



MORPHOLOGICAL CHANGES IN THE LUNGS CAUSED BY INTRAVENOUS HEROIN ABUSE

Al. Alexandrov¹, B. Landzhov^{2*}, St. Hristov¹, D. Hinova-Palova², T. Todorov³,
A. Palov², L. Malinova², D. Nikolov¹, T. Alexandrova⁴

¹Department of Forensic Medicine and Deontology, Medical University, Sofia, Bulgaria

²Department of Anatomy and histology, Medical University, Sofia, Bulgaria

³Department of Pathology, Medical University, Sofia, Bulgaria

⁴Department of Dialysis, Hospital "Alexandrovska", Sofia, Bulgaria

ABSTRACT

Upon examining cadavers of addicts with a long history of intravenous heroin use, we found a number of macroscopic and microscopic morphologic pathological changes in the lungs connected with an acute inflammatory reaction in the alveolar wall with exudation, a large number of round structures without nuclei in the pulmonary alveoli surrounded by a pale, foam-like substance, round structures without nuclei in the pulmonary alveolus surrounded by mononuclear cells. We established the causes of lungs diseases both by means of histochemical studies and on an ultrastructural level by means of electron-microscope study. Their characteristics, localization and severity depend on the period of intravenous use of heroin, adhering to the main principles of aseptic treatment and the purity of and other substances in street heroin. We studied the morphologic (macro- and microscopic) changes of the lungs and also carried out a chemical analysis of blood, urine and internal organs to check for heroin (or its metabolites) in the body, as well as the quantity of narcotic substances relative to the cause of death, i.e. whether death resulted from severe intoxication as a result of the dose taken or from the morphologic pathological changes as a result of prolonged intravenous heroin use.

Key words: heroin, heroin addiction, lungs disease, morphological changes.

INTRODUCTION

Heroin (diacetylmorphine, diamorphine) was first produced in London in 1874 with the purpose to serve as a unique painkiller and to aid physicians in treating their patients. It is a polysynthetic derivative of morphine with a stronger and more prolonged effect. It is one of the opium alkaloids and is derived after processing opium from opium poppy seeds. It affects the nervous system directly with several direct and indirect effects on vital organs and systems.

Heroin-induced pulmonary edema during an autopsy has been described first by Osler in 1880 (1, 2). The first time it is used, heroin

often has unpleasant effects, such as headaches, nausea and vomiting. The second and third time these effects tend to disappear. Two of the main factors behind the lethal outcome of taking "street" narcotics is that the pure content of street doses varies (in Bulgaria it is between 0% and 20%, rarely more) and the presence of additional substances (3).

Heroin is the most powerful drug contained in opium (around three times stronger than morphine). It can be snorted after it is heated up or mixed with tobacco or marijuana and smoked, but the best and fastest "high" is after injecting. Addicts prefer this way because they get the best result with the smallest possible amount and save money. Either way it is taken, once it has entered the body heroin is quickly metabolized into morphine and has higher lipid solubility, a much faster effect and a shorter half-life than morphine. The characteristics, localization and severity of lung disease depend on a number of key factors – the period of intravenous use of heroin; adhering to the

***Correspondence to:** Assoc. Prof. Boycho V. Landzhov, MD, PhD, Medical University, Sofia-1431, Bulgaria, Department of Anatomy and Histology, 1 Georgi Sofiiski blvd., Tel: +359+29172608, Fax: +359+28518783, E-mail: landzhov_medac@abv.bg

main principles of aseptic treatment and the purity of and other substances in street heroin.

According to some authors (4-7) the morphological pathological changes in many organs are a result from changes in the immune system, which are in turn due to the impact of painkiller drugs on the humoral immune response and cell-mediated immunity. The direct effect of analgesic drugs on the immune system is lower resistance of the body to specific and non-specific infections, which is one of the main causes of morphological changes to the organs observed both during treatment of patients and upon examining the cadavers of long-term heroin addicts.

The object of our study was to establish light- and electron-microscopic changes in lungs of heroin addicts, who died following long-term intravenous use.

MATERIALS AND METHODS

We examined 45 patients (25 men and 20 women), who died following long-term intravenous heroin use (between 12 and 84 months), at the Centers of forensic medicine and Clinical pathology of Alexandrovska University Hospital between 2005 and 2011. We studied the microscopic (incl. electron-microscopic) pathological changes in lungs to determine their type and the damage of the

toxic substance. The obtained cadaver material was fixed in 10 % formalin for light-microscopic examination. Paraffin-embedded material was cut on 6 µm sections and stained with Hematoxylin-eosin, Gomori-Grocott silver impregnation and PAS-rection. For ultrastructural study we used a solution of: 2% paraformaldehyd and 2% glutaraldehyd. The material was rinse in a 0, 1 M phosphate buffer, placed in a 1% solution of Os tetraoxyde, washed with the phosphate buffer and dehydrated in an increasing alcohol order until 100%. Afterwards, it was thoroughly washe in order to eliminate debris of bloody elements and other external particles and was include in durkopan. Ultra thin slices were made (80 nm). The contrasting of the ultra thin slices was implemente with Pb nitrate and then was examine with electron-microscope Hitachi.

RESULTS

We observed inflammatory changes in the lungs, which were usually non-specific: bronchitis, bronchiolitis and focal pneumonia (**Figure 1**). In other cases the morphological study showed that *Pneumocystis carinii* – lung damage described in medical texts by many leading scientists – had caused pneumonia (**Figures 2, 3**).

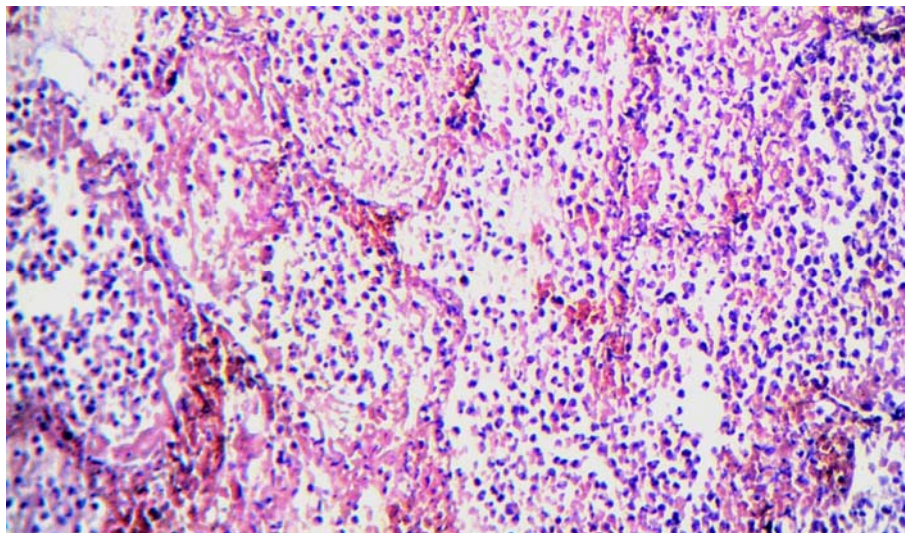


Figure 1. Non-specific inflammatory changes in the lungs (pneumonia) of deceased heroin addicts. Hematoxylin-eosin staining. Magnification (x100).

We determined the specific and non-specific inflammatory changes observed in the lungs of deceased heroin addicts. Foreign bodies such as pieces of crystal-like substances, as well as

other undissolved and poorly filtered foreign bodies injected with the drug can be found in the central part of the blood capillaries, which progress at different rates (**Figure 4**).

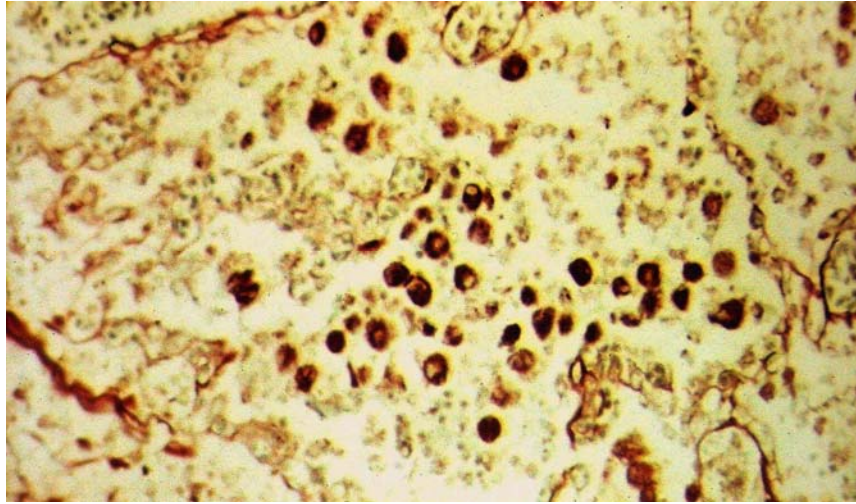


Figure 2. A large number of round structures without nuclei in the pulmonary alveoli (*Pneumocystis carinii*) surrounded by a pale, foam-like substance. Silver impregnation technique a.m. Gomori-Grocott. Magnification (x250).

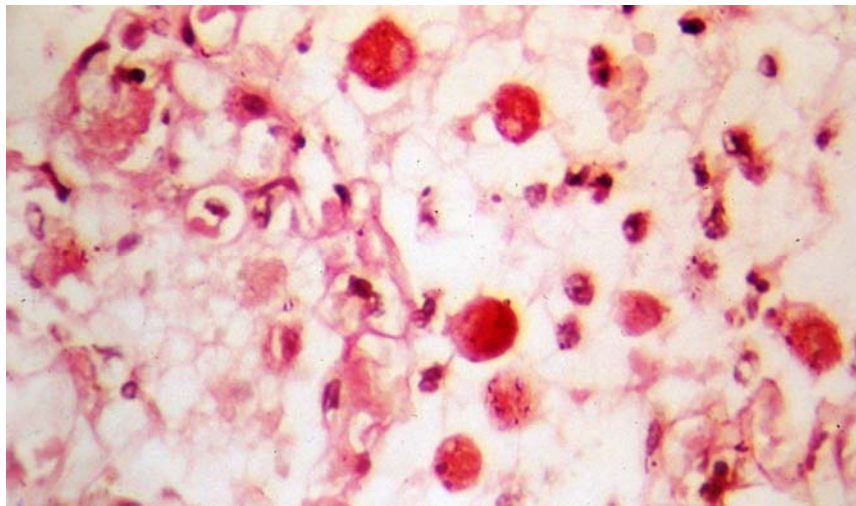


Figure 3. Round structures without nuclei in the pulmonary alveolus surrounded by mononuclear cells. Staining procedure PAS-reaction. Magnification (x400).

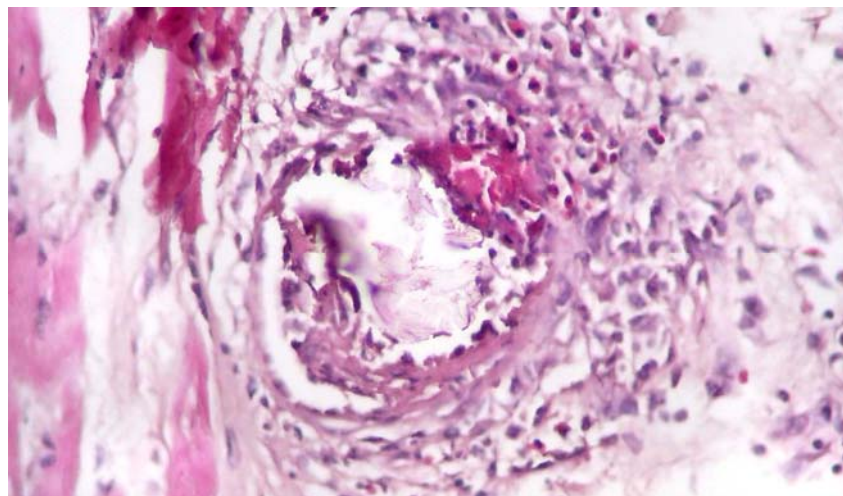


Figure 4. Inflammatory changes observed in the lungs of deceased heroin addicts. Foreign bodies such as pieces of crystal-like substances. Arteritis granulomatosa. Hematoxylin-eosin staining. Magnification (x600).

We were able to establish the cause of pneumocystic pneumonia both by means of histochemical studies (silver impregnation technique a.m. Gomori-Grocott and staining

procedure PAS-reaction) and on an ultrastructural level by means of electron-microscope study (**Figures 5, 6**).

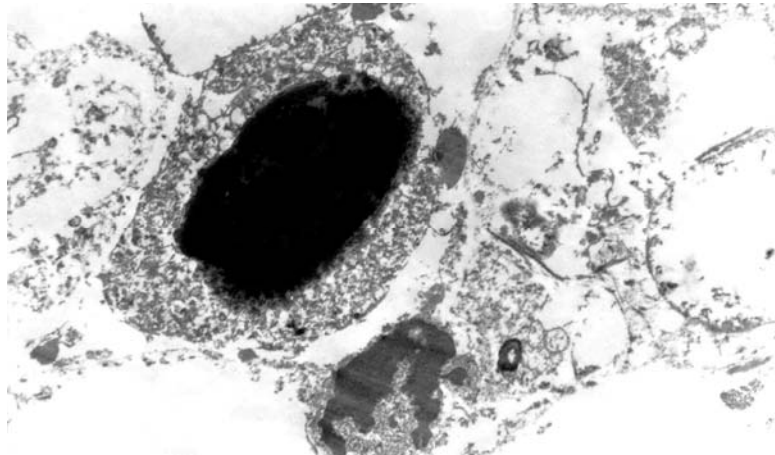


Figure 5. Small cyst formation with thick osmiophilic wall in the cytoplasm of Type II pneumocyte. Original magnification (x6400).

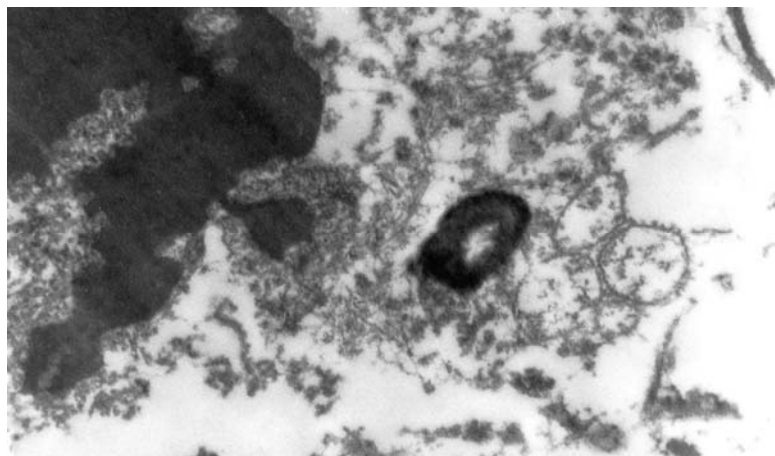


Figure 6. Small cyst formation with thick osmiophilic wall in the cytoplasm of Type II pneumocyte. Original magnification (x12000).

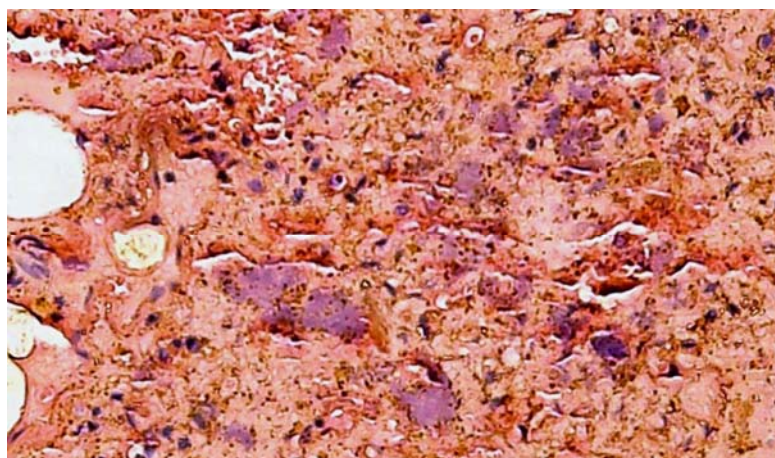


Figure 7. Case with specific inflammatory damage to the lungs and fungal colonies among the parenchyma. Hematoxylin-eosin staining. Magnification (x 250).

In other cases we observed severe chronic specific inflammatory damage to the lungs – secondary fibrous cavernous tuberculosis with large areas affected by caseous pneumonia and fungal colonies among the parenchyma (Figure 7).

DISCUSSION

The common agents associated with drug-induced lung diseases include heroin abuse, chemotherapeutic drugs, antiarrhythmic drugs, antibiotics, anticonvulsants, anti-inflammatory agents. Heroin is associated with pulmonary toxicity. The lungs can be damaged by injection or inhalation of illicit drugs. Since Osler first described heroin-induced noncardiogenic pulmonary edema during an autopsy in 1880, illicit drugs have been implicated in these diseases. Bhadra and Suratt, 2009 discuss drug-induced lung diseases related to cocaine, opiates, and talc, a common contaminant of injectable drugs of abuse (8). Vascular congestion and pulmonary edema are the most common findings in users who died within 3 hours of overdose. In contrast, lobar pneumonia was the predominant finding in those who died more than 12 hours after the overdose. Pulmonary edema and hypoxic respiratory failure are the classic complications of heroin overdose (9). The immunosuppressive effect of heroin is not well known. We determined the specific and non-specific inflammatory changes observed in the lungs of deceased heroin addicts. It appears that prolonged abuse of “street” heroin is the most frequent cause of severe immunodeficiency along with HIV. This makes the user vulnerable to pneumocystic pneumonia, which is sometimes the direct cause of death. We should point out that other drugs have this immunosuppressive effect as well. Chronic exposure to morphine suppresses cytotoxic T-lymphocyte activity in the spleen and peritoneum via μ -opioid receptors. Opiate-induced asthma and other conditions provoked by drug abuse can make death more likely to occur (10). A case in point is that of a 29-year old male with ulcerations that did not heal and skin necrosis of the lower limbs, which developed over a period of six months, caused by injecting heroin and cocaine under the skin (11). Other authors describe the case of an HIV-positive intravenous addict with diffuse thrombosis of the superficial veins all over the body and periphlebitis with perivascular abscesses, who injected cocaine and heroin into his neck veins. He also suffered from oral

candidiasis, Hepatitis C, bronchopneumonia, endocarditis and tricuspid valve insufficiency (12).

Lungs infections and pneumonia of different geneses, resulting from aspiration, septic lung emboli, etc., lung abscesses, tuberculosis, yeast infections, and vascular disorders such as arteritis, thrombosis and fibrosis of lung arteries, arterioles and capillaries (which can lead to cor pulmonale with time). Foreign bodies such as pieces of talc and/or crystal substances (from undissolved pills for peroral administration mixed with the heroin), as well as other undissolved and poorly filtered foreign bodies injected with the drug can be found in the central part of the blood clots (thrombus), which progress at different rates. Other complications include mycotic aneurysms of the blood vessels in the lungs, hypertrophy of the media of lung arteries, parenchymal diseases – pulmonary edema, progressive massive fibrosis, emphysema, hemosiderosis, and interstitial pneumonia with fibrosis (13, 14).

J.B.Downie et al. describe a patient abusing heroin by intranasal use that developed pemphigus vegetans, Neumann type (15). The connection between intranasal heroin use and development of pemphigus vegetans is a subject of analysis. According to Bhadra and Suratt, 2009, alveolar hypoventilation does not directly affect the lung parenchyma. Alveolar hypoventilation results from decreased ventilatory function. Narcotics, salicylates, tocolytics and protamine are usually implicated in noncardiogenic pulmonary edema with increased alveolar capillary membrane permeability. Bronchiolitis obliterans is a chronic form of drug-induced lung diseases characterized by inflammation and occlusion of the airways (16).

In chronic cases can be viewed fibrotic changes, including honeycombing and traction bronchiectasis (17). Lung biopsy specimens demonstrate loosely formed granulomas near the terminal bronchioles and lymphocytic and plasma cell infiltration of the alveolar walls. Pathology may demonstrate a nonspecific or usual interstitial pneumonitis pattern. Alveolitis with or without pulmonary fibrosis is a well-recognized clinical syndrome. Patients with alveolitis typically present with shortness of breath that may be acute, subacute, or chronic. Features on physical

examination include inspiratory lung crackles, weight loss, and sometimes clubbing of the digits.

CONCLUSION

The heroin causes morphological changes and damage of varying intensity and clinical significance to lungs when injected over a long period of time. Possessing knowledge of the morphological substrate of these changes enables experts of forensic medicine and pathoanatomy to give a quick and correct diagnosis of cases in their practice, thereby assisting clinicians, law enforcement officials and investigators.

REFERENCES

1. Sternbach, G., William Osler: narcotic-induced pulmonary edema. *J Emerg Med*, 1:165-167, 1983.
2. Sporer, K.A., Dorn, E., Heroin-related noncardiogenic pulmonary edema: a case series. *Chest*, 120:1628-1632, 2001.
3. Alexandrov, A., Forensic study of deceased with evidence for use of drugs. Bulgaria: Doctor's Thesis, 2010.
4. Zaki, N.G., Osman, A., Moustafa, H., Saad, A.H., Alterations of immune functions in heroin addicts. *Egypt J Immunol*, 13:153-71, 2006.
5. Tan, A. U. Jr., A. H. Cohen et B. S. Levine. Renal amyloidosis in a drug abuser. *J Am Soc Nephrol*, 5:1653-8, 1995.
6. Stefano, G.B., Leung, M.K., Bilfinger, T.V., Scharrer, B., Effect of prolonged exposure to morphine on responsiveness of human and invertebrate immunocytes to stimulatory molecules. *J Neuroimmunol*, 63:175-181, 1995.
7. Simonart, Th., Parent, D., Heenen, M., Farber, C.M., Van Vooren, J.P., Decreased skin reactivity to codeine in patients with the acquired immunodeficiency syndrome.

ALEXANDROV AL., et al.

Clin Immunol Immunopathol, 81:12-15, 1996.

8. Bhadra, K., Suratt, B., Drug-induced lung disease: a state-of-the-art review. *J Resp Dis*, 30:1-17, 2009.
9. Wolff, A.J., O'Donnell, A.E., Pulmonary effects of illicit drug use. *Clin Chest Med*, 25:203-216, 2004.
10. Merigian, K. and Blaho, K., The role of pharmacology and forensics in the death of an asthmatic. *J Anal Toxiol*, 19: 522-528, 1995.
11. Reese, W. G. and Sullivan, L. M., Tc-99m labeled wBC of lower extremity abscesses and skin necrosis due to skin pooping. *Clin Nucl Med*, 22:865-866, 1997.
12. Maggi, P., Fullone, M., Federico, M., Angarano, G., Pastore, G., Regina, G., Drug injection in jugular veins: a new risk factor for vascular diseases in HIV-infected patients? A case report. *Angiology*, 46:1049-1052, 1995.
13. Spencer's - Pathology of the lung - 5th edition, Intravenous Drug Abuse.
14. Carr, D. J. and Serrou J. M., *Immunopharmacology*, 31, , Ref. 118, 59-71, 1995.
15. Downie, B., Dicostanzo, D. P. and Cohen S. R., Pemphigus vegetans neumann variant associated with intranasal Heroin abuse. *J Am Acad Dermatol*, 39:5 Suppl.2, 1998
16. Visscher, D.W. and Myers, J.L., Bronchiolitis: the pathologist's perspective. *Proc Am Thorac Soc*, 3:41-47, 2006
17. Silva, C.I., Churg, A., Muller, N.L., Hypersensitivity pneumonitis: spectrum of high-resolution CT and pathologic findings. *AJR*, 188:334-344, 2007.