Persistent infectious and tropical diseases in immigrant correctional populations

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SUMMARY

A number of infectious diseases amongst travelers and the immigrant populations are a major public health concern. Some have a long incubation period or remain asymptomatic or paucisymptomatic for many years before leading to significant clinical manifestations and/or complications. HIV, hepatitis B and C, tuberculosis or latent syphilis are among the most significant persistent diseases in migrants. Schistosomiasis and strongyloidiasis, for instance, are persistent helminthic infections that may cause significant morbidity, particularly in patients co-infected with HIV, hepatitis B and C. Chagas disease, which was initially confined to Latin America, must also now be considered in immigrants from endemic countries. Visceral leishmaniasis and malaria are other examples of parasitic diseases that must be taken into account by physicians treating incarcerated migrants. The focus of this review article is on the risk of neglected tropical diseases in particularly vulnerable correctional populations and on the risk of infectious diseases that commonly affect migrants but which are often underestimated.

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INTRODUCTION

Persistent infections and tropical diseases may be caused by many different agents as protozoa, virus, helminths and bacteria. As these diseases hugely vary in their characteristics such as symptoms and clinical manifestations, it is often hard to make the correct diagnosis and treatment of patients.

Some persistent infections such as hepatitis B and C, HIV, tuberculosis, helminthiasis and syphilis, represent a huge problem in incarcerated population, especially when they are underdiagnosed1. This underdiagnosis may allow the progression of these infections and facilitate the transmission to inmates and to other people after release. Another threat to incarcerated population is the helminthic diseases, such as schistosomiasis and strongyloidiasis. As they are imported tropical infections, in many cases, immigrants may be misdiagnosed in European countries, since in many areas there is not an active surveillance service.

Owing principally to long asymptomatic periods, the presence of chronic or persistent infectious diseases in immigrants is proportional to the prevalence of these conditions in their countries of origin or the countries where they have spent part of their lives. This is particularly relevant in prison settings, because in most countries the correctional population includes a high proportion of immigrants. In 2012, it was estimated that there were about 1.73 million detainees in the prisons of the 47 Member States of the
Council of Europe, with foreigners accounting for 21% of inmates. This proportion has progressively increased over the past 20 years; in a number of Western European countries it is more than one third, and the vast majority of these foreign detainees are from countries with a low per capita income. For example, the proportion of foreign prisoners in Spain is 34% and in Switzerland 71%.

In Western countries, HIV, hepatitis B and C, tuberculosis and syphilis are usually more frequent in migrants than in the indigenous population. However, other chronic asymptomatic or paucisymptomatic diseases that can remain silent for many years should also be considered among immigrants. Schistosomiasis and strongyloidiasis are persistent helminthic diseases that cause significant morbidity in many tropical and subtropical countries of Africa, Asia and Latin America. Epidemiological, biological and immunological data suggest a causal relationship between the clinical evolution of some helminthic diseases (schistosomiasis and strongyloidiasis) and viral diseases (HIV, hepatitis B and C). Schistosomiasis can increase HIV transmission and accelerates HIV progression. Coinfection between schistosomiasis and chronic viral hepatitis is associated with severer forms of liver disease. In HIV-infected patients, strongyloidiasis infection increases the risk of immune reconstitution syndrome, and in some circumstances the risk of hyperinfection. This is a challenging problem, given the high prevalence of chronic viral hepatitis and HIV in prison populations.

This article summarizes the epidemiology of persistent infectious and tropical diseases in immigrants with a focus on the incarcerated populations. It also describes the clinical aspects of neglected parasitic diseases and coinfections with some viral diseases that follow a more severe clinical course.

METHODS

We identified references through searches of PubMed, SciELO and Google scholar. Online searches were restricted to articles in English, French, and Spanish. Targeted diseases were those that cause persistent viral, bacterial or parasitic infections. We selected keywords and medical subject headings (MeSH) related to HIV, AIDS, hepatitis B, hepatitis C, tuberculosis, syphilis, strongyloidiasis, schistosomiasis, chagas disease, leishmaniasis, fascioliasis and malaria. Scientific names of each pathogen were also selected. We used combinations of keywords related to each disease and to prisoners related search terms (inmate(s), sentenced, remand, detainee(s), felon, prison(s), prisoner(s)) and to migration related search terms (immigrant(s), migrant(s), transients and migrants, refugee(s), foreign, asylum-seekers, immigration, emigration, migration). To highlight articles related specifically to coinfections, we crossed bacterial and parasitic diseases with viral diseases of interest (HIV, HBV, and HCV). We selected diseases that are most prevalent in the prison setting and/or those whose morbidity is highest. Finally, websites from international organisations and from UN agencies (eg. WHO) were searched for relevant information.

PERSISTENT VIRAL INFECTIONS

Among incarcerated immigrants, the prevalence of blood-borne diseases is higher than in the general population. This is partly due to the following particularly relevant risk factors: exposure to infectious diseases in the country of origin, and the accumulation of negative social determinants of health as low socioeconomic status in a high proportion of this population.

Hepatitis B

Hepatitis B is a major public health problem that affects about 240 million people in the world. It is estimated that more than 780,000 people die every year due to the acute or chronic consequences of hepatitis B. In the prison population worldwide, the prevalence of chronic hepatitis B varies between 3.1 and 25.5%. In the United States of America, the prevalence of hepatitis B infection is very high in populations that have migrated from highly endemic regions such as Asia, Africa and the Middle East. In the largest detention centre in Switzerland, where more than 80% of the detainees are immigrants, the prevalence of chronic hepatitis B infection is 5.9%. Prevalence was eight time higher in detainees from sub-Saharan Africa than from elsewhere. History of intravenous drug use, number of sexual partners and level of education were not associated with a higher prevalence of infection in this study. However, a number of studies have demonstrated that intravenous drug use is the principal risk factor associated with hepatitis B in prison settings. For example, in Spain, epidemiological studies among prisoners have shown that in the past decade, during which the number of prisoners known to be injecting drug has decreased, against a background of increasing immigration, the prevalence of chronic hepatitis B infection fallen from 3.8 to 2.6%.
Hepatitis C

Hepatitis C is a global public health problem that affects about 185 million people in the world and cause 350,000 deaths each year. In many European countries, the prevalence of HCV in the general population is between 0.5% and 6.5% and it may reach peaks in people between 40 and 59 years old. In Western countries, seroprevalence of hepatitis C is 10-20 times higher in the prison population than in the community. The principal risk factor for this population is intravenous drug use.

Few studies have investigated the prevalence of hepatitis C in immigrants. In the Netherlands, Urbanus et al. demonstrated a higher prevalence of hepatitis C in first-generation immigrants than in the indigenous population; while statistically significant, this higher rate of prevalence was not marked. In addition, phylogenetic studies reveal that infection invariably occurs in the country of origin. In a study conducted in a German prison, Meyer demonstrated a significantly higher rate of prevalence among incarcerated migrants from countries of the former Soviet Union that in the indigenous population. Moreover immigrants from some countries like Egypt, Pakistan and China are at particular risk.

HIV

The HIV is one of the major health challenges worldwide, that causes relevant economical and social consequences for public health. It is estimated about 35 million people living with HIV around the world. An estimated 0.8% of adults aged 15-49 years worldwide are living with HIV, although the burden of the epidemic varies between countries and regions. Sub-Saharan Africa remains most severely affected, with nearly one in every 20 adults living with HIV and accounting for 71% of people living with HIV worldwide.

In many Western countries, HIV prevalence is several times higher in prisons than in the rest of the population, largely due to the high proportion of injecting drug users. In other countries, particularly in sub-Saharan Africa, the high prevalence of HIV in prisons reflects high endemicity in the local population. In the past 20 years, in Spain, HIV infection among inmates has decreased by a 4-fold factor. However, HIV prevalence among immigrant prisoners, although moderate (3% in Catalonia, for example), is not decreasing and remains high among new detainees.

Tuberculosis

Tuberculosis is one of the most leading causes of death worldwide, with about nine million new cases each year and 1.5 million deaths per year. The prevalence of tuberculosis among incarcerated immigrants is high and correlates with the level of endemicity in the country of origin. The incidence of the disease is 10-100 times higher than in the rest of the population of the host country, and is associated with the high proportion of prisoners from endemic areas with latent Mycobacterium tuberculosis infection. In the event of coinfection with HIV, the risk of developing active tuberculosis is 113 times higher than in seronegative patients. This observation is crucial in prison, given the high prevalence of HIV in this setting. Drug use, low body weight, both being prevalent in prison settings, and diabetes can also reduce the body's immune defences. In prisons, the detection and treatment of latent tuberculosis should therefore be prioritized in prisoners presenting with these risk factors.

Syphilis

Syphilis is a sexual transmitted disease with an estimated number of annual new cases of 10.6 million worldwide, Untreated Treponema pallidum remains in the body throughout the life course, resulting in serious neurological and cardiovascular disorders in 30% of patients. Syphilis also facilitates the transmission of HIV, as it increases the viral load and reduces the CD4 cell count. Syphilis continues to be a public health issue in Western countries. In addition, rates of infection by Treponema pallidum and other sexually transmitted diseases are higher among immigrants than in the general population. Prevalence can reflect morbidity rates in countries of origin, or it could also be the result of local exposure to particular risk factors. Likewise, a number of international studies have shown that prison inmates present greater vulnerability to syphilis and other sexually transmitted diseases. In Spanish prisons, the incidence of syphilis was 12 times higher than the rate reported in the general population.

PERSISTENT BACTERIAL INFECTIONS

PERSISTENT HELMINTHIC DISEASES

Published epidemiological data on parasitic infections in prisoners are rare; one case of schistosomiasis
has been reported in a Spanish prison. However, in a pilot project conducted in February and March 2013, asymptomatic prisoners from sub-Saharan Africa detained in a pretrial detention centre in Geneva, Switzerland, were screened by serology for schistosomiasis, strongyloidiasis, HIV and hepatitis B and C. Two and four out of 30 detainees had serologic evidence of strongyloidiasis and schistosomiasis, respectively (Gétaz L., personal data not yet published). The results of this pilot investigation suggest that persistent parasitic diseases are neglected conditions in incarcerated immigrants. For example, one of the four patients infected with Schistosoma sp was a 33 year old man who migrated from the Republic of Guinea to Europe at the age of 25 years. As a young boy, he bathed regularly in rivers and lakes. This asymptomatic patient was diagnosed as being coinfected with hepatitis B. A fibroscan and liver biopsy confirmed advanced hepatic fibrosis. This case illustrates the significance of certain viral and parasitic coinfections in immigrants, which we will further develop below.

Schistosomiasis

It is estimated that 207 million people worldwide are infected by Schistosoma sp, 93% living in sub-Saharan Africa and the rest in limited regions of Asia and South America. In endemic African countries, it is estimated that up to 25% of the population has schistosomiasis. Serological studies in immigrants have revealed prevalence rates varying from 10.7 to 44%. Only one description of schistosomiasis in prisoners has been published in the scientific literature, namely a case of Schistosoma haematobium infection in a patient with erythrocyturia from Senegal, diagnosed in a Spanish prison.

The disease is acquired through contact between intact skin and fresh water (lakes, rivers, etc.) contaminated by larvae. Depending on the species of Schistosoma, the adult stage tends to concentrate in the mesenteric veins of the intestine (S. mansoni, S. japonicum, S. mekongi, S. intercalatum) or vesical plexus (S. haematobium). The adults normally survive for 5-6 years, although some may survive much longer. In some cases it’s possible to find worms eggs many decades after the infection.

In Western countries, acute clinical manifestations (cercarial dermatitis and Katayama fever) occur mainly in travellers returning from endemic countries. In contrast, the chronic form of the disease is mainly seen in migrants from endemic areas. The chronic pathology is secondary to inflammation triggered by the deposition of eggs in host tissues. In the case of intestinal schistosomiasis, the eggs lodge in the wall of the large intestine and rectum. The patient presents with abdominal pain, diarrhoea with or without mucus, and loss of appetite. The inflammatory process occurs locally, with small ulcers, micropolyps and microbleeding. Eggs can migrate through the portal system and embolize in the portal spaces of the liver, causing progressive fibrosis and secondary portal hypertension. The most feared complication is an upper gastrointestinal bleeding caused by esophageal varices.

Genitourinary schistosomiasis may be asymptomatic or it may cause micro- or macroscopic erythrocyturia, painful urination and occasionally fibrosis and calcifications. The lesions in the ureters can lead to urethral stricture with hydronephrosis and secondary renal failure. The literature suggests a link between schistosomiasis and bladder cancer. Involvement of the genital organs may also occur, causing in women ulcerative lesions of the vulva, vagina or cervix, and occasionally lesions of the ovariens. Men may experience disorders of the testes, epididymitis and prostate.

SeroLOGY is very useful for diagnosis as 95% of infected individuals have positive antibodies. Serology could remain positive years after treatment. Examination of stool and urine for schistosome eggs can identify the species, but this method has low sensitivity. The absence of hypereosinophilia does not rule out infection with schistosomiasis, particularly in the chronic phase. Treatment with praziquantel is well-tolerated and generally effective, although resistance begin to emerge in some endemic countries.

Schistosomiasis and coinfection with HIV, hepatitis B and C (Table 1).

Schistosomiasis increases susceptibility to HIV-1 infection and the likelihood of viral transmission, and can accelerate the progression of HIV disease. Although S. haematobium is most commonly associated with HIV coinfection, S. mansoni is also involved.

In patients infected with the hepatitis C virus, schistosomiasis will result in increased viral load, development of chronic hepatitis and accelerated progression of hepatic fibrosis. The rapid course of the disease is particularly marked in the case of coinfection with Schistosoma mansoni. Furthermore schistosomiasis reduces response to interferon therapy and increases the hepatitis C relapse rate. Finally, the literature suggests that coinfection of S. mansoni or S. japonicum with hepatitis B results in a more severe clinical course, with accelerated deterioration of liver function and poorer prognosis.
Strongyloidiasis

Strongyloidiasis (*Strongyloides stercoralis*) is an helminthic infection typically acquired in tropical and subtropical regions. According to recently published estimates, approximately 370 million people are infected worldwide. Epidemiological studies using serological techniques in migrant populations from endemic areas have indicated seroprevalence of 11-42%. There are practically no epidemiological data from prisons. In 1988, Bourée et al. reported a prevalence rate of 4.3% among a correctional population from sub-Saharan Africa in a French prison. However, the prevalence was probably underestimated, given the low sensitivity of the coproparasitological techniques used.

The parasite larvae penetrate the body through skin contact with damp or muddy ground. After transiting through the lungs, the larvae concentrate in the small intestine until they reach adulthood. The females produce a large quantity of eggs that hatch rapidly. The larvae can complete their life cycle in the environment, following excretion in the host’s faeces, but also inside the body, as they pass through the intestinal wall or the perianal region. This process is called endogenous auto-infestation, and explains the protracted nature of the infection, which may last more than 40 years, as already described.

Clinical manifestations vary according to the phase of larval migration. The cutaneous penetration phase can cause pruritic papular dermatitis, and more rarely pseudo-Loeffler syndrome. The phase of intestinal colonization is usually asymptomatic, but can sometimes manifest itself by abdominal pain, diarrhoea, urticaria or rapid-progression linear dermatitis (larva currens) on the buttocks and abdomen. When the patient’s immunity is conserved, the body’s defence mechanisms and the auto-infestation are in balance. The risk of a disseminated form of the disease increases with the use of corticosteroids and other immunosuppressive therapies (e.g. in the context of rheumatic diseases), chemotherapy for haematological tumours, and in transplant patients. Larvae multiply massively and invade the organs, potentially leading to hyperinfection (accelerated auto-infestation), with severe symptoms and a mortality rate as high as 87%. Since *S. stercoralis* infection facilitates the translocation of enterobacteria across the intestinal mucosa, Gram-negative bacterial sepsis can occur.

Serological or coproparasitological diagnostic techniques are used. The detection of larvae in stools samples requires specific procedures (Baermann technique, Agar culture). The treatment of strongyloidiasis is straightforward with ivermectin, which is efficacious and safe.

Table 1: Consequences of viral and parasitic coinfections

<table>
<thead>
<tr>
<th>Coinfections</th>
<th>Consequences</th>
<th>Ref</th>
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<tbody>
<tr>
<td>HIV-schistosomiasis</td>
<td>Schistosomiasis =&gt;</td>
<td></td>
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<tr>
<td></td>
<td>† susceptibility to HIV-1 infection</td>
<td>4-7</td>
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<tr>
<td></td>
<td>† likelihood of HIV transmission</td>
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<td></td>
<td>† facilitates accelerated progression of HIV</td>
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<tr>
<td>HIV-strongylopidiasis</td>
<td>Strongyloidiasis =&gt;</td>
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<td></td>
<td>† risk of immune reconstitution syndrome</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HIV =&gt;</td>
<td>14-15</td>
</tr>
<tr>
<td></td>
<td>† risk of disseminated strongyloidias in subgroups of patients (e.g. corticosteroid treatment for opportunistic infections)</td>
<td></td>
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<tr>
<td>HIV-Chagas disease</td>
<td>HIV (CD4&lt;200/µl) =&gt;</td>
<td></td>
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<tr>
<td></td>
<td>† Reactivation with meningoencephalitis, nodular lesions in the cerebral white matter, acute myocarditis</td>
<td>70-71</td>
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<td>Hepatitis C-schistosomiasis</td>
<td>Schistosomiasis =&gt;</td>
<td></td>
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<tr>
<td></td>
<td>† Hepatitis C viral load</td>
<td>8-10</td>
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<tr>
<td></td>
<td>† Accelerated development of fibrosis</td>
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<tr>
<td>Hepatitis B-schistosomiasis</td>
<td>Schistosomiasis =&gt;</td>
<td></td>
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<td></td>
<td>† Accelerated development of liver impairment</td>
<td>11-13</td>
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<tr>
<td>HTLV-1-strongyloidiasis</td>
<td>HTLV-1 =&gt;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>† risk of disseminated strongyloidias</td>
<td>64</td>
</tr>
</tbody>
</table>

— 61 —
Strongyloidiasis and coinfections with viral diseases (Table 1).

In HIV-infected patients, strongyloidiasis infection increases the risk of immune reconstitution syndrome, in the period following initiation of antiretroviral therapy. There is no clear evidence of increased risk of disseminated strongyloidiasis in HIV-infected patients; the literature describes only 40 cases. The risk is however increased in some HIV-infected patients, such as patients treated with corticosteroids for toxoplasmosis, pneumonia caused by *Pneumocystis carinii* or non-Hodgkin’s lymphoma.

Coinfection with HTLV-1 has been commonly described in the literature and has been shown to increase the risk of disseminated strongyloidiasis. This coinfection is particularly prevalent in parts of Asia and Latin America. In the few studies on the prevalence of infection with HTLV-1 in immigrants in Spain, the prevalence of this infection is very low at 0.06%.

Chagas disease

This disease occurs predominantly in Latin America, in both Central and South America. The World Health Organization estimates that over 8 million people are infected worldwide. Studies in immigrants from endemic areas have revealed prevalence between 4.2 and 12.6% in Spain, Italy and Switzerland. Chagas disease is usually asymptomatic for decades before it can cause significant clinical complications. Between 20 and 30% of infected individuals develop clinical cardiac manifestations (arrhythmias, heart failure, dilated cardiomyopathy), and 10% may have motility disorders of the oesophagus (with difficulty in swallowing) or colon (with constipation), with or without organ enlargement (with occasional fecal impaction). These manifestations are primarily caused by damage to striated cardiac muscles, smooth intestinal muscle and the autonomic nervous system. In the case of immunosuppression, particularly in cases of HIV infection (CD4 count <200 cells/mm³), reactivation of Chagas disease may occur (Table 1). Chagas reactivation is characterized by high parasitaemia, myocarditis and/or central nervous system manifestations such as acute meningoencephalitis and nodular lesions in the cerebral white matter, which may mimic cerebral toxoplasmosis.

Visceral leishmaniasis

Visceral leishmaniasis (VL), or kala-azar, is a severe systemic hemoprotozoan disease caused by protozoa of the genus Leishmania, which are transmitted to humans by phlebotomous sandflies in South America, Asia, Africa and the Mediterranean region of Europe. An estimated 200,000 to 400,000 people are infected each year; there are approximately 50,000 fatalities annually. In Spain, cases of secondary infection have been recorded following the use of contaminated needles by intravenous drug addicts. This type of transmission, albeit rare, is significant, especially in prison populations where intravenous drug use is common. Available data on immigrants with *Leishmania* infection are scarce (i.e. case reports or small case-series), and there is no report among inmates. Studies in England and Germany show that the Mediterranean region is the most common area of infection in imported cases in Europe.

In most individuals, Leishmania infection does not progress to VL and individuals remain asymptomatic. The presentation of VL is characterized by a mean incubation period of 2-6 months, but reactivation can occur years after initial infections in case of immunosuppression. VL presents with fever, weight loss, palpable splenomegaly, and various degrees of anaemia, leukopenia and thrombocytopenia secondary to bone marrow suppression and/or hypersplenism. Diagnosis can be made by bone marrow aspiration, splenic aspiration and/or serology. Severely immunosuppressed HIV-coinfected patients (CD4 count <50 cells/mm³) may present with atypical clinical features (e.g. gastrointestinal, skin or lung manifestations).

Malaria

Human malaria, a vector-borne disease, is endemic in many parts of sub-Saharan Africa, Asia, and Latin America. About 3.4 billion people in the world are at risk of malaria, although the risk is relatively low outside Africa and Asia. The international literature contains no studies or case descriptions of prisoners with malaria. However, descriptions of delayed-onset malaria, with an incubation period exceeding 2 months, are common in immigrants and travellers alike. The causes of delayed onset are numerous and may include the specific immunity of the infected individual, the *Plasmodium* species involved and the effect of the chemoprophylaxis drugs used. In addition, secondary relapses on activation of hypnozoites (in *Plasmodium vivax* and *ovale*) may occur months or even years after the mosquito bite. Because of a latent parasitic stage in the liver responsible for this phenomenon, malaria should be suspected when immigrants from endemic areas incarcerated in non-endemic countries present with fever.
CONCLUSIONS

The fact that the literature provides inconsistent data on the epidemiology of persistent tropical parasitic diseases in immigrant populations, coupled with the rarity of reported cases among migrants in prison, suggests that these diseases are overlooked and neglected in this vulnerable population. The pilot project described in this article, reinforces this hypothesis and indicates a need for additional studies. Moreover, the coinfection of several of these neglected bacterial or parasitic diseases with chronic viral infections (i.e. HIV, hepatitis B and C) may lead to increased morbidity and reinforces the need to develop strategies to detect these persistent — often asymptomatic — infections among inmates originating from endemic countries.

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REFERENCES

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