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## The Value of the Histopathological Examination in Medicolegal Autopsies

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### Abstract

#### Introduction

An autopsy can be requested for several reasons: it will usually be requested by a hospital, less frequently in a judicial context. And whilst the two types of *post-mortem* investigation can differ in their aim and methodological approach, histological sampling is common to both types of enquiry. Two studies published recently in the *American Journal of Forensic Medicine and Pathology*, have challenged the effective value of the histological examination in a medico-legal investigation ascertaining the causes of death. With the aim of verifying this claim, we conducted a retrospective study regarding the autopsy activity at the *Institute of Legal Medicine in Palermo* during 2009-2012; because in this Institution, the methodological approach to a forensic autopsy has nearly always included (93%) the use of histopathological diagnostics.

#### Materials and Methods

The case records involved in our research were revised in the light of medicolegal issues and the information available: the death scene, the family and pathology history, and toxicological analysis. As a source of study, the *Registry of Forensic Autopsies* was used (including background information, gross and microscopic autopsy findings, and medicolegal opinion) and the *Registry of Forensic Histopathology Laboratory*.

Moreover, we evaluated data relating to several foreign Institutes (eg. the USA and the Ukraine): by specifically reflecting different rules regarding medicolegal expertise, the data could establish differing evaluations for the use of histopathological examinations, by means of a different pre-sectorial selection.

#### Results

463 medicolegal autopsies were performed from January 2009 to December 2012, of which 426 (93%) included a histological examination of organs and parenchyma. 235 cases (55%) were the result of violent deaths and 191 cases (45%) due to natural deaths. The histopathological examination modified the macroscopic autopsy diagnosis in 61 cases (32%) of natural death and 37 cases (16%) of violent death.

### Conclusion

The data from our Study confirmed the importance of the microscopic diagnostics in medicolegal autopsies. The histopathological identification of physiopathological events, which are responsible for death, effectively enabled us to maximise the evidence of background information, pathology history, macroscopic and toxicological findings. A histopathologic evaluation maximised the degree of certainty in determining the causation of natural and violent deaths.

**Key Words:** Histopathology, medicolegal autopsy, violent death, natural death.

### **Introduction**

An autopsy can be requested for several reasons: it will usually be requested by a hospital, less frequently in a judicial context. And whilst the two types of *post-mortem* investigation can differ in their aim and methodological approach, histological sampling is common to both types of enquiry.

A hospital autopsy is a methodical examination of the cadaver, which is undertaken to: ascertain the cause of death, the extent of pathological processes, verify the diagnosis made when the patient was alive, and/or an assessment of the therapies undergone with the main aim of making a diagnosis. Dissimilar in nature is the medico-legal autopsy, which is undertaken for legal purposes and which entails: knowing the cause, manner and time of death, the viability of any lesions, and the survival time of the patient, according to the circumstances of each case, in addition to diagnostic matters regarding the cause of death. From a methodological point of view, in a forensic autopsy the results of a meticulous external examination are gathered and photographed and, where necessary, tests on biological liquids are performed and/or organ samples taken for toxicological examination; these are elements which as a rule are not taken during a hospital autopsy.

The value of a histological examination in a forensic autopsy is often subordinate to the outcome of the results of a death scene investigation, external examination, toxicological enquiry and the macroscopic examination, all of which facilitate a thorough response to the demands of judicial authority. Only in a few cases does a histological examination play a predominant role at the start of an expert investigation. For this reason, there still exists controversy surrounding the necessity of performing a histological examination as part of a

medico-legal autopsy; this is also dictated by financial considerations. During bibliographical research carried out on *PubMed*, the attention of the authors of this Paper was attracted by a fascinating discussion relating to this issue between two American, medico-legal centres: the first study cast doubt on the value of a histological examination with a challenging title in the form of a question: “*Is routine histopathologic examination beneficial in all medicolegal autopsies?*” [1]; the second study, entitled “*The Importance of Histological Evaluation in Death Investigation*” [2] was, however, favourable in this regard.

A comparison of the provisions in force regarding the value of a histological examination in an autopsy in various European countries initially revealed unanimous agreement when entrusting the decision to extend a supplementary histo-pathological investigation at the discretion of the pathologist [3,4]. Recently such regulations have, however, been modified to oblige the use of this investigation in all cases of forensic autopsy [5,6,7].

The aim of this study is to demonstrate how evaluating the role of the histological examination in a legal autopsy may not depend only on the number of cases (where such an examination plays a diagnostic and fundamental role in resolving medico-legal questions) but also on the possibility that such enquiries can highlight rare or genetic pathologies. This situation prevails even if the number of histological examinations is small in number. And the highlighting of rare or genetic pathologies, unknown when the patient was alive, could prevent the deaths of family members and the exclusion of the responsibility of third-parties in the event of death.

With the aim of verifying this claim, we conducted a retrospective study regarding the autopsy activity at the *Institute for Forensic Medicine in Palermo* during 2009-2012; in this Institution, the methodological approach to a legal autopsy has nearly always included (93%) the use of histopathological diagnostics.

#### **Database resources**

Using the *Register of Legal Autopsies* and the *Register of the Forensic Histopathology Laboratory* of the *Institute of Legal Medicine* at the University of Palermo, 463 medico-legal autopsies were performed from January 2009 to

December 2012. For each case, the following were examined: medico-legal issues, information relating to investigations at the death scene, family and pathology history, toxicological investigations, the results of histological examinations and medico-legal considerations.

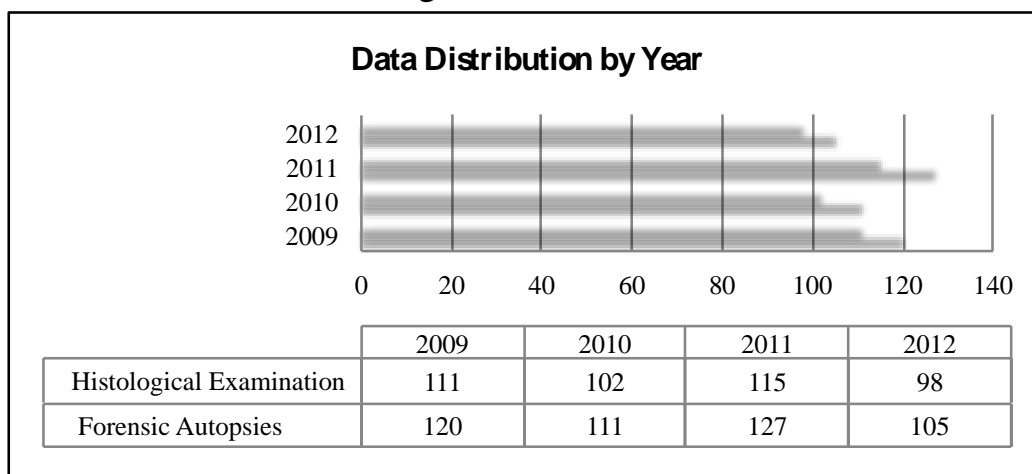


Table 1

Of these 463 autopsies, 426 (93%) included a histological examination of various organs and parenchyma tissue, which were obtained at autopsy (Table1). The 37 cases where a histological examination had not been performed related to victims of fire arms, cutting and stabbing injuries or on skeletal remains. Those autopsies including a histological examination were due to a violent death in 235 cases (55%) and a natural death in 191 cases (45%) (Table 2).

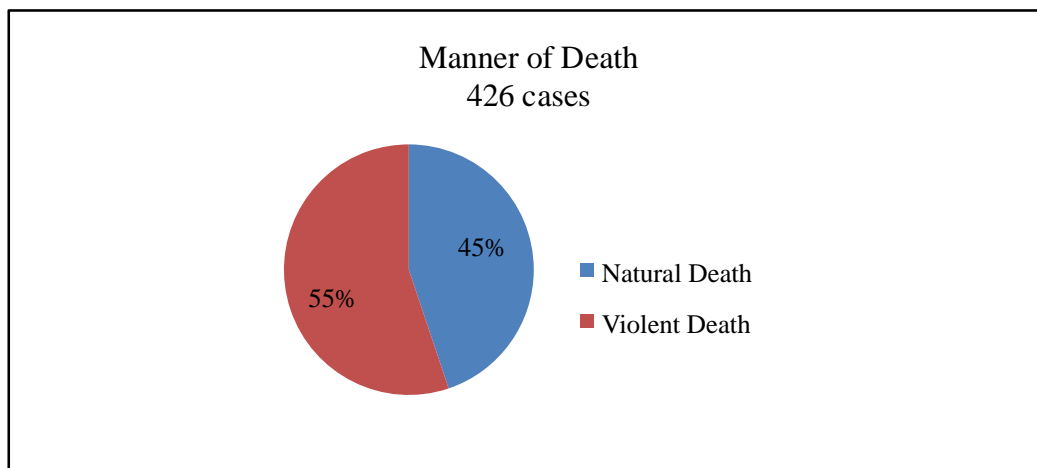


Table 2

The age of the cases reported varied from 12 weeks of gestation to 82 years (a median of 48.7); 306 (72%) of cases were male and 120 (28%) were female (Table 3).

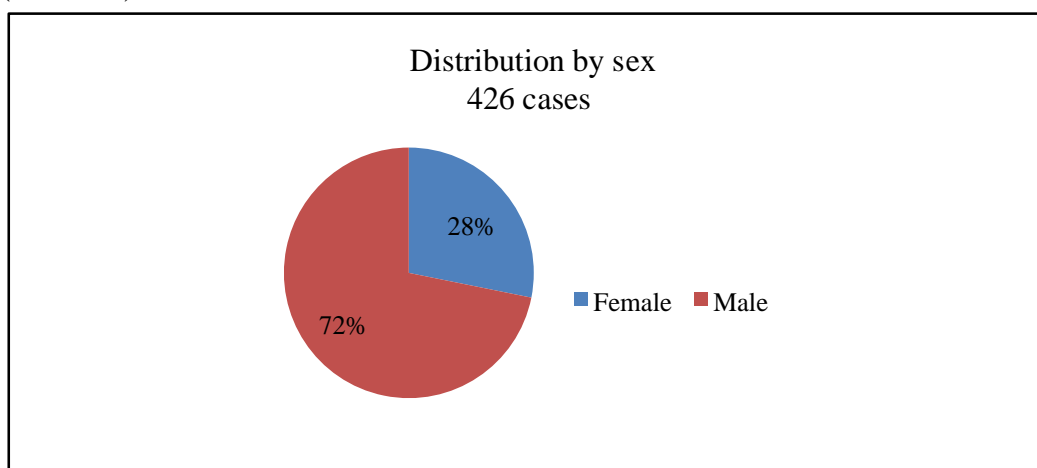


Table 3

### Results

In 426 cases involving macro- and microscopic investigations, a histopathological examination modified the diagnostic, clinical-family history and/or toxicological – circumstantial orientation in: a) 37 cases (16%) of violent death (21 due to drug use; 10 cases due to suspected medical negligence; and 6 cases due to road or work-related accidents), thereby transforming the diagnosis of

violent death into one of a natural death (Table 4); b) 61 cases (32%) of natural death (Table 5).

Manner of death	DISCORDANT AUTOPSY DIAGNOSIS		
	Histopathologic Diagnosis (n.cases)	Clinical/ Circumstances/ Toxicological Diagnosis (n. cases)	
Violent Death (235 cases)	Lymphocytic myocarditis	6	Drug intoxication 21 cases
	Myocardial infarction	5	
	Pneumonia	3	
	Bronchial asthma	3	
	Septic endocarditis	2	
	Sickle cell anemia	1	
	Pulmonary hypertension	1	
	Myocardial infarction	2	Road or work-related accidents 6 cases
	Hypertrophic cardiomyopathy	1	
	Bronchial asthma	1	
Aortic dissection	1		
Electrocution	1		
M A L P R A C T I C E	Cytomegalovirus infection	1	Pulmonary thromboembolism secondary to hip fracture 3 cases
	Heart failure	1	
	Hepatic necrosis to traumatic hematoma liver	1	
	Revascularization syndrom	1	Laparoscopic surgery with lesion of blood vessels 1 case
	Coronary aneurysm rupture	1	AMI after surgery on the heart 3 cases
	Rupture of the atrial wall	1	
	Rupture of the bronchus	1	
	Rupture of the esophagus	1	Postoperative sepsis 1 case
Placenta accreta	1	Uterine rupture 2 cases	
Staphylococcal sepsis	1		

<b>Total of cases</b>	<b>37 cases (16%)</b>
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Table 4

Manner of death	DISCORDANT AUTOPSY DIAGNOSIS	
	Histopathologic Diagnosis (n. cases)	Clinical history Diagnosis (n. cases)
Natural Death (191 cases)	Pulmonary thromboembolism	11
	Myocarditis	6
	Conduction system disorders	4
	Hypertrophic cardiomyopathy	2
	Tuberculosis	1
	Sine materia (s. Brugada)	1
	Endocarditis	3
	Cerebral hemorrhage	3
	Lung metastases	2
	Myocardial infarction	6
	Meningeal metastases	1
	Atrioventricular fistula	1
	Umbilical cord problems	7
	Chorioamnionitis	3
Myocardial infarction	3	
Coronaritis	2	
Pulmonary thromboembolism	3	
Intestinal infarction	1	
Fulminant hepatitis	1	
<b>Total of cases</b>		<b>61 cases (32%)</b>

Table 5

## TYPICAL CASES

### Case 1

A 39-year old prisoner from the Maghreb died suddenly in his cell with his cellmates, falling off his stool and hitting his head. In the last year of his life he had had frequent episodes of recurrent bronchitis. A CT scan of his thorax revealed mediastinal and pulmonary hilar lymphadenomegaly, associated with nodular formations on the both superiors lobes. A biopsy indicated chronic, granulomatous phlogosis with giant epithelioid cells, which led to a diagnosis of *pulmonary sarcoidosis*. Corticosteroid therapy was, therefore, initiated.

At **autopsy** an examination of the lungs revealed numerous lympho-nodal 'packets' on both the pulmonary hilum, oedema and congestion. There was also stenosis of the proximal segment of the left anterior descending artery and signs of myocardiosclerosis on the posterior wall of the left ventricle.

**Histology** revealed that the left anterior descending artery had been blocked by a recent thrombosis which had developed on arteriosclerotic plaque, the latter, which was vulnerable to the erosion of the fibrous layer. There was evidence of a specific granulomatous myocarditis on the myocardium of the ventricles and several histo-genetic phases could be observed. A granulomatous, caseating, disseminated miliary tuberculosis was present in the lungs. The hilar lymph nodes were characterised by fibroplastic, granulomatous phlogosis and there was evidence of stasis and polyvisceral pathosis. On the basis of all the investigations performed, it was possible to formulate a diagnosis of *cardiac arrest, secondary to acute thrombosis of the left anterior descending artery* in subjects with severe, specific granulomatous myocarditis and post-primary miliary tuberculosis.

**Medico-legal Conclusion.** The aforementioned case enabled the authors of this Paper to highlight a direct correlation between tubercular processes and the development of obstructive coronary thrombosis. By means of immunofluorescence, we could identify elevated levels of TNF, interleukins and extensive apoptosis on the coronary endothelium, the site of erosion. As is known from the literature, such mediators of phlogosis develop in tandem with chronic inflammatory diseases [8, 9]. In the case in point, the inappropriate use



of cortisone following an incorrect histological diagnosis, exacerbated by pulmonary tubercular inflammation, precipitated damage to the endothelium and thus the occurrence of acute thrombosis, a result of medical malpractice. This case underlines the value of the histological examination in the forensic investigation, one which assisted us in changing the diagnosis of *natural death* to one of *medical negligence*.

### Case 2

The second Case can be considered routine but one which occasionally attracts the attention of the forensic pathologist. Often legal authorities have difficulty in determining the responsibility of a death when, for example, death happens after an argument and the deceased is already suffering from a heart complaint. In the Anglo-Saxon literature such cases are described as *homicide by heart attack* and they are evaluated in accordance with a well-defined methodology [10].

Minutes after a violent argument relating to a parking place in a block of flats, a 56-year old man loses his balance and falls backwards, resulting in a ragged and bruised wound to his scalp. The emergency services arrive after the man has died. The witnesses inform the police officers that there had been no physical aggression other than reciprocal shoving. The judge orders an autopsy.

**Autopsy examination.** In addition to the common, non-specific signs of a sudden death, asphyxia and moderate arteriosclerosis characterised a heart weighing 550g, which revealed patches of myocardial sclerosis on the left posterior and lateral ventricle wall. The sclerosis also involved the papillary muscles with atrophy of the posterior papillary muscle, and an important obstructive arteriosclerosis of the epicardial coronary arteries with a complete blockage of the left anterior descending artery, stenosis of the right coronary artery and the first diagonal branch of the right anterior descending artery. Moreover, there were metal stents in the lumen of the right coronary and left circumflex arteries.

**Histology** confirmed a severe myocyte hypertrophy in the myocardium, which was associated with interstitial, replacement and perivascular myocardial

fibrosis. This fibrosis was advanced and multifocal, particularly on the left ventricle and interventricular septum, and the fibrosis was associated with myocardial contraction bands and wavy myocytes. The adrenal glands displayed widespread cortical hyperplasia of the intermediate fasciculata of the adrenal gland, and a degranulation of the adrenal medulla with adrenalitis and intravascular leiomyomatosis. The meninges and encephalon displayed no abnormal histology.

A histopathological examination enabled us to highlight the morphological substratum of the lethal arrhythmic event (fibrosis, hypertrophy and myofibrilolysis), in this case to the exclusion of a causal lesion of the encephalon and/or the meninges.

**Medico-legal Conclusion.** Evaluating the circumstances in which death occurred (the futility of the argument), an opinion was expressed that the stress generated in the argument, which was comparable to any type of routine emotional and/or physical stress, had triggered the events leading to death (fatal arrhythmia), thereby excluding the responsibility of any third party.

### Case 3

The third Case relates to a 34-year old man who died at home. With a long-standing drug habit, he was known to the police as a pusher of narcotic drugs.

A **medicolegal autopsy** highlighted signs of a quick death (liquid blood in the heart cavity and larger vessels, multi-visceral congestion and pulmonary oedema). Toxicology and histology tests were performed at autopsy; the former was negative. A **histological examination** highlighted the presence of sickle cells and thrombi in the capillary lumen of the parenchyma tissue, which was sampled for microscopic examination (brain, lungs, myocardium, liver and kidneys).

**Medico-legal Conclusion.** Death occurred due to cardiac arrest during an acute sickle crisis [11, 12].

## CASES OF PROFESSIONAL RESPONSIBILITY

### Case 4

The fourth Case regards a 53-year old man, who had had an aortic valve substitution and bypass surgery (via the great saphenous vein) 28 days prior to his sudden death. The patient suffered from ischemic heart disease with severe aortic insufficiency, and his symptoms had manifested themselves in the last two years. A pre-operative coronary angiography had revealed a stenosis of approximately 80% on the proximal part of the circumflex branch of the left coronary artery. The operation and post-operative periods were normal.

**Autopsy** revealed a cardiac tamponade of approximately 500ml of blood. The saphenous vein graft was intact. The mechanic valve positioned in the aorta showed regular sutures with normal disc movement. There was a parietal swelling of blood, which was adjacent to the obtuse heart margin on the atrioventricular groove, where the aortic bypass had been inserted into the left circumflex artery; this blood was surrounded by an apparent fibrous capsule. On inspection the latter was observed to be discontinuous and the origin of the haemorrhage. The other coronary arteries displayed minor, intimal, atherosclerotic lesions. The left coronary artery was surrounded by an intramural haematoma near the left margin of the heart which was partially contained by a fibrous capsule.

A **histological examination** of the left circumflex coronary artery at the site of the aneurism displayed the desiccated blood of the *tunica media* and a transmural rupture of the wall due to fibrinoid necrosis. The *tunica intima* was the location of fibrosing atherosclerotic lesions. Inflamed, granulated tissue, in the early stages of fibrotic development, could be seen in the *tunica externa* of the vessels. This inflamed tissue contained a thrombotic neoformation (capsule), which was situated between the coronary lumen and the *tunica adventitia* space (a pseudoaneurysm). This fibrous capsule appeared to have ruptured outwards as a haemorrhage.

**Medico-legal Conclusion** In the aforementioned case the bypass on the left circumflex had mechanically shrivelled the wall together with a slow, transmural rupture. The post-surgery fibrinous pericarditis acted as a temporary brake to the developing coronary haemorrhage in the pericardium. Only subsequently and on account of the extended dilation and thinning out of the

fibrotic ‘shell’ of the pseudoaneurysmic cavity did a rupture and cardiac tamponade form.

Cases of presumed medical responsibility are an issue in medicine in Italy and the daily forensic medicine activity and a histological evaluation are often fundamental in providing answers to legal questions.

### Case 5

A 55-year old woman was hospitalised at the department of Maxillofacial Surgery at a Palermo hospital due to the presence of a burning ulceration on the left-hand side of her tongue. An incisional biopsy revealed a well-defined, squamous cell carcinoma. Four days after being admitted to hospital and the intervention of a tracheotomy, the patient underwent an anterior, left hemiglossectomy with bilateral laterocervical emptying and subsequent tongue reconstruction.

A histo-morphological of the specimens taken during surgery revealed a “*moderately-differentiated squamous cell carcinoma with keratinoblast aspects which had massively infiltrated the surrounding tongue muscle tissue*”. The tumour was classified as: *G2, pT1, pN0, pMx*.

In the post-operative phase, approximately 25 hours after the operation, signs of an acute pneumothorax suddenly appeared with a contemporaneous reduction in saturation values. The tracheotomy cannula was checked with a bronchoscope and it revealed an obstruction due to the probable collapse of the tracheal mucosa; an attempt was made to unblock the cannula. A rapid deterioration of the clinical conditions, a further desaturation with bradycardia, and a rapid development to cardiac arrest followed. Advanced cardiopulmonary resuscitation was applied without success. Throughout resuscitation the tracheotomy cannula was substituted with an endo-tracheal tube.

An **autopsy** revealed a rupture of the *pars membranacea* in the trachea, which had caused the lethal pneumothorax.

A **histological examination** demonstrated the presence of an ischemic necrosis localised adjacent to the tracheal wall of the balloon cuff.

**Medico-legal Conclusion.** Medical negligence was excluded in that a histological examination revealed an ischaemic lesion and not an iatrogenic perforation made by the surgeon.

### Case 6

A 27-year old woman, 32.2 weeks pregnant, was taken to the *Emergency Department* in a state of premature labour. Upon arrival in the delivery room, she was unconscious and had unstable haemodynamic values. The patient presented with multiple ecchymoses and abrasions on her thighs, lower abdomen and the perineal; there were also signs of acupuncture on her forearms. The patient was assisted during delivery and gave birth to a deceased male foetus, weighing 1,530g. The foetal membranes were cloudy in consistency with a strong foetus smell. Immediately after delivery, the woman showed signs of tachycardia with hypotension, hypocapnia and hypothermia. Resuscitation and intensive therapy failed and the patient died some time after delivery without regaining consciousness.

Positing that the patient had been a victim of malpractice and/or mistreatment, an autopsy was requested.

A **histological examination** revealed the presence of infective endocarditis of the atrioventricular valves and the haematogenic dissemination of staphylococcus bacteria, which were subsequently isolated from skin samples.

**Medicolegal Conclusion.** On the basis of the data obtained from the histopathological investigation, responsibility for this patient's death was not attributed to a third party in that the cutaneous lesions had not been made with violence but as a result of systemic impetigo due to staphylococcus bacteria. Thus, no professional culpability could be asserted.

### Discussion

In the multi-disciplinary context of Italian legal medicine, “the sphere of forensic pathology studies consists of the *critical highlighting* of features of *harmfulness*, with the main aim of defining its characteristics, functioning and

productive procedures in the field of the so-called *factors of legal relevance*” [14].

As demonstrated by the study outlined in this Paper, the daily cases of medico-legal interest do not only concentrate on trauma (or forensic traumatology) but they encompass the entirety of general pathology. For such reasons, the application of a methodology, in essence directed at a meticulous observation-based, descriptive or morphological study, is of great pertinence to a medico-legal investigation into the cause of death.

The four elements of a pathological process which make up the basis of a disease or lesions are: 1) causes or aetiology; 2) onset mechanisms or pathogenesis; 3) structural changes induced in the cells and organs of the body, which are recorded as *morphological changes*; and 4) functional consequences of morphological changes, leading to the formulation of a diagnosis or cause of death [15]. Pathological processes regarding forensic pathology share similar mechanisms, and the objectives of forensic pathology recall the four elements of general pathology.

The field of legal medicine can be considered the totality of the sciences, and that includes forensic pathology, which applies its knowledge of medicine, pathology and biology to the resolution of medico-biological issues, emerging from the activities of the police and judicial authorities [16, 17]. The task of the forensic expert is to reconstruct the causal link in the investigation. Throughout any investigation into the cause of death, this task is undertaken by determining the cause and manner of death. Only a complete forensic autopsy, including a meticulous examination of all bodily cavities and histo-pathological sampling, will be considered fit for the purpose of medico-legal activity.

The results of medico-legal investigations into the cause of death cannot be addressed only at the legal system. Establishing the cause of death is extremely important for: epidemiological studies, clinical conferences regarding morbidity/mortality, insurance companies and the family members of the deceased person. There are aspects which concern not only legal questions but they also include the broader issues of public health and social security. A

medico-legal consultation to ascertain cause of death must be the most thorough and accurate possible.

Moreover, a histological examination performed as part of a legal autopsy is an act of interpretation and objective documentation of macroscopic autopsy findings. This is in addition to defining the cause of death, enhancing our understanding of patho-physiological processes, the latter, having determined the histological examination and improving the reliability of medico-legal expertise in court proceedings.

### Conclusion

The data from our Study confirmed the importance of the microscopic diagnostics in medicolegal autopsies. The histopathological identification of physiopathological events, which are responsible for death, effectively enabled us to maximise the evidence of background information, pathology history, macroscopic and toxicological findings. A histopathologic evaluation maximised the degree of certainty in determining the causation of natural and violent deaths.

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