 1 level, limited decontamination is carried out, consisting of clothes and personal safety equipment removal, removal of harmful agents from exposed skin areas, and application of the respective antidotes. These procedures remove up to 95% of the harmful agent. The contaminated clothes are collected by a prescribed procedure and undergo a special treatment, and the incoming patients are provided with clothing from the exchange pool. Risk of secondary exposure exists for the teams working in the reception and sorting sections. Therefore, measures for full decontamination should be planned and implemented as soon as possible for this category of personnel.

In the next levels Role 2 and Role 3 there is the necessary equipment for mass decontamination, including spray washing with use of soap, detergents and overall disinfection of the body. For this purpose, a facility for sanitary treatment is built and maintained.
With respect to the different group, the following is observed: for those, needing immediate treatment (T1), the emergency rescue and life-saving surgical interventions and diagnostic and therapeutic procedures are carried out after a partial sanitary treatment and decontamination of individual body surfaces. Full decontamination is postponed until recovery.

Delayed treatment (T2) and Minimal treatment (T3) groups, in which medical intervention can be postponed without life-threatening danger, undergo full decontamination immediately after arrival in the treatment facility. In the fourth group – Expectant treatment (T4), treatment will be impeded and will be relatively limited due to the numerous heavy wounds, bad injuries and general ill health. From an epidemiological point of view, this group is considered as a high risk for the hospital personnel.

At all levels of medical care medical personnel should be properly equipped with personal protective equipment (PPE). When decontamination of contaminated chemical and radiological casualties is carried out nonencapsulated chemical-resistant suit, gloves and boots with a full-face air purifier cartridge mask (Level C PPE) are suitable. Standard work clothes, latex gloves, eye splash protection and N-95 respiratory mask (Level D PPE) are appropriate for decontamination of contaminated biological casualties [5,8,9].

An important measure for prevention of new infections is the decontamination of vehicles, used for evacuation.

Wound decontamination

Wound decontamination presents a specific problem for the medical service. Of the whole spectrum of chemical agents, only two types, the vesicants and the nerve agents, might present a hazard from wound contamination. Of the biological agents, such hazard exists only with microorganism, causing skin infections and some from the transmissive group. Of the radiological agents, only highly energetic gamma emitters present any immediate hazard in wound contamination.

In methodological aspect, the most appropriate antiseptics for removal of microorganisms on wounds are chlorhexidines, higher alcohols and iodophores. Chlorhexidines are suitable for an overall body disinfection. However, one has to account for the fact that these are mild disinfectants and do not cover the whole spectrum of possible biological agents, e.g. the spore forms. Wound treatment necessarily includes removal of bandages and a subsequent treatment with an antiseptic preparation.

Decontamination to prevent a secondary aerosol

Biological agents in pulverized state can cause a secondary aerosolization. Upon biological contamination, a greater hazard exists when the microorganisms are highly resistant (e.g., the anthrax bacillus, the smallpox virus), penetrate through many routes and have poly-organic localization (plague, tularemia). In order for decontamination to be effective in the presence of such risks, additional measures are undertaken, such as multiple periodic treatments of surfaces and objects in the hospital facilities, mostly with sporicidal agents (aldehydes, phenols). An additional method is use of UV light inside the facilities. Chemical agents do not present a problem with respect to secondary aerosolization. For the radiological agents, after their deposition, there is a possibility for a new pulverization in the environment and migration of radionuclides.

Planning

Decontamination is an element of the suite of hygienic and counter-epidemic activities and planning in this direction should be coordinated with the general principles of medical service and with the specific tasks of the unit (mission of the hospital). In planning at different levels come into consideration: work volume, structures, teams and material resources needed for implementation of the required measures; the organization for achievement of the end goals; supplies and services required; control for ensuring correspondence between plans and practical activities for follow up of the efficiency of the decontamination that has been carried out; staff units and personnel for decontamination of the medical personnel. The plans are supplemented with scenarios and workouts for the principal activities, necessary preparations and equipment in conditions of maximal load for the unit [6,11].

Training

In addition to specialized structures in the NCB defense units, medical personnel also should maintain readiness for decontamination. The main groups who train for decontamination are teams responsible for work in the sorting and reception facilities, nurses, laboratory technicians, medical assistants. Training of individual categories should be carried out according to appropriately adapted programs. Operators should learn the technology of preparation, working solutions and methods of treatment of individual objects. Commanding staff is additionally acquainted with the persistency of the various agents into the environment, control on decontamination, side effects, organization of decontamination activities, and other topics. The principal issues in decontamination of personnel and persons needing medical help have been trained in the Bulgarian Army units in various conditions, including the Bulgarian NCB defense unit participating in ISAF.

Conclusions

1. Decontamination after the use of chemical and biological weapons is excessively difficult task and requires engagement of manpower and material resources. Even with correct planning and training, the mass implementation of decontamination procedures will involve expenditure of significant resources.

2. After the use of radiological agents, decontamination can be postponed for a longer period than for other WMD.

3. The triage priorities are imperative also during decontamination. In some cases, especially in the front ranks of the medical service, with the aim for carrying out life saving manipulations, decontamination of some conventional weapons and WMD casualties is implemented in a very limited scale.
4. On the basis of the accepted conception for operations in military medical institutions, it is necessary to enhance and optimize the instructions pertaining to decontamination in conditions of reception of WMD casualties.

References


Case Report

A case of pulmonary hamartoma diagnosed by bronchoscopic biopsy as a part of etiologic study of bronchiectasis

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Abstract. A 20-year-old man came to pulmonary department with a history of left chest pain, cough and purulent sputum production since his childhood. He expressed that he had pulmonary tuberculosis when he was 4 years old. On physical examination there was decreased expansion of left hemithorax, with decreased breath sounds. Chest roentgenogram showed shift of mediastinum to the left. Computerized tomography (CT) showed decreased volume and diffuse cystic bronchiectasis of the left lung. There was also a solid lobulated tumor (4.5x2.5 cm) extending from left hilum to the left lower lobe on CT. Flexible bronchoscopy revealed a large polypoid mass originated from lateral wall of left main bronchus which occluded almost all lower lobe bronchus. Bronchoscopic biopsy revealed the diagnosis of hamartoma. Thoracotomy was advised to the patient but he refused. Because most hamartomas are located peripherally in the lung parenchyma, we wanted to present this endobronchial hamartoma which is encountered rarely in a young patient as a part of etiologic study of bronchiectasis.

Key words: pulmonary hamartoma, bronchiectasis, endobronchial hamartoma

Pulmonary hamartomas are uncommon benign tumors with a population incidence of 0.25%, and only 10-20% of it grows endobronchially and cause symptoms. It is frequently seen in older ages but rarely seen before 30 years old [1].

Bronchiectasis is an uncommon disease with the potential to cause devastating illness, including repeated respiratory infections requiring antibiotics, disabling productive cough, shortness of breath, and occasional hemoptysis [2]. Although 50% of cases of bronchiectasis are still considered idiopathic, study of potential causes may have important implications for the management of this disease [3].

Case

20 years old male hospitalized in our clinic with left side pain and a complaint of cough which was present from childhood. Personal history revealed that he had pulmonary tuberculosis when he was 4 years old. Family history had not any characteristic features. On physical examination, trachea was minimally deviated to the left, left hemithorax participated in respiration less, and on the left side there were widespread middle cracks and polyphonic ronchus anteriorly and posteriorly. Routine biochemistry was normal. X-ray of the chest showed that mediastinum and trachea had shifted to the left. There was a volume decrease at the left lung and fibrotic, bronchiectatic changes were present. Left hemi-diaphragm had moved to the up (Fig 1).

On her respiratory function tests, FEV1 was 2.74 (71%), FVC was 3.20 (71%) and FEV1 / FVC was 86 (100%). Arterial blood gases were normal. Sputum staining and culture results were negative. Her thorax CT showed that heart and mediastinal structures were shifted to the left. There were cystic bronchiectatic changes in all segments of the left lung and the volume was clearly decreased. A tissue mass of 4.5x2.5 cm starting from hilus of the left lung was extending inferiorly and the margins of the mass were lobulated (Fig 2a, 2b).

We performed fiberoptic bronchoscopy. A polypoid lesion attached to the mucosa with thin stalk at the lateral wall of left main bronchus was observed. Left inferior lob entrance was closed with endobronchial lesion. Biopsy was taken from the lesion at left main bronchus entrance. Bronchial
biopsy revealed that cartilage tissue was seen in lamina propria in the section of bronchial mucosa, and these findings were consistent with hamartoma (Fig 3).

Fig 3. Histopathological appearance of the specimen

Discussion

Bronchiectasis is defined pathologically as the abnormal, irreversible dilatation of diseased bronchi [4]. Since the follow up and the treatment choices can be affected, it’s suggested that bronchiectasis should be evaluated for the etiology [5]. In the developing countries like our country, the respiratory system infections at childhood and bronchial obstruction are the main cause for the bronchiectasis [6,7]. In our case there is history of tuberculosis and this may be the etiology of the bronchiectasis. In advanced research with fiberoptic bronchoscopy we found that there is another reason of bronchiectasis, which was endobronchial hamartoma causing obstruction.

Pulmonary hamartoma is a kind of mesenchimal tumor which takes origin from undifferentiated multipotential cells located in the connective tissue of bronchial wall. Pulmonary hamartomas are divided into two groups as intrapulmonary and endobronchial. Intrapulmonary hamartomas which placed periferally are frequently asymptomatic. They are found incidentally with routine lung radiography. Endobronchial hamartomas are frequently seen at the proximal side of bronchial tree and they usually have stalk. Bronchoscopy is useful for diagnosis and treatment. Many endobronchial hamartomas are symptomatic related to the bronchial obstruction. Bronchiectasis and chronic pneumonia can accompany to hamartoma [8].

Although the hamartomas are benign tumors; they can cause irreversible damages in lungs as we see in our case. We think that the bronchiectasis related to tuberculosis, frequent infection and inflammatory lung disease caused the development of bronchial hamartoma.

For the treatment of bronchiectasis and endobronchial hamartoma, surgery was decided but patient refused the surgery.

References

Case Report

Breast Paget disease: clinical, histopathological and immunohistochemical aspects

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Abstract. We present some hypothesis regarding the pathogenesis of mammary Paget disease, starting from the realities encountered in one of our patients. The case aspects are discussed, with data of a 1 year follow-up. Some up-to-date information from literature is presented and personal hypothesis regarding the relationship between breast Paget disease and the underlying breast adenocarcinoma.

Key words: Paget disease of the breast, immunohistochemistry, pathology

The aim of this paper is to discuss some actual hypothesis concerning breast Paget disease and to present our opinion on this matter. It is true that Paget disease is still an important issue in women health, with a lethal outcome when left untreated or when the diagnosis is too late. Because of benign clinical aspect during most of its evolution, Paget disease of the breast is one of the great masqueraders, posing a great demand on general practitioners and specialists to having the right diagnosis in proper time, so giving good survival chances to the patient.

The idea of this paper comes from one of our patients, a female that was diagnosed in Dermatology Clinic after a long journey in different outpatient clinics. A good collaboration with specialists from several clinics of our hospital conducted to a good outcome for this particular patient.

Case

Our patient is a 57 years old female that was admitted in Dermatology Clinic for erythematous plaque, slightly squamous, located on the right areola (Fig 1). The patient does not have any subjective symptoms and no secretion. She undergone repeatedly medical check-ups in the last 12 months and treated with progesterone, estrogenic and antifungal preparations.

On the admittance, we find an erythematous edematous plaque, located on right areola, with clear, regular borders, shiny surface, scattered covered with fine scales, with no secretion. The laboratory examination was with normal values. The first glance diagnosis was that of breast Paget disease. Because of known association of Paget disease of the breast with intraductal adenocarcinoma, we requested an ultrasound examination, and a gynecological opinion regarding the treatment opportunities.

Ultrasound showed a retroareolarly located, reticulated, hypodense spicular mass, with diffuse borders, apparently adherent to surrounding tissue. The tumor had a pseudo-liquid core and an arterial-like tumoral vasculature spectrogram (PI = 1.4; RI = 0.7; PSV = 25 cm/sec; EDV = 6.5 cm/sec) (Fig 2).

The gynecologist recommended a classical surgical intervention, after a punch-biopsy. The biopsy showed Paget cells in the epidermis, near the epidermal-dermal border, associated with a sparse inflammatory infiltrate in the papillary dermis.

The surgical intervention was a classical one, with radical mastectomy and axillary lymphadenectomy, followed by breast reconstruction in second time.

The postoperative pathology results confirmed the first diagnosis, and showed the association of an in situ intraductal adenocarcinoma in the great ducts just below the areola. In the epidermis, there were PAS + Paget cells, just near the basal membrane. On immunohistochemistry, it was find a positive staining for smooth muscle actin in myoepithelial cells. There were two reactive nodes, but with no metastases on examined sections (Fig 3-5).
The actual hypothesis is that breast Paget disease is the superficial manifestation of an underlying breast malignancy.

Its first description belongs to Sir James Paget, in 1874, as a chronic eczematous areolar and periareolar skin disorder. It was considered the extension of an intraductal breast carcinoma. In 1881 George Thin published the first pathological description. In 1889 (Crocker) the first extramammary (penis gland) case and in 1901 (Dubrueuhl) the first vulvar case were published [1-3].

Nowadays, it is agreed that Paget disease is mainly a disorder of female patients, the rare published cases in males being rather anecdotic. Usually it appears as a chronic eczematous erythema of the areolar and periareolar skin.

The disease involving other areas of the body (such as penis, vulva) is similar, the pathological aspects being identical — with area particularities that implies a difference in pathogenesis and histogenesis.

Worldwide, the real incidence is not known; studies done in US showed that 1-4% of all breast cancers in female are associated with Paget disease, either of the nipple, areola, or adjacent skin. Some authors consider that 100% of breast Paget disease is associated with an underlying breast malignancy (10% in situ and 90% infiltrating). Isolated cases of Paget disease in over-countered nipples or ectopic breast tissue were reported.

The disease is encountered almost entirely on females, the male/female ratio being 1/100. The age of onset is between 24 and 84, with a median age of 53-59. In females patients with associated breast adenocarcinoma the median age is higher with 5-10 years then in general population. In male patients, the onset age is between 48 and 80, with a predominance of 5 and 6 decades. Fifty percent of Paget disease patients that associate a palpable breast tumor have axillary metastasis. From the patients with axillary lymphadenopathy, 2/3 also presents a palpable breast tumor. 30% of the patients with Paget disease and without palpable tumors may in time develop an invasive breast carcinoma. 20% of the patients with Paget disease and with no palpable tumor do associate an in situ breast carcinoma [4].

The survival is correlated with presence/absence of the palpable breast tumor. The overall rate of survival is 38-40% at 5 years and 22-33% at 10 years in patients with associated breast tumor. The death rate in patients with metastatic breast carcinoma and Paget disease is 61.3%, with a cumulative rate at 10 years of 33%. The survival rate in patients with Paget disease and no associated breast malignancy is 92-94% at 5 years and 82-91% at 10 years [4].

We must notice that the prognosis is very much affected by the presence of an underlying breast malignancy, fact that allow us to consider that the two breast diseases — the Paget disease and adenocarcinoma — are separate entities that coexist in a majority of cases, but one does not imply the presence of another and so they are not strictly linked [5].

The Paget disease pathogenesis is still a subject of debate. There are two dominant hypotheses: the epidermotrop hypothesis which states that Paget cells originate from ductal epithelium, from were they migrate towards epidermis; the alternative theory, considering the existence of malignant keratinocytes originated from areolar epidermis.

Both theories have strong and weak points, both being strongly supported by some authors and denied by others. In few words, the difference between those theories is that that in the first case the Paget disease is only an extension to the skin of the underlying breast cancer, and in the second case, there are two different diseases that coexist in the same patients in the same time [3,6].

The most widely accepted idea today is that the case is that of an intraductal carcinoma of the breast, that backward extends in the neighborhood epidermis by the way of breast ducts. That implies that Paget cells are derived from luminal ductal epithelial cells and that they share microscopic aspects of glandular epithelial cell. In evolution, Paget cells infiltrate and proliferate in epidermis, just near the border with dermis, conducting to a thickening of nipple and surrounding skin. The dermatitis is such explained by the epidermal-tropism of malignant cells that will promote the ductal malignant cells spreading through the breast ducts to the skin [7].

The weak point of this hypothesis is that until today there are no published cases (to our knowledge) that will demonstrate...
the presence of Paget-like cells in the lactiferous ducts of a patient with no apparent Paget disease, and not even in advanced cases of Paget disease no identical Paget cells were demonstrated in the ducts of breast at some distance from the dermatitis [8].

**Pathology**

In our case, the patient does present the association of a Paget disease with an in situ breast carcinoma. The immunohistochemical aspects suggest a different origin of the two malignancies. There are two questions that need to be answered – is really the case of two different diseases coexisting in the same patient, or is the case of a glandular-originated cell that migrates and differentiated in the epidermis, or is the case of a malignant epithelial cell evolving in deep tissue?

The immunohistochemical properties are solid arguments for the coexistence of two different diseases with no direct relationship. The Paget cells discovered in the specimens from our patient were great size malignant cells, with pale, vacuolated cytoplasm, great, polymorph, hyper-chromatic nuclei, with significant nucleoli and relatively frequent mitosis.

Paget cells express cellular markers similar to those of associated mammary carcinoma: glandular epithelial cellular markers (small molecular weight cytokines) and tumoral markers (characteristic for breast ductal carcinoma malignant cells): CEA (carcinoembriogenic antigen), AC 15-3 (milk fat globule protein), EMA (epithelial membrane antigen), GCDFP-15 (gross cystic disease fluid protein); oncogenes (p53, c-erb, B-2) [16, 25].

The immunohistochemical aspects are similar to those of glandular epithelial cells from eccrine and apocrine glands. The CK 7 (cytokeratin 7) is a specific marker with almost 100% sensibility for breast Paget disease, and CK 20 (cytokeratin 20) is negative in breast Paget disease cells and positive in 30% of extra-mammarian Paget diseases.

Paget cells are specifically defined by mobility factor heregulin, which acts on Her2/neu receptor. This mobility factor favors migration, extension and infiltration of malignant cells in the neighborhood skin; normal epidermal keratinocytes also produces heregulin [9].

Furthermore, Paget cells possess Her2/neu receptors and Her3 and Her4 co-receptors, which are responsible for chemotaxis of ductal carcinomatous cells [10]. Pathology is the only diagnostic mean that allows radical intervention – radical mastectomy. There are common aspects described, such as hyperkeratosis, parakeratosis, akantosis and an infiltration with malignant round-oval cells that infiltrate all epidermis layers, with pale cytoplasm and big nuclei, with voluminous nucleoli. Occasionally, mitosis may be encountered. Paget cells are either isolated or grouped in nests [9,11].

Paget cells are PAS positive for neutral mucopolysaccharides, positive on alcin blue stain for acid mucopolysaccharides (sialomucin). Occasionally, a DOPA negative melanin-like pigment may be present. On haematoxyline and eosin staining, the absence of intercellular bridges is evident [9].

Basal epidermal cells are compressed between Paget cells and papillary derm. Paget cells are negative for estrogen and progesterone receptors, even if they coexist with an underlying breast cancer with positive receptors of this type. They are also negative for breast glandular markers (lysozime, lactalbumine etc).

Several histology variants of Paget cells are mentioned in literature: adenocarcinomatous (columnar), fusiform (angular cells, elongated, grouped in nests or compact masses), achantolitic (overlap with anaplastic variant, with marked achantolysis), anaplastic (similar with those from Bowen disease, pleomorphic cells with numerous nuclei, frequent mitosis, grouped in nests on the entire thickness of the epidermis, which is highly distorted), pigmented (several cases communicated in male patients, with DOPA negative cells filled with melanin from adjacent cells) [9]. In more advanced lesions exists an active periphery, with clusters of great cells with numerous mitosis. In ulcerated lesions, epidermis is completely replaced by malignant cells; dermis also may be invaded and frequently malignant cells are present around hair follicles and sweat glands. In the dermis exists a dense infiltrate with lymphocytes, histiocytes and plasmocytes, occasionally also with eosinophils.

A generous biopsy is recommended, one which to contain also glandular tissue to detect an eventual breast carcinoma [5,12].

Immunohistochemistry is today a very useful tool for the clinician, because of high degree of specificity of the stains. For Paget disease must be taken into consideration, some of them being useful for differential diagnosis also:

- **small weight keratin**
- **erb B-2**
- **CEA – negative in surrounding keratinocytes and in Bowen disease**
- **S-100 protein – positive in melanoma, negative in Paget disease**
- **HMB-45 – positive in melanoma, negative in Paget disease**

**Clinical aspects**

Clinical manifestations of Paget disease of the breast are eczematous cutaneous associated with erythema, scales, itching, burning sensation, ulceration with sero-hemorrhagic discharge, bleeding [13,14].

Early signs and symptoms of breast Paget disease are: excoriations secondary to pruritus and recurrence of small vesicles in the lesional skin. In time, erythematous squamous plaques develop around areola, covered with thick crusts. Plaques’ borders are very sharp, thickened [16]. Often may be encountered retractions of the areola, with bloody-serous discharge. The diameter of lesions varies from 3 mm and 15 cm, with a median value of 2.8 cm. Usually areolar alterations are associated (in 98% of cases) with ductal breast malignancies (in situ or infiltrative) [15,16].

The rule is one side ailment, but with the possibility of exceptions [17].
A 4 stage classification is used nowadays in assessing the prognosis of breast Paget disease patients (Table 1) [18].

Table 1. Classification of Paget disease of the breast

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
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<tr>
<td>0</td>
<td>Lesion limited to skin, with no in situ carcinoma of the breast.</td>
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<tr>
<td>1</td>
<td>Skin lesion associated with in situ ductal carcinoma, just under areola.</td>
</tr>
<tr>
<td>2</td>
<td>Skin lesion associated with extensive in situ carcinoma.</td>
</tr>
<tr>
<td>3</td>
<td>Skin lesion associated with invasive breast cancer.</td>
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</table>

On cytology (Papanicolaou, Giemsa) Paget cells are present, as great cells, with an increased nuclear/cytoplasm ratio, occasionally with intracytoplasmatic vacuole, diagnostic aspect for Paget cells [19].

Very useful are immunohistochemical stains for epithelial mucin, CEA and SMA (smooth muscle actin).

**Differential diagnosis**

The differential diagnosis should be done extensively, because of numerous diseases that may mimic breast Paget disease (Table 2).

Table 2. Differential diagnosis

<table>
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<tr>
<td>Intuitive contact dermatitis</td>
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<tr>
<td>Drug eruptions</td>
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<tr>
<td>Areolar ductal carcinoma</td>
</tr>
<tr>
<td>Areolar erosive adenomatosis</td>
</tr>
<tr>
<td>In situ malignant melanoma</td>
</tr>
<tr>
<td>Bowen disease</td>
</tr>
<tr>
<td>Toker benign hyperplasia</td>
</tr>
<tr>
<td>Localized cutaneous amyloidosis</td>
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<tr>
<td>Breast carcinoma with skin extension</td>
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The diagnosis is supported by imagistic procedures [20]:

- **Radiodiagnosis** [15,21]:
  - Microcalcification just under areola (the evaluation of subjacent breast adenocarcinoma)
  - Architectural distortions
  - Nipple and areolar thickening (edema)
  - Nipple alterations
- **Ultrasound** [22]:
  - Tumoral aspect under nipple
  - Malignant vascularization
  - Tumoral extension
  - Glandular aspect

The only 100% sure diagnosis is the pathology one, comprising cytology and immunohistochemistry. Toker hyperplasia is a benign disease with well defined pathology picture. Great clear cells, with no epithelial mucin, negative for S-100 and CEA are present. It is not associated with breast malignancy.

On EM, Paget cells are epithelial cells, with the absence of dense cytokeratin granules, numerous free ribosome, lysosomes, great mitochondria, prominent endoplasmic reticulum, tonofilaments, Golgi corpuscles, membranous microvilli and rare desmosomes. Those cells do not have a contact with lamina densa.

Included in the pathology report must be the existence or non-existence of an associated breast carcinoma, with distended ducts, pleomorphic cells with hyperchromatic nuclei and increased nucleus/cytoplasm ratio, often with nuclear cribriform pattern.

**Treatment alternatives**

The treatment of breast Paget disease is related to the coexistence of the underlining breast carcinoma. In cases with palpable breast cancer, the only choice is considered to be radical mastectomy (either classic or modified) with axillary node excision. When there is no palpable tumor one may try conservative interventions, with or without node excision, such as: nipple excision, conical-shape excision, drug treatment (with tamoxifen), radiotherapy [23,24]. Studies shows in those cases recurrences after a median period of 4.6 years. The presence of metastases, either of the Paget disease, or of the breast cancer, modifies the prognosis and such the first intention surgical option [25].

The prognosis is related to the coexistence of other ailments, but overall is similar to that of other breast cancers. Some studies presents a small number of patients with breast Paget disease with no palpable breast tumor and with negative mammography, that were conservative treated (nipple excision with large excision of the underlying gland), that were free of recurrences after 10 years. In most of the patients treated by local excision, with or without other treatment methods, there were recurrences in 11.4%. Some rare cases of recurrences in patients that were treated per primam with wide enough excision were also presented. The protocol for patients with breast palpable tumor implies the first use of radiotherapy, either alone or associated with wide surgical excision. After 7.5 years the median recurrences rate was 1.5%. All those studies support the opinion that the only right choice for the proven Paget disease of the breast, associated with breast carcinoma, is the radical mastectomy, either classical or modified procedures [26,27].

**Conclusions**

In our case, pathology results suggest that could be the situation of two different diseases, parallel evolving in the same patient: breast Paget disease and in situ adenocarcinoma of the breast. Despite of early stage of breast carcinoma (Stage I), radical mastectomy associated with axillary lymphadenectomy is recommended, because it appears to be associated with better prognosis. Postoperative, we recommended association of radiotherapy and regular medical check-ups for the next 5 years.

In conclusion, Paget disease of the breast is a disease characterized by parallel manifestations on the skin and inside breast gland, which seems not to be compulsory, but associated in a very important percent, easy and cheap to be diagnosed. The election treatment nowadays seems to be radical mastectomy, followed in advanced cases by chemotherapy and radiotherapy, with minimum 5 years follow-up. Pathology study of the operative specimen is compulsory, in order to detect an underlying breast carcinoma.
References

**Case Report**

**V-Y island flap to cover a defect in the perianal region from perianal Paget’s disease: case report**

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Abstract. Perianal Paget’s disease (PPD) is a rare entity which requires surgery with complete excision of the lesion leading a large skin defect in the perianal region. V-Y Island flap technique is a feasible way to cover the large skin defect in perianal region. Care must be taken to the base of the graft which should be placed in a good shape into the anal canal. Perianal Paget’s disease was diagnosed in two patients after biopsy and they were treated with entire surgical excision. Both are alive at present. No important complication was experienced and there was no need to ostomy. No recurrent disease was experienced in a year follow up. Anal canal function and life quality of the patients are also in good condition. Despite of the fact that the treatment after wide local excision is challenging, we used V-Y island flap which is a simple and helpful surgical procedure to cover the wide skin defect in the lesion located around the perianal region.

Key words: perianal diseases, Paget’s disease, V-Y flaps

Perianal Paget’s Disease (PPD) is a rare condition which engages the whole circumference in perianal region. Paget’s disease is pathognomonic with Paget’s cells that contain pale-staining cytoplasm and large nucleus located peripherally [1,2]. These cells come from glandular basis. The lesion reveals a well-demarcated erythematous plaques which is often pruritic and eczematous. Paget’s disease in perianal region is frequently (about 40%) together with invasive carcinoma of the region [2-4]. Generally Paget’s disease in perianal region is secondary to prostate or colorectal cancers or transitional cell cancer [5]. On the other hand primary PPD has been appeared from intra-epidermal cells of the apocrine gland ducts (or from pluripotent keratinocyte stem cells) [6,9]. The potentially aggressive characteristics of invasive Paget’s disease has assessed distant metastasis; although, minimally invasive Paget’s disease with invasion less than 1mm deeper is similar to non-invasive Paget’s disease [6-8]. Then accepted treatment is wide local excision [2-5]. Significant rate of recurrence is the other challenging problem [4,5]. Several techniques have been described to cover the large perianal defect that can not be easily closed primarily [1,2,4,5].

**Case**

In the last 4 years, 2 patients with perianal Paget’s disease were evaluated for surgery after preoperative diagnostic biopsy. Both had entire physical and ano-rectal exam. Then flexible sigmoidoscopy and Guiac stool test were done for each. The day before surgery bowel cleaning utilized with fleet phospho-soda and fleet enema together, and prophylactic antimicrobial agent with ornidazole 2x500 mg per oral. (Nidazol®) were employed and continued 5 days postoperatively. Patients were instructed to ingest merely liquids the day before surgery. Two patients were taken to the operating room to perform wide local excision with V-Y flaps covering.

**Operational technique**

Under epidural anesthesia, patients were laid down on the table in prone Jack-Knife position. Rectum was cleaned by 10% Povidon- Iodine solution. Lesion (Fig 1) exposed clearly by using Lone-Star perianal retractor to perform multiple biopsies for frozen section and they all were 1cm from the edge of the lesion in all four quadrants of the perineum as suggested in the paper by Beck and Fazio [10].

**Fig 1.** The perianal Paget’s disease around the perianal region

At the dentate line biopsies were taken under care. Excision of the lesion was progressed deeper to the subcutaneous tissue until negative margins were confirmed by frozen section. A V-Y island flap was prepared on side of the perianal region with size matching to the defect (Fig 2).

**Fig 2.** A V-Y island flap on perianal region is displayed

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The dissection for the flap was made deep down to the subcutaneous fat and continued till the island of the flap reached to the dentate line without tension. After the preparation of the inner side of the flap, it was slid to the dentate line and sutured the mucosa of the anal canal all around by using 3/0 vicryl which was used to suture the rest of the flap. The completed flap was in Y shape (Fig 3). Drain was not used in routine.

Fig 3. A V-Y Flap slid in to the anal canal and sutured to the anal mucosa of the anal canal, Note Y shape at completion

Postoperative period
Patients were started on elemental diet and clear liquid diet was advanced with return of bowel function, if necessary, Lomotil for 5 days were also engaged to prevent defecation. was advanced with return of bowel function, if necessary, to prevent defecation. There was no complication disturbing the patients’ life quality.

Results
Graft survival was full in both patients. Dressing was kept 3-4 days postoperatively. Sit baths were prescribed after first defecation. The wound completely healed after 3 weeks using simple water baths, soap-water baths and dry dressing after defecation. After 12 weeks anal function was evaluated using fecal incontinence severity index (FISI) and the SF-36, quality of life questionnaire was performed to determine the patient’s anal canal function. While FISI scores [1-3] for two patients were not challenging in the preoperative period, FISI scores for both were also same as in the previous ones. SF-36 questionnaires stated anal canal function was well and there was no restriction at each patient’s daily life.

Discussion
It is not easy to make estimation about the true incidence of PPD because of the rare nature of this disease. It typically presents with a reddish elevated, crusty and scaly lesion which appears in 6th or 7th decade [5,11,12]. Characteristic presenting symptoms are pruritis, irritation, rash and sometimes maceration in the perianal region. It happens to be treated by dermatologists as a benign dermatologic condition in the first place. If the lesion is not healed by any treatment biopsy is performed (12, 13). PPD could be associated with an underlying gastrointestinal cancer, in 12-15% [4,5,14]. Two patients certainly had no underlying carcinoma. It is reported by Goldblum and Hart that PPD with rectal adenocancer have a tendency of endodermal differentiation with gastrointestinal-type glands, frequently positive for CK20 and negative for GCDFP15. In the other type primary intraepidermal neoplasm, Paget’s cells display sweat gland differentiation with GCDFP15 positivity [5,6,9]. It is also reported about the different Paget’s disease that the sialomucins were present in normal anal ducts but they were not present in transitional epithelium of the anal canal. A patient with perianal Paget’s disease showed strongly positive staining, both in the underlying mucinous adenocarcinoma and in Paget’s cells of the affected anal and perianal region. In contrast, stains of other forms of Paget’s disease were completely negative, as well as malignant melanoma and Bowen disease [12].

The treatment of PPD is surgical; wide local excision is the accepted approach and adjuvant therapy has remained controversial [2,4,15,16]. Four-quadrant biopsy mapping is advocated preoperatively, because of the existence of Paget’s cell beyond surgical margins of the lesion [4,10]. In the study, the surgical margins was found positive in 53% of 30 patients with primary PPD [17], and another literature reported microscopically positive margins in more than 50% of cases [18]. On the other hand, the report stated that the use of frozen on punch biopsy has limited value and is so demanding for the pathologist. St. Peter et al. declared that recurrent disease developed in spite of negative margins in their series [20]. Wide local excision has been carried out by large tissue loss which should be covered by using local muscle and/or myocutaneous flaps or skin grafts [1,2,19,20]. As in here, two cases underwent local wide excision covered by V-Y flaps after multiple biopsies on all 4 quadrants taken preoperatively. Frozen section gave no involvement on surgical margins then the flaps were run to the ano-cutaneous line. In this study our technique of V-Y island perianal flaps mentioned above, was found very useful. It was associated with almost none flap-related complications but in just two patients. In the literature the complication about flaps which are frequently seen as anal stenosis and ectropion, are in wide range from 12 % to 65 % [20,21]. In our experience cases are very limited and the flaps were small and they involved only one side of perianal region. Thus strong confirmation is not available at now.

Conclusion
Because coverage after wide local excision is challenging, several different surgical procedures have been described and employed. V-Y island flap is simple and valuable method to cover the wide skin defect in the lesions located in perianal region.

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Case Report

Laparoscopic extraperitoneal paraaortic lymphadenectomy in advanced cervical cancer

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Abstract. In order to determine the zone of radiotherapy, laparoscopic extraperitoneal paraaortic lymphadenectomy (LEPL) was performed in a patients with advanced (Stage IIIb) cervical cancer. The operation time was 148 minutes. The average blood loss was 40 ml. Eight lymph nodes were removed and all were free of tumor. The patient was discharged 2 days after operation without any complication. Pelvic chemo-radiation therapy was planned following the operation. The LEPL seemed to be an accurate procedure to decide the mode and the zone of radiotherapy. To our knowledge this is the first LEPL performed in our country.

Key words: cervical cancer, extraperitoneal paraaortic lymphadenectomy, laparoscopic surgery

Recently, chemoradiation has been used primarily in advanced cervical cancer therapy. The purpose of endoscopic surgery is to determine the paraaortic lymph nodes in advanced cervical cancer. Laparoscopic extraperitoneal and transperitoneal approaches have been used for this purpose. Transperitoneal route was defined by Querleu and Childers in 1992 and extraperitoneal technique was reported by Dargent [1-3]. At the moment, extraperitoneal approach is preferred in order to protect the postoperative adhesion formation which may be related to increased rate of radiotherapy complications [4]. In advanced cervical cancer, laparoscopic interventions may be used for two indications; first, to determine the zone of radiotherapy and second, to choose the patients for pelvic exenteration surgery. In this case study, our aim was to determine the zone of radiotherapy.

Case

The patient was 49 years old and admitted to our clinic with postcoital bleeding. She had 4 pregnancies and 2 normal deliveries. Rectovaginal examination under general anesthesia revealed a tumor which was about 5cm. The cervix was barrel shaped and the tumor was invading right parametrium up to the lateral pelvic wall. Left parametrium was tumor free.

Fractional probe curettage and cervical biopsy were performed. Pelvic MR indicated a mass lesion which was 55x40x40 mm, protruding through the vagina narrowing the endocervical channel, pressing the bladder from the posterior and infiltrating the anterior walls of the uterus and cervix totally.

Rectoscopic and cystoscopic examinations were performed as part of the routine evaluation. Cervical biopsy was resulted as squamous cell cervical carcinoma and the patient was staged as IIIB cervical cancer. After having the informed consent, Laparoscopic extraperitoneal paraaortic lymphadenectomy was performed in 148 minutes with an average blood loss of 40ml. The patient was discharged 48 hours after operation without any complications. Eight reactive lymph nodes were reported after postoperative histopathological diagnosis. Chemoradiotherapy with pelvic radiotherapy was planned.

The patient was operated at lithotomy position. In the first part of the operation, infraumblical diagnostic laparoscopy was performed for cytological examination, abdominal washing procedure was performed and pelvic structures were examined. A 4x5cm tumor was seen in the cervix. A 1.5 cm incision including the fascia was made to the left symmetrical region of Mc Burney. In this stage, the process was guided by the laparoscope which was in the abdominal cavity. The peritoneum was dissected by finger. The psoas muscle and iliac artery were identified. Then, pneumatic laparoscopic trocar was placed and fixed in the dissected area. Intraperitoneal gas was evacuated while the extraperitoneal laparoscopy was started. Carbon dioxide (CO2) has been insufflated until the pressure reached 10mmHg. Over the iliac zone, by following mid-axillar line the entrance for the second trocar was found. For safety, a spinal needle was inserted into the extraperitoneal area. Through this entrance, a 5mm trocar was inserted. Laparoscopic forceps was placed and the dissection was progressed over the iliac artery through the aortic bifurcation.

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The ureter and the ovarian vein were swept away from the operation area. The dissection was advanced through the right part of the aorta. In this stage, we reached to the parasympathetic plexus and inferior mesenteric artery. The plexus was dissected and the ventrolateral part of aorta became free (Fig 2).

Then the dissection was made until the left renal vein. When the dissection was over, lymphadenectomy was started (Fig 3). A 2x3cm sized suspicious lymph node was removed out using the endobag.

While we were waiting for frozen section a dissection on the other side was performed. At the level of bifurcation, first right ovarian artery and vein, then, right ureter were identified. Dissection was enlarged along the right common iliac artery on the inferior side and along vena cava inferior on the superior side.

The lymph nodes were reported as ‘‘malignancy negative’’. Then left paraaortic and iliac, paracaval and right iliac lymph nodes were removed. At the end, retroaortic lymph nodes were dissected.

At the end of the operation, the all sites were irrigated and aspirated and parietal peritonium left open in order to prevent lymphocele formation. Bipolar laparoscopic cautery was used to control bleeding. The patient was mobilized completely at the first day postoperatively. Blood loss was calculated as 40 ml.

Discussion

In advanced cervical cancer, the most important advantage of extraperitoneal laparoscopic procedure is prevention of unnecessary morbidity of the radical surgery [5-9]. Besides, intraoperative and postoperative complications, hospital stay and infection rates will be decreased [5,7-10].

Ouerleu and Dargent’s study including 53 patients had the largest series and the average operating time was 125.9±31.8 minutes. Our operating time was 148 minutes. One factor that may affect the operating time is surgical equipment. Using laparoscopic forceps which specially developed for this surgery may ease dissection. During lymphadenectomy using Dargent Extractor may not only shorten the operating time, but also may increase the number of lymph nodes which removed. Successful arrangement of the distance between the trocars may enhance the effective use of the forcepses [5-7,11]. Keeping the distance between the trocars as much as it could be supplies more comfort during the operation. Some authors suggest clipping and cutting lumbar arteries at this situation [1,4,7]. But Ouerleu and Leblanc who performed this technique successfully, suggest saving these arteries.

In Querleu and Dargent’s study, the technique was successful in 42 patients and 10-44 lymph nodes were removed in patients that Balloon used in extraperitoneal approach. In open surgery the average of lymph node removed is 9.8. In our case 8l lymph nodes were removed and they were all free of tumor.

The most important complication is vessel injury during the dissection [5,7,10-13]. The reason why the pressure in extraperitoneal laparoscopy is kept approximately at 10 mm Hg is to decrease the risk of pulmonary obstruction when there is a vessel injury [1,5,11,12]. In Dargent’s series, a case of ureter injury was treated by placing stent [5,11,12]. One of the most important points for preventing the intraoperative complications is that both of the trocars including the pneumatic one must be inserted very carefully. We determined the best place for the trocar entry by a spinal catheter. To prevent lymphocele formation, parietal peritoneum must be opened by incision and intraperitoneal and extraperitoneal areas must be conducted at the end of the operation [1,5,11-14]. If the continuity of the peritoneum is spoiled, the extraperitoneal fixed pressure can not be reached and the operation will get more difficult but not impossible. In this occasion, laparascope was placed through a third helper product and the peritoneum will be placed upper.

In conclusion, extraperitoneal paraaortic lymphadenectomy might be a reasonable method to prevent aggressive surgery
and also it may shorten the time period to begin a
postoperative radiotherapy in patients with advanced cervical
cancer.

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Medical History

Asclepions in Turkey

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Abstract. Asclepions had a place in Greek Pantheon since 5th century BC as the physician-god or the god of healing. His cult spread to whole Antique World and over than 200 healing temples were built in the name of Asklepios. His family started to develop together with his myth. He and is wife Epione have two sons named Machaon and Podalirios and five daughters named Hygieia, Panacheia, Acheso, Iaso and Aigle. His daughters have some of his powers. The most famous one of his daughters is Hygieia. She became a symbol of preventive medicine. The temples established in the name of Asklepions are called Asclepion. According to Strabon who was the most famous historian and geographer in Antique World, the oldest Asklepios is in Epidaurus. It is predicted that there are over than 200 temples in the west coasts of Anatolia, in Aigean Islands and in Greece, but many of them are not known yet. The most famous Asklepions are in Bergama, Rhodes, Epidaurus and Cos. The new healing centers belonging to the Antique World, except Bergama Asklepios, were discovered in Trace in the last digs. The most important ones are Allioni, which is 15 km northeast of Bergama and Heraion Telchis (Karacalıları), which is 15 km. away from Tekirdag. As a result of the digs, there are some setting places such as Karahoyuk village in Eskipir, Kaidos, Ephesos and Yumurtalik in Adana, which are not proved to be an Asclepion yet. However, there is some evidence that show that these places are health centers. In addition to this, Vitruvius (90-20 BC) who was a famous architect mentioned that there was an Asclepion Temple in Troia Region and Tralles (Aydın).

Keywords: asklepion, antique world, asklepios, temple

In Ancient Greek culture, Asclepios (Esculap, Aesculapius), as the “physician god” or “god of medicine”, was the most important god of health. His cult spreads to an era of approximately thousand years. Its source is unknown, as is the case with other Greek and Roman mythologies, and there are various stories about his birth. In general, the accepted one is the way it is depicted in the third Pythonikon lyric poem written by Pindaros in 5th century BC. In the Iliad of Homer, Asklepios is described as a very famous physician. He is reported to have sent his two sons, who were also good physicians, to the War of Troia [1,2].

Asclepios was added to Greek Pantheon in 6th century BC. As his cult became popular, his myth and his family have broadened as well. He and his wife Epione have two sons, Makhaon and Podalirios, and five daughters named Hygieia, Panakeia, Akeso, Iaso and Aigle. His daughters also possess some of his powers. In the Asclepios cult, Asclepios, Telesphoros and Hygieia constitute an inseparable ternary. Telesphoros, the symbol of convalescence and dreams, became famous in Bergama at the end of Hellenistic period in 2nd century. He was perhaps a great physician in his lifetime and after his death he had been turned into a god [3-6].

The temples, which were established in the name of Asclepios, are called “Asclepion”. The first Asclepion had been built in Epidaurus and other famous Asclepios are in Cos and Bergama. On the other hand, it is known that there are many other Asclepios in west Anatolia and the Aegean coasts. Famous architect Vitruvius (c. 90-20 BC) explained the conditions to be paid attention to in the architecture of Asclepios. “Especially, for Asclepios and other health gods who are supposed to heal a lot of sick people, little temples can be built. If the place of these temples is chosen near appropriate spring water, this appropriateness can rely on natural reasons. Because, when sick bodies coming from unhealthy places are bathed with health giving mineral water, they can get recover faster and so the respect for the god can be increased by using entirely the natural properties of the place” [7,8].

At first the Asclepios were established outside the city, close to rivers and water sources and in places with fresh air. They resembled today’s sanatoriums. After that their structures and proportions had changed. In the early times Asclepios contained a fountain, a temple, and an altar, whereas libraries and monumental health buildings were added later on to Asclepios. In addition, different treatment methods had been developed. In Roman culture, psychotherapy and also hydrotherapy became important for treatment of obstetrics, dermal and rheumatic diseases have been shown interest in [9-12]. The physicians in Asclepios, called Asclepiads, were considered as the sons and daughters of Asclepios. Hippocrates, Calos, Antipos, Galenos, Nikamedes, Flavius, Hermokrates, Claudius are among the famous asclepiads.

Asclepion of Bergama

Archeologist B. Aziz Ogan and Prof. Dr. Von Theodore Wiegand, director of Berlin Museum, discovered Asclepion of Bergama in 1927. To define the place of this Asclepion, Prof. Wiegand used a work of Aristeides (Hieroi Logoi), which he came across in the Library of Vatican Palace. According to the famous ancient writer Pausanias, the first Asclepios Temple in Bergama was established in southwest of the city of Bergama, at the site of the sacred water devoted to Asclepios in the first half of 4th century BC. It has been determined that this sacred place has existed since the 4th
century BC, and progressed in the Hellenistic Period. However the golden age of Bergama Asclepion was the 2nd century BC. The remaining buildings were mostly built by Emperor Hadrian (117-138 BC) [13]. With the addition of a theatre and a library in the 2nd century BC, the Asclepion of Bergama became a center in which sick people were healed. Healed people used to visit the Asclepios Temple and grant money in proportion to their wealth. A miniature sculpture of healed organs was usually offered as a vow. This tradition also appeared in Rome [14].

Allianoi Health Center

Allianoi is in Pasha Illicesi region, close to Bergama – Ivrindi Highway. In the 2nd century BC, Aelius Aristides of Mysia wrote a book called Hieroi Logoi (Sacred Words) and mentioned that when he was traveling from Hadrianoterai to Bergama, he became ill and he went to Allianoi, drank its thermal spring water and got better. He said that he dreamed of God Asclepios and felt himself better with the inspirations of Asclepios. He said that the distance of this thermal spring water center to Bergama was 120 stadia (23-25 km). There is not any other important thermal water complex known of Asclepios. He said that the distance of this thermal spring water center to Bergama was 120 stadia (23-25 km). There is not any other important thermal water complex known between Bergama and Balkesir. Although there is no epigraphic finding, relying on Aristeides work it is claimed that this place is Allianoi [7,16].

Allianoi was established in Hellenistic Period (323-330 BC) and its golden age was in the reign of Roman Emperor Hadrian (117-138 BC). It is thought that this place was not really an ancient city, but a health center belonging to Pergamum Kingdom. The biggest evidence for this is the fact that no coin in the name of the city existed. This center was used continuously between 3rd century BC and 11th century AD [7,17]. This site is thought to be a general cult site belonging to the God of Health Asclepios, for there are many works of art related with him. Two Asclepios statues, small bas-reliefs of Telesphoros, two altars belonging to Asclepios and many medical tools made of bronze were found. All these artifacts are kept in the Bergama Museum. These artifacts also suggest that the cult of Telesphoros existed before the cult of Asclepios [7,18]. Apart from the bath structures indicating intense use of thermal therapy, there are also a large number of findings in the site of Allianoi. Among these are spatulas, urogenital catheter (aenea fistula), various forcepuses used for different purposes, and bronze scalpel handles which prove that surgical interventions had been performed.

Karaevlialti (Heraion Teichos) Health Center

Archeological research is going on in Karaevlialti under the directorship of Associate Prof. Dr. Nese Atik from Mimar Sinan University. Karaevlialti, known as Heraion Teichos in antiquity, is at a 15 km. distance from Tekirdag. Early findings suggest that the site first became populated around 3000 BC and contains various floors of cultures till the 13th century. A large ebony courtyard with walls surrounding it was found at the site in 2001. The ongoing research at the area revealed many medical tools. Later on, baked soil figurines (symbolizing offerings) dating from the 1st century were discovered [19]. In addition, remnants of some kind of mashed seashell, known as Murex in Latin, were discovered in some parts of the courtyard. The seashell was boiled in water to produce a certain type of dye giving claret red-purple tones, known as Purpur. This dye was very precious for thousands of sea shells were required to make only one gram of dye, and it was used in the dresses of kings. Later, studies on sources dating from antiquity revealed that the Murex in mixed and burnt form was used in the making of drugs rather than dyes, and the mashing was a part of this procedure. This drug was first used for cleaning of the teeth and in the treatment of ear infection when combined with pork oil and honey. This drug is also mentioned in the Materia Medica of Dioscorides to be used for abscess drainage and cleaning of the teeth [19,20]. In the light of all these findings, it is suggested that an Asclepios temple must have existed here.

Datca (Knidos) Health Center

Datca (Knidos), situated on the coast of Southwestern Anatolia, was a competitor of Istankoy (Cos), a leading center of medicine of the antique age. Knidos was one of the important schools of medicine that educated physicians, and it supported a doctrine that classified diseases according to the organs involved. Knidos defended the same principles of medicine with Cos, and distinguished physicians such as Herodikes and Europhon were among its students. However, no remnants of an Asclepion temple have been found yet in Knidos [9].

Efes (Ephesos) Health Center

Ephesos Health Center was famous in the whole Mediterranean region in the Roman Empire era. Rufus of
Ephesus and Soranus are two distinguished physicians of this school. No remnants of this center have been found yet. However, evidence about the names and studies of physicians from writings found in the digs of the Church of Virgin Mary suggest that the place had been a health center in earlier times [9].

**Troia Asclepion**

Strabon, who was born in Amaseia, Pontos in 64 or 63 BC, was a famous geographer and historian. While he was giving information about Troia, he mentioned an Asclepion established by Lysimachos.

**Aydin (Tralles) Asclepion**

Vitruvius (c. 90-20 BC), a famous architect and writer of De Architectura, a book on architecture, which was dedicated to Roman Emperor Augustus, mentioned books written by architects that lived before him. Vitruvius wrote about the existence of an Ionian Asclepion in Aydin (Tralles), and in addition he said there was a book written by Arcesius about the Asclepios Temple of Tralles.

...... Arcesius, Corinth proportions, on the Ionian Asclepios Temple in Tralles which he was said to have built it himself, and Staurus and Pytheos on Mausoleum, each wrote a book [8].

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Abstract. For Greece, the 19th century signifies, one of the most important periods, if one takes into consideration that after the successful completion of the Greek Revolution of 1821, its national consciousness has been formed and it has been created the bases of the creation of the modern model of the European nation, and of which the ethnic and territorial integration has taken place at the beginning of the 20th century. In the phase of these developments the Army is the cornerstone of the Hellenic society. The social and political influence of the Army, and especially of the highly qualified Generals, such as military doctors, was important during the 19th century, during a period in which the roles of army officers, politicians and civilians are not perfectly distinct among themselves. The Health Department of both the Army and Navy, played an active role in the Hygienic organization of the country in contrast of other European countries in which the State Hygienic Services and hospital units were ahead of the development of the Hygienic service of the Army.

Key words: Greece, Greek revolution, military doctor, society

For Hellas (Greece), the 19th century signifies, one of the most important periods, if one takes into consideration that after the successful completion of the Hellenic (Greek) Revolution of 1821, its national consciousness has been formed and it has been created the bases of the creation of the modern model of the European nation, and of which the ethnic and territorial integration has taken place at the beginning of the 20th century [1].

In the Hellenic society, after the establishment of the independent nation, there has been prevailed a mixture of various political and cultural trends, with the Great Idea being eminent of the romantic nationalism.

The insecurity for the future and the economic adversity, which are the main characteristics of that era, and the social reformations political and social aiming at the re-organization and modernization of the society.

In the phase of these developments the Army is the cornerstone of the Hellenic society. After the incorporation of the unruly armed forces into organized army by the first Governor of Greece called Ioannis Kapodistrias, the fact that philo-Hellenic military remains after the Revolution, improved the situation. At the beginning, the Army was developed according to the Bavarian system under the authority of the Bavarian monarch, called Othon and later, according to the French system and therefore a modern and in good fighting condition army, was created [1,2].

The social and political influence of the Army, and especially of the highly qualified Generals, such as military doctors, was important during the 19th century, during a period in which the roles of army officers, politicians and civilians are not perfectly distinct among themselves.

In a country such as Hellas of the 19th century, in which the functioning of the Medical Faculty of the University of Athens started in 1837, the burden and the responsibilities were born by doctors who had studied abroad and Hellenic (Greek) military doctors, who had remained in the country after the Independence in Hellas (Greece) and by the Bavarian doctors of Othon.

Despite the intense presence of the National Health system in the country of the above mentioned scientifically educated doctors, the Hellenic society is plagued with quackery, illiteracy, prejudice and empirical medicine, phenomena which appeared and prevailed, during the Ottoman period. With the creation of the “Medical Conference” in 1834 and the “Medical Society of Athens” in 1835, the licensed doctors were under legislation and therefore the above phenomena were decreased [2].

The Health Department of both the Army and Navy, played an active role in the Hygienic organization of the country in contrast of other European countries in which the State Hygienic Services and hospital units were ahead of the development of the Hygienic service of the Army. Therefore the military doctors, with their high scientific background and their training in famous universities abroad took part in the “Medical Conference” and in the teaching and scientific work of the newly established Medical Faculty [1,2].

With the training of new doctors, and the development of the medical press in our country, and with stunning announcements, many of which are reference points for foreign doctors, they form the Hygienic Policy of the state with the publishing of Hygienic counseling, which support the health of the Army. Thus the health of civilians was protected (such as the vaccine of cox pox which was practiced in the Army since 1835, whereas it wasn’t compulsory for the Hellenic population).
References
