TWELVE YEAR RETROSPECTIVE STUDY ON THE FORENSIC ASPECTS AND MORPHOLOGICAL CHANGES IN VITAL ORGANS AND SYSTEMS IN CASES OF LONG TERM DRUG ABUSE

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Abstract

Drugs are substances that affect the psychic, emotional and physical state of the individual. They have health-related consequences as they pose increased risk of internal organ damage in varying degrees, as well as intoxication and death. Today drug addiction is still of great social, medical, legal and criminological significance regardless the worldwide measures taken to combat drug distribution and use. In the Department of Forensic Medicine and Deontology, Medical Faculty, Medical University - Sofia, Bulgaria, a retrospective study on the forensic aspects and morphological changes in vital organs and systems after long-term use of narcotic substances has been carried out for the period of 2006-2017. The performed chemical analysis showed that the most frequently used drugs were from the opioid group, alone or in combination with other psychoactive substances, impurities or alcohol. In connection with the prolonged abuse of narcotic substances, we observed different morphological changes in the heart, lungs, brain, liver and kidney tissue. Even though the identified changes are mainly non-specific, considered together, they could be classified as characteristic in cases of people abusing with psychoactive drugs. Knowing the morphological characteristics of the changes in different tissues and organs could enable forensic and pathology specialists to properly diagnose the various cases and thus direct and assist the investigating authorities.

Key words: *Drug addiction, chronic use, morphological changes, forensic medicine*

Introduction

Drugs are substances that affect the psychic, emotional and physical state of the individual [1, 2, 3]. At present, drugs are generally referred to as substances to which tolerance and dependence are created [4, 5, 1, 6]. They have health-related consequences and are of great social, medical, legal and criminological significance regardless the worldwide measures taken to combat drug distribution and use. For a substance to be classified as an illicit one it is necessary to be listed in special government lists, which are updated periodically. Drug addiction involves mainly young people and a significant percentage of them start taking drugs in childhood. In recent years, the spread of natural, semi-synthetic and synthetic psychotropic substances has become more prevalent, with the increasing number of crimes and fatalities associated with their misuse [7, 8]. Drug toxicity is generally due to direct effects of the drug or its metabolites on the human body, direct effects of impurities or excipients injected with it, infectious complications, mechanical and lifestyle factors in the drug addictive practices [9, 10, 11, 12].

The purpose of this study is to reveal the morphological changes in vital organs such as the heart, lungs, brain, liver and kidneys of deceased with different in length history of illicit drug intake and to clarify their involvement in the genesis of death.

Materials and methods

A thorough forensic analysis of deceased with data of prolong drug abuse was carried out in the Department of Forensic Medicine and Deontology, Medical University, Sofia, Bulgaria for the period 2006-2017. In each case, samples of blood and/or urine were obtained for chemical analysis and examined for the presence of alcohol and drugs that do not give visible morphological changes in tissues and organs. The chemical analysis was conducted by the methods of thin-layer chromatography, UV spectrophotometry and gas chromatography (gas chromatography with nitrogen-phosphorus detector GC / NPD THERMO FINNIGAN and gas chromatography with mass spectral detector quadrupole GC-MS model Thermo scientific). Necropsy material was fixed in 10% formalin solution, paraffin blocks were made as well as permanent histology samples stained with hematoxylin and eosin using standard techniques. All the anamnestic, medical and criminological data, and results from the toxicological analysis, were compared with the macroscopic and microscopic changes in the heart, lung, brain, kidney and liver tissue of the deceased.

Results and discussion – forensic aspects

In the Department of Forensic Medicine and Deontology, for the period 2006-2017, 12299 autopsies were performed, and 488 of them were with data of drug abuse, with the following breakdown by years and gender (Figure 1 and Figure 2).

In the beginning of the studied period, it has been found that in the distribution curve of the case of deaths associated with drug abuse there is a significant, gradual increase, with the formation of peaks in 2007 and 2010. They were followed by a notable decline in 2012. There is a new peak in 2013, again followed by a decline, with the formation of a kind of a three-year plateau between 2014-2016. In 2017, there is a new increase in the observed cases. On the one hand, this characteristic of mortality can be attributed to the quality and composition of the drugs offered. On the other hand, the amendments described above may be related to various legislative changes introduced in connection with the drug policies after Bulgaria joined the European Union.

The gender distribution revealed the prevalence of men over women, as the deceased men were 85,4% of the observed cases.

The performed chemical analysis showed that the most frequently used drugs were from the opioid group (64,5%), alone or in combination with other psychoactive substances, additional substances (impurities) or alcohol. Even though heroin was widely used – more than half of the investigated cases were positive for this psychoactive drug (commonly combined with other narcotics or alcohol), there is an increase in the cases of death after methadone use, which in 2017 exceeded those after heroin use. Significantly less deaths were associated with stimulant use – 15,8% of the observed cases (cocaine, amphetamines, methamphetamines and "designer drug"). Often they were combined with opioids, especially heroin. The incidence of deaths after stimulant drug use is increasing form the beginning of the observed period and in 2017 is almost equal to the group of opioids. Death that occurred after marijuana use was found to be 6,9 % of the observed cases. It should be noted that it often accompanies the use of opioids and stimulants. In 12,7%, deaths occurred after the use of non-prescribed drugs (benzodiazepines, barbiturates, etc.) in people with evidence of sporadic or long-term use of narcotic drugs (Figure 3). The number of death cases after drug abuse of only one narcotic substance has been greatly reduced, taking into account the tendency for simultaneous combined intake of several substances - polytoxicomania or polynarcomania. Commonly used combinations are opioids and stimulants, opioids and hypnotics, as well as various drugs and alcohol (Figure 3).

Morphologycal analysis

In connection with the long-term use of narcotic drugs, tissue and internal organ damage causing diseases leading to death develops. The current idea of the effects, diseases, cause and genesis of death associated with the intake of psychoactive substances is based on an in-depth study, comparing all data - from the scene, criminal and anamnestic information from relatives, acquaintances and eyewitnesses to available morphological macro- and microscopic changes of organs and tissues, supported by the relevant chemical analysis. The presented results show a great variety in the combination of the respective factors in each individual case, which ended in death. Below are described some of the morphological changes in vital organs and tissues, observed during the investigated period.

Myocardium: In the cases we studied, the following macroscopic changes were observed - left ventricular cardiac hypertrophy, myocardiofibosis, coronary atherosclerosis, calcification of the venous and arterial walls, acute venous stasis. The most common histological changes in the myocardium that we observed in cases of deceased with prolonged history of illicit drug were undulation and fragmentation of the cardiomyocytes (Figure 4A), and focal lipomatosis (Figure 4B), as well as pronounced perivasal and interstitial fibrosis, and oedematous changes. In some cases, we found circular cell infiltrates in the interstitium - evidence of myocarditis (Figure 4B). In other cases, we observed the presence of foreign bodies in the form of particles of crystalline substance (undissolved oral tablets, talc, etc., mixed with the "street" dose of heroin), as well as other undissolved and poorly filtered elements injected with the drug into the bloodstream, reaching the coronary vessels. Such alterations also exist in the lungs, where, like in the heart, foreign-body granulomas are formed (Figure 4C).

Lungs: Frequent findings in the lungs were interstitial and intraalveolar edema (Fig. 5A). In most of the cases macroscopically lungs filled the chest cavity, they were heavy, grayish-purple in color, under pressure there were dimples left, and from the cut surface and under lateral pressure a yellowish-pink oedema fluid was observed. In the last years there have been frequent cases where the intake of a narcotic substance (most often heroin) results in vomiting with subsequent massive aspiration of stomach contents and death occurred from mechanical asphyxia due to the aspiration of food particles. Other frequently observed changes affecting pulmonary parenchyma were of an inflammatory nature (Figure 5B), mainly of non-specific origin, such as bronchitis, bronchiolitis, pneumonia with involvement of a significant portion of pulmonary parenchyma, sometimes pleural effusions with pleuritis, and subsequently pleural adhesions. There have been cases where the morphological finding showed a particular cause of the infection /Pneumocystis carinii, Mycobacterium tuberculosis and others/ (Figure 6A-C). In one single case, epitheloid cell granulomas was formed, with giant Langhans cells. (Figure 6D).

Central nervous system (CNS): Due to the impact of psychoactive substances on the CNS with related blocking of neurotransmitters, prolonged drug abuse may result in irreversible damage to neurons and synapses. Additionally, there is an increase in cerebral blood flow leading to haemodynamic and liquor-dynamic disturbances. In most of the cases, macroscopic brain edema is evident, as the brain becomes soft and smooth and overfills the cranial vault, gyri (ridges) become flattened, sulci (grooves) become narrowed, and ventricular cavities become compressed. These changes are also demonstrated histologically - pericellular and perivasal cerebral edema of histological material stained with hematoxylin and eosin, presented in varying degrees depending on the speed of dying. In addition macroscopically, cerebral cortex atrophy was also observed, as well as at the same time the change was demonstratively seen during the microscopic examination of the cerebrum. Furthermore, there was a disruption in the normal architectonics of the cells in the brain cortex, the latter being chaotic (Figure 7A). These changes were observed in a large number of people with evidence

of longer-term use of narcotics, especially in cases where heroin and marihuana were used. In single cases where the death was a result of a brain disease we observed inflammatory changes in cerebral tissue such as focal leukoencephalitis (Figure 7B), inflammatory changes in the meninges with adhesions, and also vascular changes (Figure 8A). We have also observed cases where the death was a result of encephalitis, meningoencephalitis, and opportunistic infections such as toxoplasmosis, Epstein Barr virus infections and others. A common morphological finding in most cases is the presence of acute venous stasis. In some cases, we observed severe changes in the wall of the cerebral blood vessels due to its erosion and extravasation around the vessel or separation of the layers of the vessel wall with absorption of liquid components (proteins). Often, in cases of proven stimulant abuse we have seen massive intracerebral hematomas or basal subarachnoid haemorrhages (due to vascular wall damage of an arterial blood vessel), with the rapid development of compression syndrome and death (Figure 8B).

Liver: The most common morphological finding in liver tissue was the fatty degeneration (Figure 9A), expressed in varying degrees. In some of the cases it is in combination with inflammatory infiltrates of mononuclear cells and segmented leukocytes in the portal spaces - toxic hepatitis (Figure 9B). In single cases, we have established solitary and disseminated abscesses.

Kidneys: Chronic use of narcotic drugs, especially intravenous ones, may lead to the development of kidney disease, although the factors determining individual sensitivity are still poorly studied, and it is not always clear whether it is the result of injecting the drug itself or is also due to other factors. Kidney changes associated with prolonged drug abuse are most commonly associated with the presence of focal to diffuse interstitial fibrosis, mononuclear or segmented leukocyte infiltrates and renal tubular atrophy, the latter depending on the degree of interstitial fibrosis and the amount of fully sclerosed glomeruli (Figure 10 A). Another common findings were degenerative changes in the epithelial cells (mainly involving the proximal tubules) to the degree of necrosis with the tubular basal membrane being exposed and, in some cases, the rupture of the latter (Figure 10B). Changes common for some types of glomerulopathies (with minimal changes, membranous and membranoproliferative type) were rare. In some cases, amyloid deposition occurs in the kidneys, especially in long-term heroin addiction, in addicts with compromised immune system (Figure 10 C).

Drug addicts are experiencing the above-described changes that are potentiated by both the disease itself and the immune deficiency caused by it, and by reducing the body's resistance due to the chronic psychoactive substance abuse.

Conclusion

In the genesis of death there is an overlap of the effects of the drug with disease alterations in various organs and tissues occurring due to the prolonged intake of psychoactive substances. The observed changes in the myocardium, lungs, brain tissue, liver and kidneys can be an independent cause of death, create conditions for the development of other diseases, most often of an inflammatory nature with severe complications, or are beneficial factors for mortal outcome for another reason. These disorders are due to the direct toxic effects of the narcotic substances as well as a consequence of reduced humoral and cellular immunity, resulting in decreased resistance of the organism to infections of different origin.

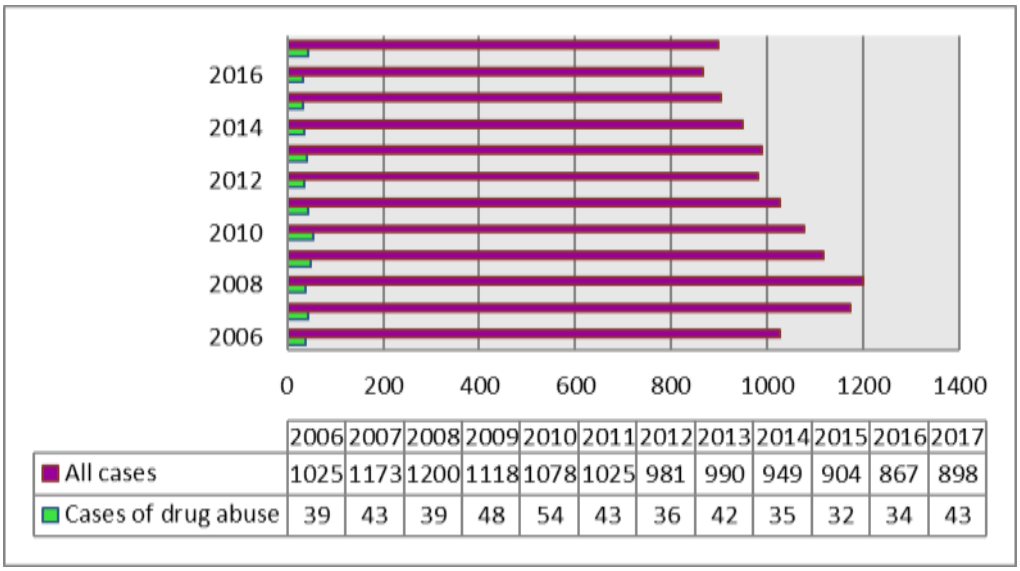
In our study, we have found that there are multiple and diverse morphological changes in different tissues and organs that are not specific for the different types of drugs, but combined they are characteristic for a prolonged abuse with psychoactive substances. Knowing the morphological characteristics of the changes in different tissues and organs could enable

forensic and pathology specialists to properly diagnose the various cases and thus direct and assist the investigating authorities.

Statement for potential conflicts of interest: The authors declare that they have no conflict of interest.

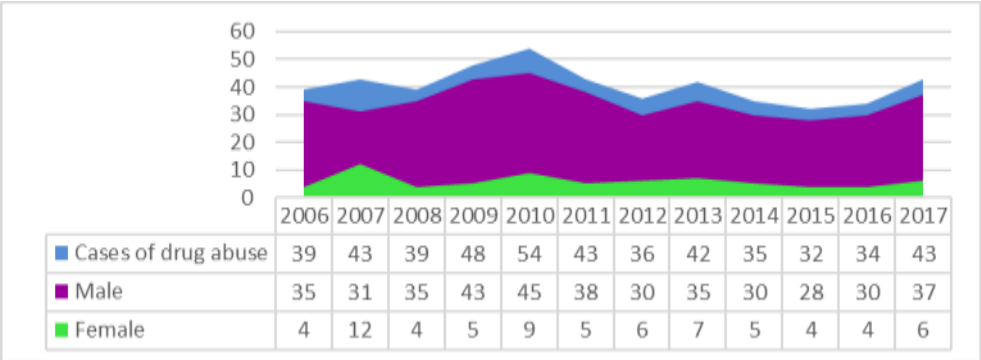
References

1. Караджов, Юл. н.с.: Наркотиците - почти всичко за тях, София 2003г. Издателство: Дилок
2. Edland, J. F. (1972). Liver disease in heroin addicts, Hum. Pathol., 3(1), pp. 75–84.
3. Louria, D. B., Hensle, T. et al. (1967). The major medical complications of heroin addiction, Ann. Intern. Med., 67(1), pp. 1–22. 42
4. Дьони Ришар, Жан-Луи Сенон: Дрогите, Енциклопедия Larousse, 2003г.;
5. Игор Куценок, Георги Димитров: Злоупотреба и зависимост от психоактивни вещества, София 2004г.;
6. Milroy CM, Parai JL. The histopathology of drugs of abuse. Histopathology. 2011; 59: 579–593.
7. Bakir, A. A. and Dunea, G. (1996). Drugs of abuse and renal disease, Curr. Opin. Nephrol. Hypertens., 5(2), pp. 122–126.
8. Dettmeyer R, Friedrich K, Schmidt P, Madea B. Heroin-associated myocardial damages—conventional and immunohistochemical investigations. Forensic Sci Int. 2009; 187: 42–46.
9. Adelman, L. S. and Aronson, S. M. (1969). The neuropathologic complications of narcotics addiction, Bull. N.Y. Acad. Med., 45(2), pp. 225–234.
10. Arnett, E., Battle, W. et al. (1976). Intravenous injection of talc-containing drugs intended for oraluse: a cause of pulmonary granulomatous and pulmonary hypertension,Am. J. Med.,60, pp. 711–718.
11. Dettmeyer, R., Schmidt, P. et al. (2000). Pulmonary edema in fatal heroin overdose: immunohistological investigations with IgE, collagen IV and laminin: no increase of defects of alveolarcapillary membranes, Forensic Sci. Int., 110(2), pp. 87–96.
12. Karch, S.B., MD, Karch's pathology of drug abuse, Third edition, 2002



	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
All cases	1025	1173	1200	1118	1078	1025	981	990	949	904	867	898
Cases of drug abuse	39	43	39	48	54	43	36	42	35	32	34	43

Figure 1. The cases of drug abuse compared to all autopsies of deceased, performed in the Department of forensic medicine and deontology for the period 2006-2017.



	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Cases of drug abuse	39	43	39	48	54	43	36	42	35	32	34	43
Male	35	31	35	43	45	38	30	35	30	28	30	37
Female	4	12	4	5	9	5	6	7	5	4	4	6

Figure 2. Cases of confirmed drug abuse and gender distribution.

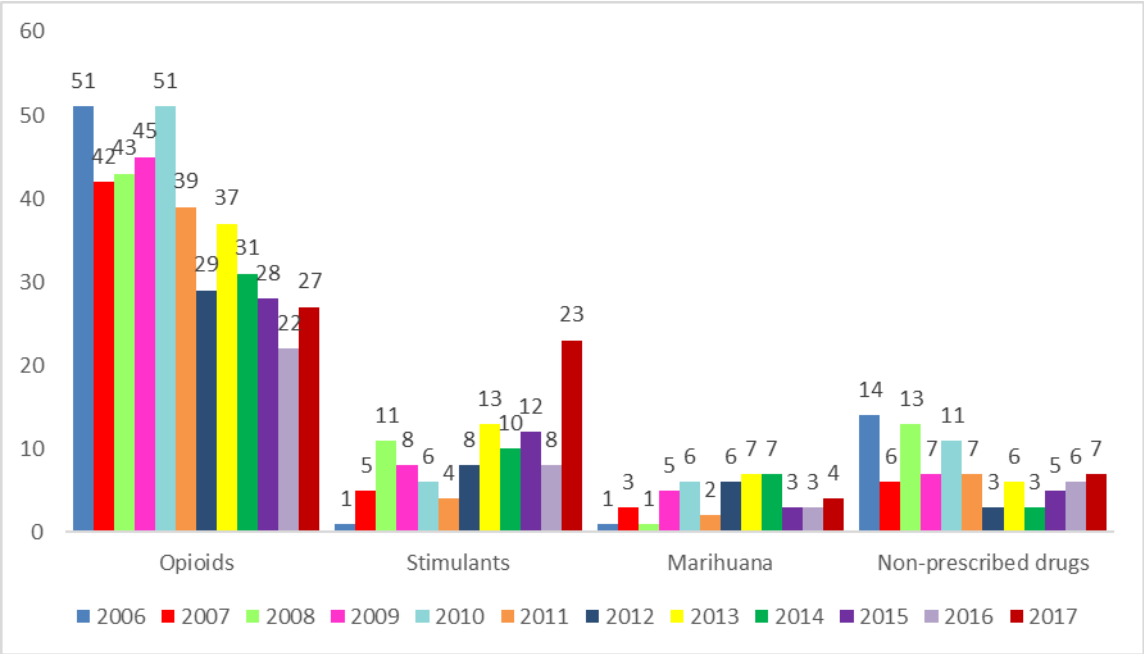


Figure 3. Results from the chemical analysis of the deceased for the period 2006-2017.

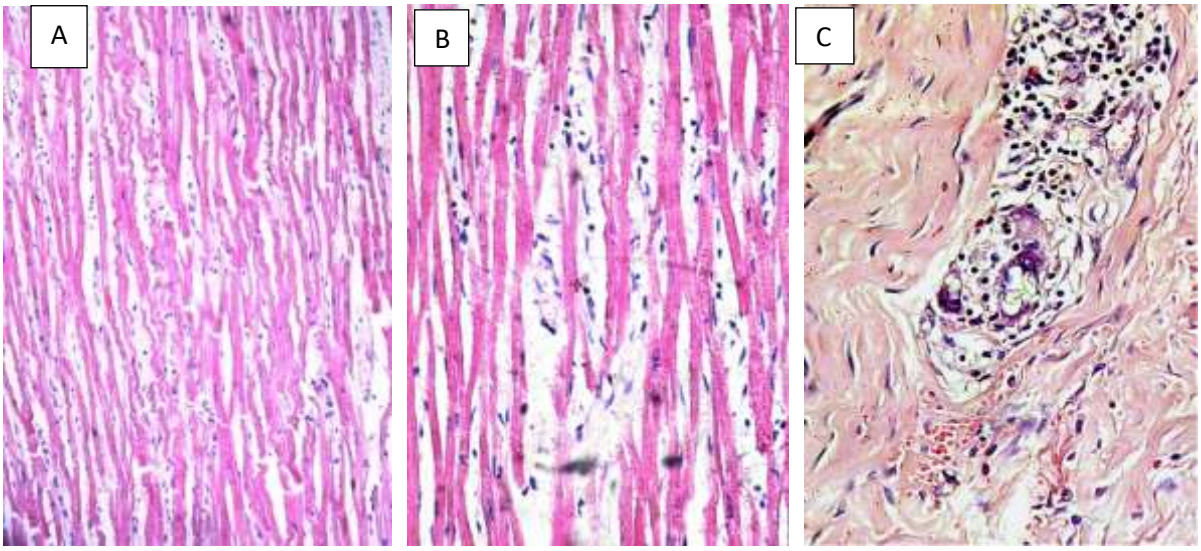


Fig. 4 Myocardium – **(A)** Focal undulation and fragmentation of cardiomyocytes, general degenerative changes in the heart muscle. Expressed perivasal fibrosis. Hemaloun-eosin. Original magnification 10x25; **(B)** Myocarditis - cardiomyocyte fragmentation, general

degenerative changes, lipomatosis and oedema in the interstitium, scarring inflammatory infiltrates in the interstitial, predominantly lymphocytes, Fig. Hemaloun-Eosin; Original magnification 10x40; **(C)** "Foreign body" granuloma with the presence of a crystal-like substance in the lumen of a small coronary blood vessel. Hemaloun-eosin. Original magnification 10x40.

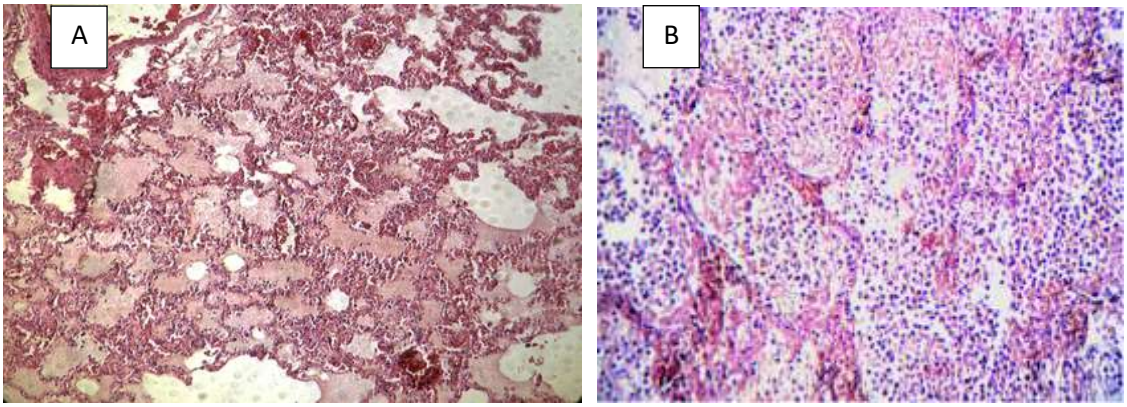


Fig.5 Lung – (A) Interstitial and intraalveolar edema, bleeding - mostly interstitial. Pic. hemaloun-eosin. Original magnification 10x10; (B) Abundant intraalveolar infiltration with segmental leukocytes and mononuclear cells with fresh hemorrhage. Hemalaun - Eosin. Original magnification 10x25

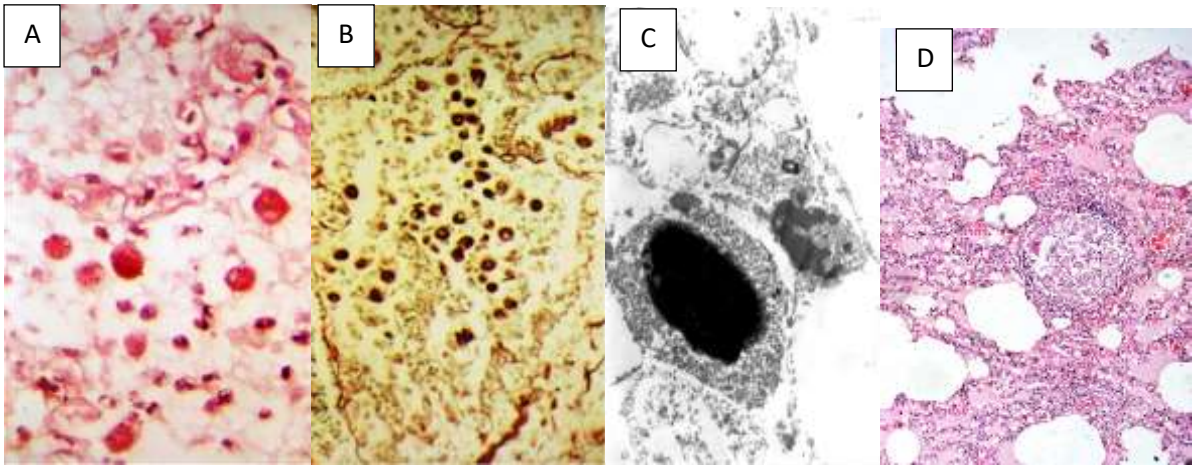


Figure 6. Presence of many round non-nuclear structures in the pulmonary alveoli (Pneumocystis carinii), with the presence of foamy matter around them. Hemalaun-Eosin. Original magnification 10x40 (A) and Silver impregnation according to Gomori - Grocott. Original magnification 10x25 (B); (C) Presence of an infectious agent in the cytoplasm of a lung cell - Pneumocystis carinii. Electronogram. Original magnification x 6400; (D) Interstitial and intraalveolar edema, presence of epitheloid cell granuloma with the presence of giant Langhans cells; Hemaloun-eosin. Original magnification 10x25

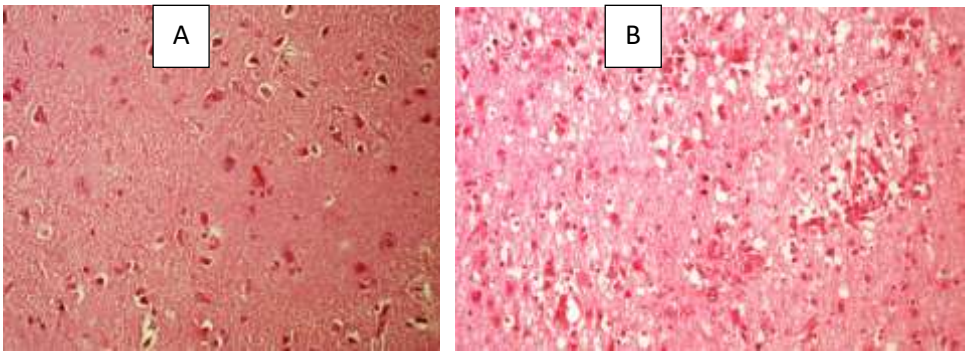


Figure 7. (A)Cerebral cortex - atrophy (devastation, reduced number of cells, in some places only shadows of cells remain, as the cells are indiscriminately arranged with different orientation); Hemalaun-Eosin, original magnification 10x60; (B) Leukoencephalitis (focal changes) - pericellular accumulations of lympho-plasma and giant cells (giant cell encephalitis) color. Hemalaun-Eosin, original magnification 10x60;

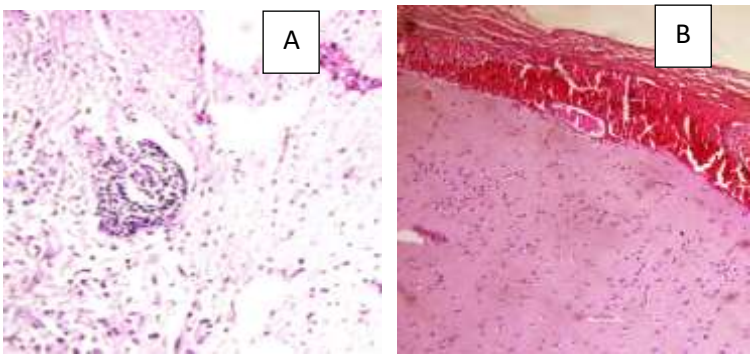


Figure 8 (A) Brain tissue with pericellular and perivascular edema and vascular alterations in single microcirculatory vesseles, Hemalaun-Eosin, Original magnification 10x40; (B) Subarahnoid hematoma - Hemalaun-Eosin, original magnification 10x25

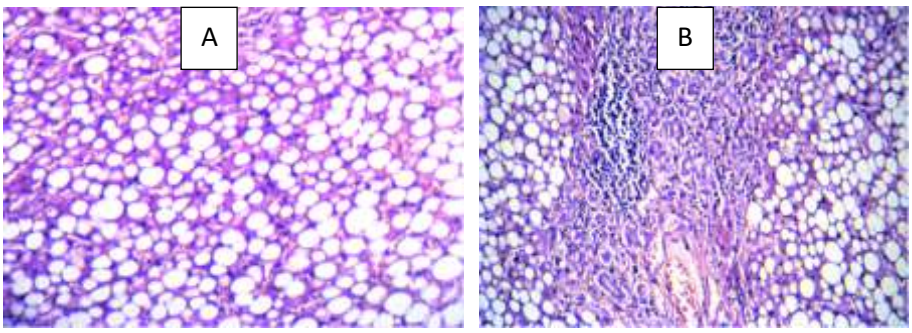


Figure 9. Liver – (A) Fatty degeneration, Hemaloun-Eosin, Original 10x20 magnification; (B) Mononuclear infiltration in the portal space with proliferation of bile ducts and fatty degeneration of hepatocytes. Hemalaun-Eosin. Original magnification 10x20.

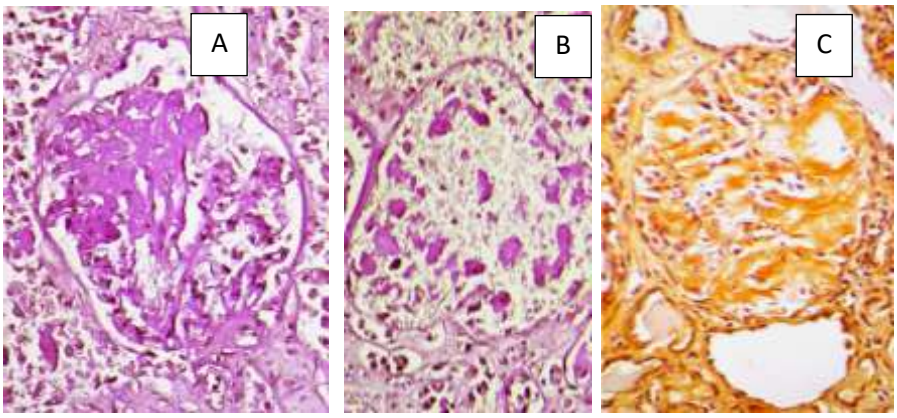


Figure 10. (A) Segmental sclerosis and hyalinosis in the glomerulus. PAS reaction. Original magnification 10x25. (B) Severe dystrophic to necrotic changes in the glomerulus with exposure and rupture of the tubular basement membrane. PAS reaction. Original magnification 10x25. (C) Abundant deposition of homogeneous matter (amyloid) in the mesangium and basal glomerular capillaries. Congo red. Original magnification 10x25.