

# Infective Complications of Drug Addiction

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## Introduction

First of all I would like to thank the organizers for asking me to participate in this congress and of entrusting me with this important subject; I believe this invitation is not meant as a personal acknowledgment, but rather as an acknowledgment of the association that I am representing here today, namely the San Patrignano Community, which in turn adds greater importance to my presentation.

The San Patrignano Community has been dealing with drug addicts and social outcasts for over 20 years; since 1985, over 10,000 people have been hosted and treated at the Community; I myself entered the Community at the beginning of 1980. Subsequently, I decided to study medicine, graduated in 1987 and specialized in Infectious Diseases in 1991. It goes without saying that when I entered the Community I did not realize that that would be the beginning of a difficult and yet fruitful period. Only Vincenzo Muccioli anticipated my future development and supported me and spurred me as long as I needed help.

The rapid transformation of the Community into a huge centre, the constant flow of new arrivals, and the emergence of the notorious diseases associated with drug addiction, called for the creation of new organization patterns and of more efficient health facilities in order to ensure that all guests, including those in severe health conditions, receive appropriate medical assistance during the therapeutic program.

The new Medical Centre provides a large variety of health care services: (a) preliminary screening; (b) follow up according to the type of basic pathology (HIV infection, hepatitis, etc.); preventive medicine (vaccinations, etc.) and formulation of sanitary guidelines; (d) general and specialized treatments according to the guests' needs, supported by an outpatient department; (e) hospitalization of patients affected by acute pathologies or by disabling chronic illnesses jeopardizing their

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self-sufficiency (34 beds); (f) separate accommodation for self-sufficient AIDS patients requiring infusion therapy on a daily basis (16 beds); (g) day hospital.

The Medical Centre and its staff necessarily had to specialize in complications associated with drug addiction; today I will try to briefly discuss the problem of infective complications on the basis of our experience and case record, and to review the most important literature on this subject.

The first concept that I would like to make clear is that San Patrignano has never considered drug addiction as a medical problem, but rather as a social or existential problem affecting the individual; the term medical problem applies only to the complications associated with drug addiction, namely:

- the abstinence syndrome
- the direct toxicity of drugs such as for example the toxicity connected with narcotics (overdose, non-cardiogenic pulmonary oedema), the acute toxicity caused by cocaine, crack and amphetamines (psychosis, convulsions, cerebrovascular accidents, myocardial infarction and arrhythmia), the toxicity caused by ecstasy (psychosis, rhabdomyolysis, hyperthermia, chronic damage to the serotonergic system, etc.).
- infectious diseases associated with drug addiction that in turn can be divided into: (1) infectious diseases associated with the use of infected needles (HIV-infection, viral hepatitis, bacterial infections, etc.); (2) infectious diseases caused by the incautious behaviour that is frequently associated with drug addiction (sexually transmitted diseases); (3) diseases that are more common among drug addicts than among other people, presumably associated with their lifestyle or with alterations in their immune defence (pneumonia, tuberculosis, etc.).

### **Infective Complications of Drug Addiction**

The main infective complications of drug addiction, both in terms of incidence and gravity are the viral diseases transmissible by sharing needles, HIV-infections and infections caused by other retroviruses (HTLV I/II), hepatitis type B, C, Delta and G.

Since the problem of HIV-infection has already been discussed in detail, I don't think that it is necessary to dwell on the epidemiological

- and clinical aspects. I will just confine myself to a few considerations:
- the sharp drop in the prevalence of HIV-infections among drug addicts reported in our Community (from 55 percent in 1985 to less than 10 percent after 1993, and probably even less if we consider only those who started taking drugs in the last few years); these data have been confirmed also at the national level and are mainly attributable to the sharp drop in the sharing of needles, moreover, they were recorded before the introduction of methadone and independently of it;
  - the adoption of other forms of incautious behaviour, especially unprotected sex and the frequent change of partners, is not perceived as dangerous by drug addicts; according to our data, most of the new infections, even among drug addicts, are sexually transmitted, which means that also in this case the distribution of methadone does not reduce the risk, and that only education proves effective;
  - the important and negative role of new drugs that cause HIV-infections due to the reduction in the level of sexual protection (cocaine, ecstasy, crack), rapidly induce people to prostitute themselves (crack) and increase the risk of needle sharing (intravenous cocaine and the repeated injections that come with it). Today, needle sharing still poses a major risk, especially in certain circumstances: patients with mental disorders, convicts, very young drug addicts, outcasts, homeless people and restricted groups of drug addicts, such as couples, close friends, etc.

Other viruses similar to HIV (retroviruses) can be transmitted by the needle: some years ago great importance was attached to HTLV I. The virus was associated with a certain number of neurological diseases and rare forms of lymphoma and was thought to accelerate the evolution of HIV-related diseases. HTLV I appeared to be quite common among drug addicts (especially in the urban areas of the US and southern Italy); scientists found out later that it actually was another similar retrovirus, HTLV II and that there was no association with any type of disease.

In the past, viral hepatitis was the most common infectious disease associated with drug addiction; over the years, the precautions taken by drug addicts to avoid HIV infection have dramatically reduced the cases of hepatitis B, a typical disease of drug addicts; also the recent introduction of vaccines has contributed to a reduction in the incidence rate. The very high incidence of hepatitis C, which currently runs as high as 80 percent (a few years ago it had almost reached 95 percent),



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still remains a mystery to me. Why is the incidence of hepatitis C so high despite the reduced sharing of needles and the lower risk of sexual transmission? There is no answer to these questions; probably, the practice of warming up the drug in a spoon disactivates the virus but not the HCV, or probably it is enough to warm up the drug in a single container to cause the infection without necessarily sharing the needle. Since there is no time to discuss the clinical aspects of hepatitis C, I will just underline a few facts:

- the only approved therapy, alpha-interferon, is not very effective (25 percent) and is associated with a low level of tolerability. This therapy is very difficult to apply to ex drug addicts since it can trigger latent mental or psychiatric disorders or compensated disorders, such as states of depression, anxiety and even psychotic states.

- It is possible that the interferon-ribavirin combination increases the rate of response.
- people infected with HIV are exposed to a greater risk of developing cirrhosis, however there aren't enough data to justify the use of interferon, both because it appears to be less effective and because it can activate the HIV virus (it should be associated with anti-retroviral drugs). Moreover, in some cases it has caused a sudden “drop” in CD4 lymphocytes.
- Apparently, the presence of a virus C infection does not aggravate the evolution of the HIV infection.

We still know very little about the hepatitis G virus. Probably it is quite common among drug addicts, however, we don't know to what extent it causes damage to the liver, because it is often associated with the hepatitis C virus.

The intravenous use of drugs paves the way for other infections which are not caused by the sharing of needles, but simply by the use of needles, especially if there is a lack of personal hygiene and if the same needle is used several times. In this case the infections are bacterial or fungal.

Bacterial infections are mostly caused by cutaneous Staphylococci; there is a wide range of infections including local infections (thrombophlebitis, cellulitis, abscesses) and systemic infections such as endocarditis, sepsis, pulmonar septic emboli, etc. Endocarditis is one of the most common infective complications connected with drug addiction. It usually affects the tricuspid valve and is caused by the *Staphylococcus aureus*. Contrary to what was generally assumed, endocarditis is more common among drug addicts infected with HIV. Moreover, the incidence is three times higher among patients with more than 350 CD4 lymphocytes and eight times higher among patients with less than 350 CD4 lymphocytes.

Fungal infections are caused by *Candida* which is not found on the skin but in the drugs themselves; these infections usually affect the patient's eyes (endophthalmitis); it is worth mentioning the outbreak of infections caused by *Candida* (eyes, scalp) that spread among Italian, French and Swiss drug addicts in the 70s.

As regards sexually-transmitted diseases, I will just focus on HPV and scabies, since our impression is that the other famous venereal diseases, such as syphilis and gonorrhea, represent a minor problem considering that they are easy to cure and that their incidence is on the de-

crease among drug addicts (at least in Italy) as compared to 10 years ago.

HPV-infection is very widespread, probably also among people who don't use drugs. In males this virus causes condylomas that tend to relapse after surgery and that are sometimes very widespread and difficult to cure. Female patients affected by HPV would generally develop condylomas on their external genitalia as well as cell alterations (coilocytosis) in the cervix uteri which in turn can result in dysplasias (localized, moderate or severe) or even intraepithelial neoplasms or invasive carcinomas. The main risk factors of HPV-infection are premature sexual activity, the duration of infection and the number of partners. The risk factors of dysplasia and cervical neoplasm are the duration of HPV-infection and above all the presence of HIV infection and a low number of CD4 lymphocytes.

Scabies is often included among sexually-transmitted diseases. In reality, very often the transmission occurs also with other types of contact, or simply by living together. I mention this disease because it is re-surging and because it is a major source of concern. I personally reported a few cases in the early 80s. Then, the disease literally disappeared for more than 10 years. Yet, over the last few years we have seen so many cases that we decided to have newly-arrived patients undergo a routine examination by a specialist. The diagnosis is very difficult, especially if the patient affected by the disease shows an adequate personal hygiene: in this case the clinical picture is atypical and subtle and the disease might manifest itself simply as night itching. In immunodepressed patients the disease may not be clinically manifest (eczema, radzyge, etc.) and is difficult to cure since it can affect certain areas that are normally unaffected (pavilions of the ear, nose root, etc.)

Other infections that are statistically associated with drug addiction are not caused by the sharing of needles or by incautious sexual behaviour: the most important among these are tuberculosis and pneumonia.

Anglo-Saxon authors have always mentioned drug addiction as a risk factor for tuberculosis. Actually, the picture is not very clear since it is necessary to make a distinction between tuberculous infection and disease.

Tuberculous infection revealed by positive skin tests (Test Tine – Mantoux) has a fairly high incidence (about 10 percent in Italy) and is usually contracted during childhood or adolescence. Generally speaking, the infection does not evolve into a disease (the risk is 10 percent

during a whole lifetime, 5 percent of which in the first year of infection). Apparently, drug addiction is a risk factor for tuberculous infection: the prevalence of positive skin tests for tuberculosis among drug addicts in the US exceeds 20 percent and in certain areas of Europe (Spain) the rate is even higher: the reason behind this increase is mainly social, since drug addicts are often outcasts and sometimes have no fixed abode.

According to our data, out of over 6000 patients hosted in our Community only 7 percent show a positive skin test for tuberculosis. It follows that the incidence is not higher than that reported among other people in the same age group. In order to reduce the risk of falsely negative reactions, the study has been limited to HIV-negative patients. According to our data, the risk factors of tuberculous infection increase with age and with the duration of drug addiction. Moreover, the infection mostly strikes people coming from other countries and former convicts; on the other hand, in a multivariate analysis only the national origin and age are statistically significant risk factors.

We don't know whether drug addicts with a positive skin test for tuberculosis face a greater risk of developing tuberculosis; however, we have reason to believe that malnutrition, the lack of sanitary controls and a weaker immune system favour the development of a clinically manifest tuberculosis.

Undoubtedly, HIV-infection is the main risk factor for tuberculosis both due to (a) the reactivation of latent infections (the annual risk of tuberculosis among HIV-positive and PPD-positive patients is 10 percent) and (b) to the rapid development of new infections (high risk of epidemics in the Community, in the lodgings, in the Aids department, etc.) This is why we recommend preventive therapy (Isoniazide) for HIV-positive patients and for patients with a positive skin test for PPD. We don't know for sure whether after the cycle of preventive therapy (12 months) there is still a risk of tuberculosis (or if it has increased due to a weaker immune defence) since it is difficult to sterilize the foci of latent tuberculous infection. Another problem is the unreliability of skin tests in patients whose immune defence has been weakened by the HIV infection. In order to overcome this problem we suggest to integrate the PPD test with a number of skin tests based on antigens that are very common in nature (multitest); only if these tests turn out to be positive can a negative PPD test rule out the possibility of a latent tuberculous infection.

The protocol adopted by the San Patrignano Community for the prevention of tuberculosis envisages chest X-ray and skin tests (Mantoux + multitest) upon arrival and subsequently every 12 months. Chemoprophylaxis with Isoniazid is prescribed to HIV-positive and PPD-positive patients (Mantoux reaction of at least 5 mm in diameter) with less than 500 CD4 lymphocytes (a higher number of lymphocytes is usually not associated with tuberculosis); with this protocol the number of cases of tuberculosis among our guests has been reduced to a minimum (less than 10 cases in 10 years out of 2000 patients infected with HIV, excluding the patients in the inpatient department who were diagnosed with tuberculosis from the very beginning); moreover, no case has caused an infection among the other guests in our Community.

Well before the appearance of HIV-infection, the international medical literature featured a number of studies underlining the high risk of pneumonia among active drug addicts (2.1 percent per year as compared to the 0.3 percent for the rest of the population). There are several possible reasons for this: (a) depression of cough reflex induced by narcotics; (b) increase in pathogenic bacteria in the oral cavity due to poor hygiene; (c) weak perception of the first symptoms of respiratory infection due to active drug use; (d) systemic immunodepression due to malnutrition and repeated antigenic stimuli; (e) pulmonary talcosis due to the intravenous use of drugs formulated for oral administration; (f) direct toxicity of drugs on the respiratory tract, already demonstrated with regards to heroin (asthma-like reactions, depression of ciliary activity) and cocaine. The risk of pneumonia increases significantly (9.7 percent) among patients infected with HIV, especially those with a low number of CD4 lymphocytes. This is due to the above-mentioned factors and also to dysfunctions in humoral immunity which pave the way for bacterial infections.

Recently (July 1996), the Medical Centre of San Patrignano has published a study on the incidence and aetiology of pneumonia among 5000 patients with a three-year follow up. The incidence of pneumonia was 1.4 percent among HIV-negative drug addicts and 9 percent among HIV-positive ones. The study has provided some new information:

- a high prevalence of “atypical” forms of pneumonia, in particular those caused by *Chlamydia pneumoniae*, the main cause of pneumonia, both among patients infected with HIV (1.1 percent) and seronegative patients (0.4 percent);

- among the atypical forms of pneumonia we reported a high incidence of pneumonia caused by *Coxiella burnetii* (Q fever) which is probably associated with the surrounding rural environment;
- the infections caused by encapsulated bacteria (*Streptococcus pneumoniae* and *Haemophilus influenzae*) are by and large the main cause of bacterial pneumonia among HIV-positive patients (with an annual incidence of 1.9 percent and 1.2 percent respectively). Unlike what has been written by other authors, the clinical picture of these infections is far more severe among HIV-seropositive patients and is often accompanied by a septic onset, acute kidney failure (especially following the use of antipyretics to control fever) and by the risk of shock.