ABSTRACT
A complex forensic study of deceased with data of drug abuse is presented. Both morphological changes in different target tissues and organs related to prolonged intake of drugs and illicit substances and statistical representation of the frequency of such kind of deaths were investigated. The causes of death are compliant with drug types found in the chemical analysis of biological fluids and/or internal organ samples taken during the autopsies. The purpose of the study is to investigate and track the statistical changes for the indicated period to enrich and update the data from the systematic and periodic targeted mortality surveys conducted in the Department of Forensic Medicine and Deontology in deceased with data on long-term use of narcotic substances, as well as the characteristic morphological changes identified therein. The conducted survey covers a five-year period (2013-2017) concerning all deceased undergoing forensic examination at the Department of Forensic Medicine and Deontology at the University Hospital "Aleksandrovsk". Both macroscopic and microscopic morphological methods of investigation, autopsy and light microscopic examination of necropsy with classic and special stains, as well as statistical approaches, were used to schematically illustrate the obtained results. During the reported period, a total of 179 cases of deceased with drug abuse data were examined, taking into account their annual distribution as frequency, their causes of death and characteristic morphological changes in tissues and internal organs. The periodic statistical follow-up of cases of deceased drug abusers compared to their causes of death permits a wider and more up-to-date look at the type and distribution of drugs offered on the "black market", which in turn allows for timely referral to the various institutions involved in countering drug trafficking, prevention and treatment of drug addicts.

Key words: drugs, drug addicts, morphological changes, statistical study

INTRODUCTION:
A complex forensic study of deceased with data of drug abuse is presented. Both morphological changes in different target tissues and organs related to prolonged intake of drugs and illicit substances were investigated and statistical representation of the frequency of such kind of deaths. The causes of death are compliant with drug types found in the chemical analysis of biological fluids and/or internal organ samples taken during the autopsies.

OBJECTIVE:
The purpose of the study is to investigate and track the statistical changes for the indicated period to enrich and update the data from the systematic and periodic targeted mortality surveys conducted in the Department of Forensic Medicine and Deontology in deceased with data on long-term use of narcotic substances, as well as the characteristic morphological changes identified therein.

MATERIAL AND METHODS:
The conducted survey covers a five-year period (2013-2017) concerning all deceased undergoing forensic examination at the Department of Forensic Medicine and Deontology at the University Hospital "Aleksandrovsk", who died on the territory of Sofia-city and Sofia region. Both macroscopic and microscopic morphological methods of investigation, autopsy and light
microscopic examination of necropsy with classic and special stains, as well as statistical approaches, were used to schematically illustrate the obtained results.

RESULTS:

During the reported period, a total of 179 cases of deceased with drug abuse data were examined, taking into account their annual distribution as frequency, their causes of death and characteristic morphological changes in tissues and internal organs.

In 2013 we examined a total of 42 cases, as follows: 35-men and 7-women; Acute poisoning with heroin – 5 cases; Acute combined poisoning with narcotic substances – 9 cases; Acute combined poisoning with narcotic substances and alcohol – 4 cases; Different traumatic incidents (suicide, murder and accidents) after drug use – 3 cases; Death due to disease after drug use – 9 cases; Mechanical asphyxia due to aspiration (inhalation) of vomiting (as a reaction to the body of acute poisoning) after drug intake – 11 cases; Suicide by other medicines in people with prolong drug abuse – 1 case

In 2014 a total of 35 cases were examined, of which: 30-men and 5-women; Acute poisoning with heroin – 5 cases; Acute combined poisoning with narcotic substances – 2 cases; Acute combined poisoning with narcotic substances and alcohol – 11 cases; Different traumatic incidents (suicide, murder and accidents) after drug use – 7 cases; Disease due to drug abuse – 8 cases; Mechanical asphyxia due to aspiration (inhalation) of vomiting (as a reaction to acute poisoning) after drug intake – 1 case; Suicide by other medicines in people with prolong drug abuse – 1 case

In 2015 we observed a total of 32 cases, of which: 28 men and 4 women; Acute poisoning with heroin – 3 cases; Acute combined poisoning with narcotics – 10 cases; Acute combined poisoning with narcotic substances and alcohol – 1 case; Different traumatic incidents (suicide, murder and accidents) after drug use – 7 cases; Disease due to drug use – 6 cases; Mechanical asphyxia due to aspiration (inhalation) of vomiting (as a reaction to acute poisoning) after drug intake – 4 cases; Suicide by other medicines – 1 case

In 2016 the total cases of drug abuse were 34, of which: 29 men and 5 women; Acute poisoning with heroin – 6 cases; Acute combined poisoning with narcotic substances – 9 cases; Acute combined poisoning with narcotic substances and alcohol – 4 cases; Different traumatic incidents (suicide, murder and accidents) after drug use – 5 cases; Disease due to drug use – 7 cases; Mechanical asphyxia due to aspiration (inhalation) of vomiting (as a reaction to acute poisoning) after drug intake – 3 cases; Suicide by taking other medicines – 0 cases

In 2017 we examined a total of 36 cases, of which: 31 men and 5 women; Acute poisoning with heroin – 7 cases; Acute combined poisoning with narcotics – 8 cases; Acute combined poisoning with narcotic substances and alcohol – 6 cases; Different traumatic incidents (suicide, murder and accidents) after drug use – 3 cases; Disease due to drug use – 6 cases; Mechanical asphyxia due to aspiration (inhalation) of vomiting (as a reaction to acute poisoning) after drug intake – 6 cases; Suicide by taking other medicines – 0 cases

The most frequently observed macroscopic morphological changes depending on the type and mode of intake of the drug are:

- When smoking a variety of marijuana products, pigmentations (darkening) on the tooth enamel, mainly on the crown of the incisors, can be observed due to the presence of more tar than in the mass of tobacco products. Smoking of the so-called laced weed, combined with other psychoactive substances like cocaine, amphetamines, heroin, or psychoactive drugs (benzodiazepines, barbiturates, etc.) can lead to atrophy of the gingiva with gum retraction, tooth collapse, paradontosis and loss of teeth. Such changes are also observed when stimulants are
taken, by rubbing the narcotic substance into the gums (often with a sample of the "merchandise" offered by the dealers);

- The use of stimulants and / or laced weed often leads to bruxism with the result of faster erasing of the tooth enamel on the chewing surface of the teeth with dental pulp opening [2, 5, 7]. As a rule, prolong drug addicts often lack oral hygiene, as there are numerous cases with cavities, broken teeth, present root parts, or complete tooth loss (Photo 1).

Morphologically, in the investigated cases, both local changes in the area of application of the drug (skin, subcutaneous and peripheral blood vessels) were observed, as well as disease changes related and due to the direct toxic effect of the narcotic substance and the manner of the drug intake and the type and quantity of the impurities in the street dose (mainly heroin abuse)[8, 13, 17, 18]. Most commonly skin and mucous membrane traces of needle marks were detected in areas over venous blood vessels in typical as well as "hidden" areas (photos 2 and 3).

These needle-like traces are usually overlapping in the same place when the basic principles of aseptic and antiseptic are not followed, leading to constant local inflammation of the soft tissues, resulting in ruptured tissue, abscesses, and even phlegmons (Photo 4) - life-threatening diseases. As a result of the overlapping needle impacts at the same site, peculiar femoral-vein fistulas are formed in the form of so-called tunnel-like scars (Photo 2), a characteristic morphological sign for long-term injecting type of drug use.

Subsequently, the observation of such tunnel-like scars revealed contusions, fibrous tissue in the subcutaneous soft tissue and around blood vessels. Also, cases with narrowing of the lumen of the vessels, sometimes with thrombus formation, and an inflammatory reaction around them were examined. The formation of thrombus in the venous vessels at the sites of injection may be the cause of pulmonary embolism and death - a complication of the drug addiction. Histologically, inflammatory changes of the skin, the subcutaneous and the underlying soft tissues are observed at the injection site (Photos 7 and 8).

The respiratory system most often experience changes of inflammatory nature of the airways and lungs, mostly of a non-specific, such as on one hand bronchitis, bronchiolitis, pneumonia (Photo 9) involving a significant part of the pulmonary parenchyma, and on the other - those with the specific nature of the developing disease, such as tuberculosis. In some cases, the infecting agent can also be identified, and in our case histological findings suggest that pneumonia is most likely caused by Pneumocystis carinii, which are difficult to treat due to the background of reduced immunity and often end up with a fatal outcomes [19, 20, 21]. In case of doubt about such cases, apart from histological examinations with hematoxylin-eosin, a silver impregnation on Gomori-Grocott (Photo 10) and PAS-reaction (Photo 11) could be performed.

Inhalation intake of drugs also creates an opportunity for the inhalation of impurities in the respiratory tract, and lungs. A frequent histological finding is the presence of fungal colonies in the lungs (Photo 12), as well as vascular lesions - arteritis (Photo 13), thrombosis, fibrosis of the pulmonary arteries, arterioles and capillaries (which may lead to overlapping of another infection as well as to the development of pulmonary hypertension with right ventricular hypertrophy - "pulmonary heart").

Changes in blood vessels and myocardium are not a rare finding in the case of death of persons with evidence of long-term drug use. We observed pericarditis, myocarditis, endocarditis and valvulitis with different bacterial genesis due to reduced immunity [9, 12, 16, 21]. In some cases, foreign particles of crystalline substances (most often particles of unspoilt oral tablets, talc, etc., mixed with the "street" heroin dose), as well as other undissolved and poorly filtered elements injected with the drug into the blood vessels in the lungs and hearts form "foreign body" granulomas (Photos 14 and 15).
Often, in chronic drug users there are initial to marked changes in the myocardium with undulation and fragmentation of cardiomyocytes, focal lipomatosis and general degenerative changes, as well as pronounced perivasal fibrosis (Photo 16).

In the brain study of some individuals with evidence of prolonged drug use, we found a significant reduction in the thickness of the cortex (Photo 17) and predominantly marked cerebral perivasal and peri-cellular edema (Photo 18), as well as infection diseases, cerebral vessel vasculitis and others [6, 11, 14, 15, 22].

At liver level, in almost all cases there was fatty liver degeneration (vacuolization in the cytoplasm of hepatocytes – Photo 19), expressed to varying degrees. In some cases, it is accompanied by inflammatory infiltration of mononuclear cells and segmented nuclear leukocytes in portal spaces (toxic hepatitis data - Photo 20). In some cases, intravenous drug administration may lead to the development of solitary abscesses in the liver [1, 3, 4, ] (Photo 21).

In the kidney study, long-term drug users (mainly heroin ones), as a frequent histological finding in renal parenchyma, we had observed damage of the tubulointerstitial apparatus with interstitial fibrosis expressed to varying degrees from focal to diffuse, presence of mononuclear infiltration or segmental leukocytes and atrophic canals, as well as degenerative changes in epithelial cells, primarily proximal canals, sometimes to a degree of necrosis of the tubular basal membrane. Although renal changes such as glomerulopathies are rare we observed such cases, with flattening of the podocytes, subendothelial deposits of ossophilic material in glomerular capillaries, as well as pseudo-linear granular deposition of immunoglobulins corresponding to membrano-proliferative glomerulopathy (podocyte, membranous and membranoproliferative disease). Histochemical methods (Masson's trichromatic staining, PAS-reaction, Wilder silver impregnation) were used to differentiate glomerulopathy. In one case, fibro-cavernosal tuberculosis was observed with amyloid deposition in the kidney as a finding in drug addicts associated with the decreased immunity [10, 23] (Photos 22 and 23).

CONCLUSION:

The periodic statistical follow-up of cases of deceased drug abusers compared to their causes of death permits a wider and more up-to-date look at the type and distribution of drugs offered on the “black market”, which in turn allows for timely referral to the various institutions involved in countering drug trafficking, prevention and treatment of drug addicts. On the other hand, the knowledge of the characteristic morphological changes and the related morbid complications allows rapid diagnosis, respectively, timely and correct therapeutic approach.

In some cases of death in people with evidence of prolonged drug use, the above-described morphological may not be seen and the only things observed during autopsy are pronounced venous congestion, brain and lung edema. This can be explained with the fact that death can occur even at first or initial intakes of narcotics. On the other hand, the individual tolerance of each addict and the presence of various impurities (in order to create a larger quantity, respectively, a larger profit for the distributor) are associated with different effects of the drugs with unpredictable results.

In some cases vomiting occurs as a reaction of the body, especially when taking heroin (with or without impurities), as the drug addict aspirates gastric content and death may result from ether form mechanical asphyxia, or as a result of Mendelson syndrome (abscessing aspiration pneumonia).

The cause of acute poisoning with one illicit drug is a result of the intake of heroin. Combined poisoning in 87% of the cases involves the combination of heroin and ethyl alcohol, the latter having a synergistic and potentiating effect, often leading to deadly acute intoxication.
In the remaining 13% of the cases, death from drug intoxication is a consequence of a consistent combination of stimulants (most of them are amphetamines) and heroin. Regardless of the type of drug and its various effects on the CNS, which determine certain effects, respectively perceptions, from a morphological point of view, the changes in the various tissues and organs can be summarized depending on the mode of drug intake – inhalation, injection, oral intake, etc. There are multiple and varied morphological changes in different tissues and organs that are not specific to different types of drugs but are characteristic of a particular mode of administration. Knowing the morphological substrate of these changes enables the correct and rapid diagnosis of the different cases. In all them, however, morphological data should be compared with the results obtained from the chemical analysis and critically analyzed.

Statement for Potential Conflicts of Interest - No potential conflict of interest was reported by the authors.

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PHOTOS

Photo 1

Photo 2

Photo 3
Photo 4

Photo 5
Photo 6