INTERNATIONAL NOTES

Infectious Complications in Drug Addicts: Seven-Year Review of 269 Hospitalized Narcotics Abusers in Switzerland

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In a retrospective survey of patients hospitalized in the Department of Medicine of the University Hospital, Basel, Switzerland, from 1980 to 1986, we found 269 patients with history of past or current drug abuse. The charts of these patients were analyzed for infectious complications according to defined criteria. Heroin was the principal drug consumed by 95%. In 127 patients (47%) at least one infectious complication was diagnosed. In 125 (31%) of 404 admissions, the infectious problem was the main reason for hospitalization. Among the 269 patients, 217 infective episodes occurred. Pulmonary infections were the most frequently occurring (52 episodes). There were 44 cases of viral hepatitis, 30 of human immunodeficiency virus infection, and 25 of minor genital infections. Bone and joint infections and sepsis/endocarditis were diagnosed in seven cases each. The overall mortality was 4.1%; however, only three of the 11 deaths were attributed to infections. Intravenous drug addiction is complicated by a high morbidity because of infections that were seldom lethal during the observed period.

Intravenous drug addicts are a population at risk for infectious complications such as bacteremia, fungemia, endocarditis, pneumonia, arthritis, osteomyelitis, septic thrombophlebitis, soft tissue infections, venereal diseases, viral hepatitis, and infections with the human immunodeficiency virus (HIV) [1–22]. Between the 1940s and the 1970s, several publications covered the whole spectrum of infections [23–29], whereas in the recent literature, more attention has been given to single infections in narcotics abusers [1–22]. The present report describes all infectious complications among drug addicts that have been diagnosed at the medical department of the Basel University Hospital (Basel, Switzerland) between 1980 and 1986. The frequencies and etiologies of the particular infections are presented and compared with those described in the literature.

Patients and Methods

The medical department of the Basel University Hospital is a 280-bed acute care facility. It is the major provider of acute medical care for the estimated 1,000 drug addicts in Basel. Drug abusers appear in the emergency room when they feel sick or occasionally they are brought by the police in cases of intoxication in public. Some patients are referred from addiction treatment facilities if they require hospitalization for acute disease. History and physical examination are recorded by house staff.

Patients were enrolled in the present study if they reported a history of drug abuse, presented with intoxication and miosis responding to naloxone, or had opiate metabolites in urine samples. Individuals with exclusively oral drug abuse other than opiates were excluded from the study. The medical charts of all patients defined as narcotics abusers and admitted to the department of medicine from January 1980 to December 1986 were reviewed. Patients who were seen on the emergency ward only (mainly for intoxication) were not included in this study.

Regarding the development of the human immunodeficiency virus (HIV) epidemic in Basel, the years before 1984 are defined as the pre-HIV era, i.e., the time before HIV-associated diseases were recognized, and the years 1985–1986 as the post-HIV era. Drug addicts suspected to have HIV infection have been

tested for the presence of HIV antibodies since December 1985, and all drug addicts have been routinely tested since 1986.

Diagnosis of infection was established according to uniform criteria. Pneumonia was defined by a typical pulmonary infiltrate seen on chest roentgenogram and by the presence of purulent sputum. Aspiration pneumonia was assumed when there was radiologic evidence of infiltration and a history of coma or bronchoscopic evidence for aspiration with fever and leukocytosis.

Endocarditis was classified as definite, probable, or possible, as suggested by Pelletier and Petersdorf [30] and Von Reyn et al. [31]. According to this scheme, cases of endocarditis classified as definite are those that have been histopathologically confirmed. Probable cases have persistently positive blood cultures and either a new regurgitant murmur or predisposing heart disease with evidence of embolization. Possible endocarditis is diagnosed in patients with persistently positive blood cultures and either a predisposing heart disease or an embolic phenomenon.

Bacterial arthritis or osteomyelitis was identified in patients with positive cultures from synovial fluid or bone and also in cases with a suggestive clinical picture and cytologic or histologic evidence of purulent inflammation or positive blood cultures. HIV infection was classified according to the Centers for Disease Control's definition [32]. Hepatic disease was assumed to be viral in the presence of positive hepatitis B surface antigen or hepatitis A IgM, histologic evidence of active viral hepatitis, or pathologic results of liver function tests and inflammatory signs (fever, leukocytosis) without any other explanation (such as alcoholic hepatitis).

An undefined bacterial infection was presumed if there were at least four of the following clinical or laboratory conditions: fever $\geq 39.0°C$, chills, leukocytosis $\geq 20,000/mm^3$ or leukopenia $\leq 3,000/mm^3$, band forms $\geq 25\%$, vacuoles and toxic granulation of the granulocytes, and favorable response to an empiric course of antibiotics. Unclear transitory fever (<12 h) after intravenous drug application was classified as pyrogenic reaction.

Those cases not clearly defined by the above criteria were separately reviewed by two investigators. Chronic infections that led to repeated hospitalizations (mainly chronic viral hepatitis and HIV infection) were recorded as single episodes. Statistical analysis was performed by Fisher's exact test.

Results

A total of 51,794 admissions were recorded in the Department of Medicine of the Basel University Hospital during the seven-year period. Among these patients, 269 narcotics addicts were admitted 404 times (0.78% of all admissions). Among those, 255 (94.8%) were principally heroin addicts. Only 14 patients (5.2%) consumed exclusively cocaine, methadone, intravenous barbiturates, or amphetamines. Drugs had been injected intravenously by 262 (97.4%) of 269 patients. Only seven (2.6%) exclusively used another route such as inhalation (four cases), oral intake, or intramuscular or subcutaneous injection. Duration of addiction was not described frequently enough to permit any conclusive statement. The mean age for the 269 individuals was 26.4 y (range 15–83 y, median 21 y); 56.3% were male. Two hundred thirty-six (87.6%) were of Swiss origin, 27 were Western European, three were Eastern European, two were from North African countries, and one was from the United States.

One hundred twenty-seven hospitalized patients (47.2%) had at least one infectious complication. In 125 of the 404 admissions (30.9%), the infectious problem was the exclusive or main cause of hospitalization, an increase from 26.4% in the pre-HIV era to 41.6% in the post-HIV era ($P < .001$). Other reasons for admissions were heavy intoxication with oral drugs (27.6%), heroin (16.6%), or alcohol (4.0%); withdrawal reactions (5.4%); and various other medical reasons (15.5%). Table 1 lists the types of infections in our patients compared with others from published series. Lower respiratory tract infections, viral hepatitis, HIV infection, and genital infections were most commonly diagnosed. Three of these infections were lethal.

Lower respiratory tract infection. Bacterial pneumonia was diagnosed in 43 patients. Aspiration was the assumed cause in 21 of these. The etiologic agents in 22 cases of alveolar pneumonia or bronchopneumonia were *Streptococcus pneumoniae* (seven cases), *Haemophilus influenzae* (two), mixed aerobic and anaerobic flora (two), and *Staphylococcus aureus* and *Streptococcus viridans* (one each). The last two patients had empyema; in nine patients the etiology remained unclear. Two drug addicts with pneumococcal pneumonia had an HIV infection (groups II and IVA, respectively) as the underlying disease. One patient with pneumococcal pneumonia died from multiple organ failure due to heroin intoxication.

Table 1. Types of infections among hospitalized drug addicts.

Diagnosis	Present series (1980–1986) No. (%)	Reference [23] (1938–1947) No. (%)	Reference [29] (1971) No. (%)	Reference [35] (1972–1983) Group I* No. (%)	Group II† No. (%)
Lower respiratory tract infection	52 (24.0)	. . .	16 (9.5)	15 (53.5)	21 (18.3)
Viral hepatitis (acute and chronic)	44 (20.3)	. . .	61 (36.1)‡	7 (25.0)	51 (44.3)
HIV infection (group II, III, or IV)	30 (13.8)	. . .	. . .	. . .	. . .
Minor genital infection	25 (11.5)	. . .	41 (24.3)§	. . .	3 (2.6)
Thrombophlebitis or soft tissue infection	13 (6.0)	72 (58.5)	24 (47.7)	. . .	5 (4.3)
Undefined bacterial infection	11 (5.1)	. . .	. . .	. . .	. . .
Bone and joint infection	7 (3.2)	. . .	. . .	1 (3.6)	1 (0.9)
Venereal disease	7 (3.2)	. . .	19 (11.2)	1 (3.6)	5 (4.3)
Primary bacteremia, fungemia, and endocarditis	7 (3.2)	15 (12.2)	8 (4.7)	1 (3.6)	9 (7.8)
Pyrogen reaction	6 (2.8)	. . .	. . .	1 (3.6)	. . .
Enteritis due to *Salmonella* species	3 (1.4)	. . .	. . .	. . .	. . .
Acute nonbacterial gastroenteritis	2 (0.9)	. . .	. . .	. . .	. . .
Malaria	. . .	29 (23.6)	. . .	. . .	. . .
Tetanus	. . .	7 (5.7)	. . .	. . .	. . .
Undefined fever	. . .	. . .	. . .	2 (7.1)	11 (9.7)
Candidal endophthalmitis	. . .	. . .	. . .	. . .	5 (4.3)
Various conditions	10 (4.6)‖	. . .	. . .	. . .	4 (3.5)
Total no. of episodes	217	123	169	28	115
Total no. of patients	269	365	200	492	191
Mortality due to infection (%)	3/269 (1.1)	10/365 (2.7)	0/200 (0)	1/492 (0.2)	2/191 (1.0)

* Patients admitted for intoxication.
† Patients admitted for other reasons.
‡ All patients with acute hepatitis.
§ All patients were female.
‖ Purulent tonsillitis, febrile dental infection, upper respiratory tract infection, enterocolitis (*Shigella* species), anorectal abscess in Crohn's disease, urinary tract infection (*Escherichia coli*), catheter-related thrombophlebitis, nosocomial bacteremia (*Enterobacter cloacae*), acute cytomegalovirus infection, acute Epstein-Barr virus infection (one each).

Four patients with fever and cough had purulent bronchitis without pneumonia. Three HIV-infected drug addicts had interstitial pneumonia with *Pneumocystis carinii* (two) and cytomegalovirus (one). Active tuberculosis was diagnosed in two patients. One with tuberculous pleurisy had no HIV antibodies; the other with cavitary tuberculosis was not tested.

Viral hepatitis. Of the patients with active viral hepatitis, 25 had acute and 19 had chronic infections. Acute episodes were caused by hepatitis A virus (three) or hepatitis B virus (18 cases), one of them with δ-agent superinfection. Four patients were presumed to have non-A, non-B hepatitis. Of the 19 patients with chronic hepatitis, 16 were diagnosed by liver biopsy. Histopathologic examination revealed chronic aggressive hepatitis in nine and chronic persistent hepatitis in seven drug addicts. In three patients clinically diagnosed as having chronic viral hepatitis, no histologic confirmation was attempted during the study period. One patient died from progressive hepatic coma with underlying chronic aggressive hepatitis.

HIV infection. We have tested for HIV antibodies in our patients since December 1984. Among 62 drug addicts tested from December 1984 to December 1986, 30 were positive for HIV antibodies. In 1986, when HIV antibody testing was performed in all hospitalized drug addicts, 26 (49%) of 53 patients were seropositive. Seroconversion could not be documented during the study period. Asymptomatic HIV infection (group II) was diagnosed in 19 patients (63.3%) and lymphadenopathy (group III and IV, respectively) in two (6.7%) and nine patients (30%). Both individuals in group III and nine of 19 patients in group II suffered from infections not indicative of AIDS, namely, bacterial pneumonia (five), endocarditis (two), undefined bacterial infection (two), transient candidemia (one), and purulent soft tissue infection (one). The nine patients of group IV had interstitial pneumonia (three) oral thrush

(six), constitutional symptoms (six), or herpes simplex genitalis (one).

Genital infections and venereal disease. Minor genital infections were found in 25 female patients. The etiologic agents were *Trichomonas* (10), papillomavirus (six), *Candida* species (four), herpes simplex (three), and *Gardnerella vaginalis* (two). Three of 59 tested patients had latent syphilis. Two women suffered from etiologically undefined pelvic inflammatory disease, one case associated with an intrauterine device. Gardnerella epididymitis was found in one man. Gonococcal sepsis was assumed in one patient. She had fever, oligoarthritis, and typical cutaneous lesions. Gonococci could not be cultured; however, the gonococcal complement-binding reaction turned positive.

Thrombophlebitis and soft tissue infection. Thrombophlebitis at an injection site was seen in six individuals. One additional patient presented with lymphangitis and phlegmonous infection of the left forearm. In two heroin addicts, phlegmonous infection complicated a crush syndrome of the forearm due to severe intoxication. Furunculosis was seen in two patients. One individual developed disseminated ulcerative *S. aureus* lesions unrelated to injection sites. Finally, granuloma pyogenicum of a thumb occurred in one patient.

Bone and joint infection. Spondylitis was diagnosed in three patients. In each biopsy material revealed purulent inflammation and/or microbial growth (*S. aureus* and *Pseudomonas aeruginosa*, respectively). The *S. aureus* spondylitis (fifth and sixth thoracic vertebrae) was complicated by a paravertebral abscess and pleural empyema. Sternal osteomyelitis caused by *S. aureus* was diagnosed from a presternal collection. A heroin addict (patient no. 7, table 2) with endocarditis had arthritis in multiple joints. *S. aureus* was isolated from blood and the synovial fluid of his right knee. *Enterobacter cloacae* was isolated in the blood culture of a woman with unilateral acute sacroileitis. Finally, purulent gonarthritis without bacterial growth in the synovial fluid or several blood cultures was seen in one patient.

Unclassified bacteremia, fungemia, and endocarditis. Table 2 summarizes the data of seven patients who each had several positive blood cultures on admission. Five patients (nos. 1-3, 6, and 7) injected heroin alone, two injected dissolved tablets in addition. Patient no. 4 was diagnosed as having

a possible endocarditis on the basis of two positive blood cultures and a predisposing heart disease. Patient no. 6 was classified as "probable endocarditis" because of persistently positive blood cultures and a new regurgitant heart murmur. Patient no. 7 had definite endocarditis; he presented with endocarditis of the aortic valve, cutaneous embolic manifestations, septic arthritis of both knees and hips, and right hemiparesis. Primary replacement of the affected valve was not performed because of continual drug abuse. Despite adequate antibiotic therapy and supportive care, the disease progressed, and the patient died with progressive heart failure during a desperate attempt at valve replacement. Autopsy confirmed destructive endocarditis of the aortic valve, with embolic manifestations in the skin, brain, kidneys, and spleen. In addition to these seven patients, one individual who was on treatment with cefoxitin and tobramycin for presumed aspiration pneumonia developed signs of septicemia. Four of five of his blood cultures were positive for *E. cloacae* on the 11th day of hospitalization. This episode was classified as nosocomial bacteremia and consequently does not appear in table 2.

Discussion

This study represents a retrospective analysis of infections in drug addicts. Diagnoses have been established on the basis of data from the patients' charts according to preset criteria. Several types of infections that are common in drug addicts may be underrepresented in this study because patients with venereal diseases, skin infections, or endophthalmitis are generally not hospitalized in the medical department.

The reasons for the increased risk of infections in drug abusers are several: (*1*) people who inject themselves are often carriers of *S. aureus* [33]; (*2*) unsterile drugs are injected with dirty needles and syringes; (*3*) dental hygiene is often poor; (*4*) bacterial clearance by the tracheobronchial system is decreased during intoxication; (*5*) cell-mediated immunity may be impaired not only by HIV infection but also by intravenous drug abuse itself [34]; and (*6*) promiscuity and prostitution increase the risk of transmitting numerous infective agents.

To our knowledge, three other series [23, 29, 35] have shown similar results, although there are substantial differences in the study design. In these

Table 2. Characteristics of seven patients with sepsis and endocarditis.

Patient no.	Age (y)/ sex	Time to last injection	Clinical presentation, WBC count (per mm³)	No. of positive blood cultures/ total no.	Microorganism	Treatment, route	Comments
1	19/F	<24 h	Fever 39.0°C, suspected withdrawal reaction; WBC 14,900	3/4	*P. acnes*	No antibiotics	Spontaneous defervescence within 6 h
2	30/F	Unknown	Fever 39.0°C; marked paradontosis; WBC 4,200 (25% band forms, toxic granulation, and vacuoles)	3/4	*S. aureus*	Cloxacillin iv, tobramycin iv	
3	20/F	10 h	Fever 38.9°C; pelvic inflammatory disease (clinical diagnosis); normal WBCs	2/2	*S. aureus*	Cefoxitin iv, doxycycline iv/po	Cervical cultures negative for gonococci and chlamydiae
4	24/F	<12 h	Fever 38.1°C, chills; WBC 9,000 (26% band forms, toxic granulation, and vacuoles)	2/2	*S. aureus*	Flucloxacillin iv, followed by penicillin iv	Probable tricuspid valve endocarditis due to *S. aureus* 5 y and 2 y before current episode; HIV infection group II
5	24/M	3 w (heroin); "a few days" (codeine)	Fever 39.0°C, chills, dry cough; WBC 9,400 (38% band forms, toxic granulation, and vacuoles)	2/2	*C. albicans*	Penicillin iv, followed by amoxicillin po, no antifungal drugs	HIV infection group IIIB; no pathogen in bronchoalveolar lavage; no echographic signs for endocarditis; defervescence within 48 h; no signs of disseminated candidal infection (follow-up, 7 mo)
6	21/F	Unknown	Fever 40.0°C; shock; clinical signs of tricuspid valve insufficiency; WBC 11,000 (62% band forms, toxic granulation, and vacuoles)	5/5	*S. aureus*	Cloxacillin iv	Tricuspid valve insufficiency confirmed by echocardiography, aspiration pneumonia due to *Haemophilus*; HIV infection group II; pregnant (20 w)
7	24/M	<24 h	Fever 39.3°C; cutaneous embolic manifestations; splenomegaly; hemiparesis; septic arthritis of multiple joints; WBC 15,000 (35% band forms, toxic granulation, and vacuoles)	5/5	*S. aureus*	Cloxacillin iv, tobramycin iv	*S. aureus* also isolated from synovial fluid; died on day 13 from heart failure; endocarditis and multiple embolic phenomena confirmed by autopsy

reports, diagnostic criteria are not stated. Furthermore, patients admitted to the hospital for only a few hours for intoxication were included in Quadri and Russi's study [35] but not in our study. In our series 26% of the patients were hospitalized for infections during the pre-HIV era, a number similar to the 28% of Hussey and Katz [23] but lower than the 58% reported by White [29]. The frequency of different infections in our series is compared with published data in table 1. It is obvious that Hussey and Katz [23] presented only selected cases. White [29] found fewer respiratory tract infections but more venereal and other genital infections, soft tissue infections, and cases of hepatitis. The lower rate of viral hepatitis in our series may be due to the hepatitis B vaccine campaigns since 1982 and to our reluctance to hospitalize patients with hepatitis. The fact that our patients mostly injected drugs intravenously, not subcutaneously, contributes to the lower rate of soft tissue infections and the lack of tetanus cases in our study, compared with older American series [23, 24, 26, 28]. The absence of tetanus cases in our series may also be a consequence of regular tetanus vaccine campaigns in Swiss school children.

Bronchopulmonary infections were the main infectious complication in our study. Similarly, Marantz et al. [10] diagnosed pneumonia in 38% of 87 febrile episodes in 75 drug addicts. In contrast, others reported many fewer pulmonary infections [9, 23, 29]. The low incidence of aspiration pneumonia (1%) in Jaffe and Koschmann's study [9] is particularly unusual. Opportunistic pneumonias in AIDS patients were only seen in the last year of our study. The rate of hospitalizations for infection increased from 26% in the pre-HIV era to 42% in the post-HIV era. Bacterial pneumonia, which is more common in HIV-infected individuals, has contributed to this rise. At our hospital the first case of AIDS was diagnosed in late 1984. There is therefore a lag time of about four years for AIDS cases, compared with large cities such as San Francisco and New York [36]. This explains our low incidence of AIDS-related diseases and, particularly, the lack of infections with atypical mycobacteria that commonly appear late in the evolution of HIV infection [37].

However the propagation of HIV infection among drug addicts is much faster in Switzerland than in the United States, with the exception of New York City [38]. For instance, in San Francisco in 1985, only 10% of the narcotics addicts were infected with HIV [21, 22]. In contrast, in Switzerland 22% of the ad-

dicts had already developed antibodies to HIV by 1982 and 49% by 1985 [18]. In our study four of nine patients tested before 1986 were positive for HIV antibodies. This number is biased since only selected cases were tested. However, in 1986, when each drug addict was tested for HIV antibodies, the prevalence of 49% was representative. This high prevalence of HIV infection is amazing, since there are no "shooting galleries" in Switzerland [39, 40]. However, the frequency of HIV antibody may be explained by frequent needle sharing among acquaintances before 1986, when needles and syringes were made freely available. In other European countries, HIV infection is also prevalent in drug addicts [22, 41, 42].

Arthritis and osteomyelitis are classic but rare infections in drug abusers. They are mainly caused by *S. aureus* but also by gram-negative rods, such as *Pseudomonas aeruginosa* and *Serratia* species, or by fungi. The arthritis has an unexplained predilection for syndesmoses such as the sacroiliac, sternoclavicular articulation, or symphysis pubis [11–13].

Special diagnostic problems are encountered in drug addicts with initially unexplained fever. Such individuals should be hospitalized since a major infection cannot be ruled out by history or by clinical examination [10]. The following differential diagnosis should be considered: pyrogenic reaction, fever as a symptom of drug withdrawal, occult focal infection, HIV infection group IVA, and bacteremia or fungemia with or without endocarditis.

In cases with positive blood cultures, the question arises of whether endocarditis is present; it cannot be proved by history or by clinical signs [6–8, 10]. In the present study the rate of occurrence of endocarditis was 0.7% of all admissions. Others have reported higher rates in unselected hospitalized (3.9%–8.3%) [6, 8, 9] and febrile (13%) [10] drug addicts.

S. aureus is the most common pathogen in intravenous drug abusers [2]. Methicillin-resistant strains of *S. aureus* are rarely encountered in our hospital; between 1980 and 1986 only 3.6% of the *S. aureus* blood isolates of all hospitalized patients were methicillin resistant (unpublished data). In the present study group, every isolate of *S. aureus* was sensitive to methicillin. This finding contrasts with results from other centers where up to 42% of the isolates in drug addicts are methicillin resistant [2, 39]. This may be due to the fact that Swiss drug addicts do not use prophylactic antibiotics (unpublished results from interviews), whereas in Detroit,

79 of 180 bacteremic narcotics abusers took antibiotics, mainly cephalosporins [2].

Microorganisms of low virulence, mainly from skin flora, can cause bacteremia and endocarditis without focal disease in intravenous drug addicts. Therefore microorganisms such as *Staphylococcus epidermidis*, *Corynebacterium* species [43], *Bacillus* species [44], and *Candida* species [3–5] have to be considered as relevant pathogens. In our study this is exemplified by a case in which three of four blood cultures yielded *Propionibacterium acnes*. Disseminated candidal infections have been increasingly recognized in intravenous drug abusers [3–5]. In our series the patient with candidemia (no. 5, table 2) did not receive antifungal treatment because the cultural result was ignored. An uneventful follow-up to seven months showed that this episode was apparently self-limited. The most probable source of *Candida* in such patients was recognized in the meantime. *Candida* species may colonize lemons or lemon juice, which is used to dissolve certain types of heroin [5].

Among our study patients, three died of infection — one with pneumococcal pneumonia after an overdose, one with endogenous hepatic coma in posthepatitis cirrhosis, and one with fatal cardiac failure as a consequence of aortic endocarditis. During the study period eight others died from noninfectious causes, mainly drug overdose.

In conclusion, the pattern of infections in Swiss drug addicts is different from that in patients reported in older American series [23–29]. Specifically, the rate of soft tissue infections is much lower, and cases of tetanus and malaria are completely absent in the present study, whereas lower respiratory tract infections are more frequent.

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