

Screening for infectious diseases in newly arrived asymptomatic immigrants in southern Italy

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Abstract

Background: Screenings for infectious diseases in asymptomatic immigrants currently takes place when receiving new arrivals.

Aims: We describe the frequency of infections in a cohort of newly arrived asymptomatic immigrants in Southern Italy.

Methods: We studied a cohort of 238 Sub-Saharan African and Asian men hosted at a reception centre (CARA) in Foggia between January and December 2015. The tuberculin skin test for diagnosis of latent tuberculosis infection (LTBI) and serology/virology testing for HBV, HCV, HIV were performed.

Results: From this cohort, 205 individuals agreed to be tested for serological/virological markers only, while 82 agreed to be tested for LTBI only; 49 people agreed to have both tests. Among those tested for virological markers, 23/205 (11.2%) were HBsAg positive; 12/23 (52.2%) individuals had chronic active hepatitis; 77/205 (37.6%) individuals had only anti-HBc positivity. HCV infection was present in 8/205 (3.9%) individuals, and chronic HCV infection, was diagnosed in only two people. Only 2/205 (1.0%) individuals presented with anti-HIV and HIV-RNA positivity. We found LTBI in 29.6% of TB-tested individuals.

Conclusions: Asymptomatic immigrants are at increased risk for some infections, mainly HBV and tuberculosis.

Keywords: epidemiology, infectious diseases, LTBI, newly arrived immigrants, Italy

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Introduction

The last 20 years has seen considerable migration from low- and middle-income countries to high-income nations, primarily the United States of America and Western Europe. On 1 January 2016, the number of people living in a European Union (EU) member state who were citizens of nonmember countries was 20.7 million. In Italy this represented about 4 million people or 6.7% of the population (1). This remarkable increase in people whose living conditions are often considerably disadvantaged has sometimes led to problems, not only of a socioeconomic and security nature but also in regard to sanitation and health. In fact, while most tropical diseases are absent or appear sporadically in Italy (2,3), it was observed that the prevalence/incidence of other pathologies such as HBV/HCV/HIV/TB have changed their epidemiology over the years, in accord with the immigration phenomenon. Some infections have been directly imported, in both latent and active forms. Others have been contracted by immigrants because of living conditions/habits, with an increase in some infectious diseases such as HIV (3), TB (4) and viral hepatitis (5,6) and sometimes co-infections (6).

Southern Italy has been, and still is, a major destination for illegal immigration (African, Middle Eastern and Asian) from the North African coast (7). On

arrival, the immigrants are hosted in reception centres (CARA), which are distributed in various parts of Italy. Most are young and healthy individuals, but they are often considered a source of certain infectious diseases such as Ebola, SARS etc., occasionally resulting in unjustified prejudice because of their geographic origin, ethnicity, health conditions at the departure point, and the migratory route (8–10). Therefore, the identification and treatment of any imported asymptomatic infections could reduce their incidence/prevalence and modify their outcome. This can have a significant clinical and psychological impact, both for the individual affected and for public health (10).

The health service for immigrants in Italy, particularly for clandestines, is not adequate and most assistance is currently provided by religious or lay volunteer groups. Only recently have hospitals and local health services initiated the creation of outpatient clinics for immigrants, including soliciting the help of cultural workers and interpreters (10). In such a challenging scenario, the team of volunteer doctors participating in this study have been screening immigrants hosted in the CARA in Foggia (Apulia, Southern Italy) for infectious diseases for several years.

The aim of this research, conducted in 2015, was to determine the possible presence of HIV/HBV/HCV/TB infections in a cohort of asymptomatic immigrants who

were temporarily guests at the CARA in Foggia, and to measure the burden of latent or active infections which are potentially harmful for the individuals' health and transmissible to the community.

Methods

Participants and tests

Between January and December 2015 we screened 238 asymptomatic immigrants for HIV/HBV/HCV/TB. Before screening, all guests at the CARA (728 persons) were informed about the purpose of the study and invited to participate. Subsequent recruitment was on a voluntary basis; the recruitment of minors was mediated by tutors. The study was reviewed and approved by the general manager and the medical director of the CARA, and written informed consent, provided in 4 languages (English, French, Arabic and Italian), was obtained from each participant. All study procedures conformed with the Helsinki Declaration (1975, amended 2008).

At the time of enrolment, all participants were interviewed using a questionnaire to obtain demographic and clinical information. None of the screened participants reported previous exposure to infectious diseases, nor vaccination for hepatitis B, nor vaccination or anti-tuberculosis prophylaxis. All enlisted participants went through complete clinical tests and, if necessary, we proceeded with further diagnostic tests and treatment. In addition, we implemented a strategy to prevent any transmission to other immigrants and indigenous populations who lived in close contact with infected persons. Diagnoses of infections were made using standard commercial tests. The health examination performed for all asymptomatic immigrants was based on systematic screening that included serological and virological examination for selected infections: HIV, HBV, HCV virus, and a check for possible latent tuberculosis infection (LTBI) using the tuberculin skin test (TST).

Statistical analysis

Categorical data are presented as absolute numbers and proportions. Continuous variables were summarized as mean and standard deviation (SD), and categorical variables as absolute and relative frequencies. Differences in the mean values for continuous variables (age, HBV genotypes) were evaluated by the Student t-test for independent samples. The Chi-squared test was applied to compare categorical variables (ethnicity, HIV/HCV antibodies, HBV markers and TST positivity); $P < 0.05$ was considered statistically significant.

Results

Demographic characteristics

One hundred and thirty-two (132) of the 238 participants enrolled in the study (55.5%) came from Sub-Saharan African countries (54.2% from East Africa, 35.9% from West Africa, 10.8% from Central Africa) and 106 (44.5%) were from Asia, mainly from the Indian subcontinent and Pakistan. The mean age was 25.1 (SD 5.7; range 13–40) years. All of the participants were men since the population of the CARA was exclusively male. Subjects had been in Italy for a mean period of 36 days (range 7–118 days) (Table 1). Among the study population, 205/238 immigrants (86.1%; 111 Africans, 94 Asians) agreed to be tested only for serological/virological markers (HBsAg/anti-HBc, anti-HCV, anti-HIV) and 82 individuals agreed to be tested for TB (TST). Only 49 participants agreed to have both tests (Table 2).

HBV infection

Among the individuals we tested, 23/205 (11.2%) were HBsAg positive: 17/23 (73.9%) Africans and 6/23 (26.1%) Asians ($P = 0.03$); 16 patients were anti-HBe positive while 7 (2 of whom were Asians) presented with HBV-wildtype (HBsAg/HBeAg positive). Chronic active HBV (CHB) infection, with HBV-DNA detectable using real-time polymerase chain reaction testing, was present in 12/23 (10 Africans and 2 Asians, $P = 0.03$; 52.2%) HBsAg positive individuals (mean level 1 374 231 copies/mL, range

Table 1 Baseline characteristics of immigrant patients according to geographical origin, and the pathologies for which they were screened, Italy, 2015

Geographical origin	Patients	Screened for HBV, HCV and HIV	Screened for TB	Screened for HBV, HCV, HIV and TB
Africa	132	111	56	27
East Africa	71	59	28	16
West Africa	47	41	14	6
Central Africa	14	11	7	7
Asia	106	94	26	22
Pakistan	43	41	17	14
Bangladesh	26	21	3	3
India	16	12	3	3
Other countries	21	20	3	3
Total	238	205	82	49

74 651–13 875 247). Nine CHB patients presented e-minus mutant virus and 3 had HBV-wildtype virus. Genotype distribution among all CHB/HBV-DNA positive patients was: 5/12 genotype E (51.7%), 3/12 genotype A (25.0%), 2/12 genotype D (16.7%), 1/12 genotype B (8.3%), and 1/12 genotype C (8.3%). Genotypes E, A and D were associated with the African subgroup while genotypes C and B were associated with the Asian subgroup.

A significant statistical difference was observed between genotype E and the other genotypes ($P = 0.02$); the difference in prevalence between genotypes A, B, C and D ($P = 0.08$) was modest. We found 77 individuals (37.6%) had anti-HBc positivity (OBI), a bio-marker of previous HBV infection. The prevalence among sub-Saharan Africans was 66.2% (51/77), compared with 33.8% (26/77) among Asians ($P = 0.03$). All participants denied having previous HBV vaccinations in their country of origin. Five out of 77 participants (with slight hypertransaminasaemia) had HBV-BNA positivity with a low viral load (mean level 1275 copies/mL, range 471–5743); genotyping was not performed.

HCV infection

Infection with HCV was present in 8/205 individuals (3.9%): 3/8 (37.5%) were Africans and 5/8 (62.5%) were Asians ($P = 0.02$). Chronic HCV infection, with the presence of HCV-RNA detectable by real-time polymerase chain reaction testing, was diagnosed in only 3 Asian patients; HCV genotyping was performed in these individuals: 2 presented with genotype 1a and 1 with genotype 3.

HIV infection

Only 2/205 (1.0%) individuals presented anti-HIV antibodies, and subsequently we were able to detect HIV-RNA; 1 was African and the other was Asian. The HIV-positive immigrants were not aware of their serologic status before their arrival or, at least, they did not acknowledge sero-positivity for HIV. Neither of the 2 patients showed an AIDS-defining disease or other clinical symptoms at the time of screening; only 1 patient developed pulmonary active tuberculosis during the first month of follow-up.

Table 2 Epidemiological and clinic features of infectious diseases among immigrant patients according to region of origin, Italy, 2015

Epidemiological and clinic features	Total No.	Origin								P-value ^a	
		Africa (Af)	East Africa	West Africa	Central Africa	Asia (As)	Pakistan	Bangladesh	India		Other countries
HBsAg+	23	17	6	4	7	6	2	2	1	1	0.03 ^b
HBeAg+	7	3	2	1		4	1	1	1	1	
HBV-DNA+, HBsAg+, OBI	17	13	4	5	4	4		2	1	1	0.03 ^b
Genotype	12										
A	3	3	2	1							
B	1						1				
C	1									1	
D	2				2						
E	5		1	3	1						0.02 ^c
CHB	12	10	2	3	5	2	1			1	0.03 ^b
OBI	77	51	19	16	16	26	11	3	5	7	0.03 ^b
HCV+	8	3	1	2		5	1	1	3		0.02 ^d
CHC	3					3	1		2		
Genotype	3										
1						2	1		1		
3						1	1				
HIV+	2	1				1					
Virological coinfection	5	2 (1 B, 1 C)			2 (1 B, 1 C)						
LTBI TST+	21	15	3	7	5	6	1	3		2	0.02 ^b
TB & hepatitis coinfection	5	3	1	1	1	2		2			

OBI = anti-HBc; CHB = chronic active HBV; LTBI = latent tuberculosis infection; TST = tuberculin skin test.

^aWhen the value of P is not specified, the parameters compared are not statistically significant.

^bAf vs As.

^cE vs all.

^dAs vs Af.

Viral co-infections

Five patients (3 Africans and 2 Asians) showed HBV-HCV co-infection: in 4 cases HBV infection was prevalent, while in 1 case HCV virus infection prevailed. Co-infection for HIV-HBV-HCV was present only in the HIV-positive African participant.

Latent tuberculosis infection

Only 82/238 (34.5%) individuals in the study population agreed to undergo the tuberculin test (56/82, 76.7% Africans and 24/82, 29.3% Asians) ($P = 0.02$). Among patients tested with TST, 11 (8 Africans and 3 Asians) did not return for the control. The TST was positive (> 10 mm) in 21 (29.6%) of the remaining 71 individuals. The prevalence of LTBI was significantly greater among Africans (71.4%; 15/21) than among Asians (28.6%; 6/21) ($P = 0.02$). One of the TST-positive subjects was also HIV-positive. None of the patients who were TST-positive presented radiological or microbiological signs of active pulmonary tuberculosis. All data are described in Table 2.

Discussion

The ever-increasing presence of immigrants fosters feelings of fear in the native Italian population; fear that they may introduce new and unfamiliar diseases such as SARS, MERS, Ebola, dengue, etc., or pathologies which are no longer present or have almost been eradicated from the country (11). Many of these infections may be asymptomatic for long periods and manifest themselves later in life as active diseases. This means that the incidence of certain illness may increase in host countries despite autochthonous cases declining (12).

Infection with HBV is prevalent in immigrants, particularly in people coming from Sub-Saharan African areas with a high rate of infection ($> 8\%$). This figure is most likely a result of the lack of or incomplete prophylactic vaccination in the country of origin and risky sexual behaviour (13–15). In our study we evaluated the prevalence, the typology of HBV-infection and the degree of disease, based on genotype. Our findings (HBsAg positive rate: 11.2%) reflect the current prevalent migratory flow to our geographic area, which is mostly represented by people coming from Sub-Saharan Africa. In contrast, HBV infection is rarely observed in Asian immigrants (16–18). These data, showing the differences in infection rates due to ethnicity, highlight the epidemiological pattern of the prevalence of HBV based on country of origin (13,19–21). Among our participants, more than half had CHB, indication of a previous infection, with a clear majority from Sub-Saharan Africa (10/12 patients). The prevalence of HBV infection was similar in African children (< 16 years) and adults. This result leads us to postulate that the infection may occur at an early age (by vertical transmission or in childhood), in contrast with what has been observed in Western countries (17).

Most cases were infected with genotype E, which is almost exclusively disseminated in Sub-Saharan Africa

(18,21). Other HBV genotypes were also found, like D, B, C, A, thus reflecting different areas of origin (22–24). This redistribution of HBV genotypes represents an important change in the epidemiology of infection. In Italy, this increases the number of subjects infected with a “different” hepatitis despite the risk of reinfection with a virus of a different genotype for the Italian population being low because HBV vaccination protects from all HBV genotypes. A high proportion of patients (37.56%) had only anti-HBc (OBI), a marker that can be indicative of either natural or artificial immunization or occult active hepatitis. This clinical situation seems to be quite frequent among individuals from Sub-Saharan Africa (18,24).

Careful evaluation of OBI in the immigrant population is important because OBI can be transmitted through transfusion, organ transplantation or haemodialysis; OBI may reactivate and cause acute hepatitis in immune-compromised patients; it may contribute to the progression of hepatic fibrosis in patients with other chronic liver diseases and constitute a risk factor for hepatocellular carcinoma (25–27). Therefore, it is evident that immigrants with OBI may, if not carefully controlled, represent a risk for themselves and for the indigenous population. Currently there is no agreement on how to classify and manage individuals with OBI. Some authors suggest testing for HBV-DNA when alanine aminotransferase (ALT) levels are elevated (28), while others recommend the test only if there are other risk factors for liver disease, even with normal ALT levels (28,29). We decided to check for HBV-DNA only in 5 participants who had high levels of serum ALT.

The prevalence of HCV-infection in Europe reliably indicates that about 1% of the total population is affected, albeit with regional differences (16). However, from research carried out in different countries it emerged that immigrants seem to have a very high risk of contracting HCV-infection after their arrival in host countries (30). In Italy, the prevalence of HCV among immigrants varies with both the period and the area of research (different ethnicities), but generally it is higher than that of the local population: it ranged from 2.7% in 2008 in Verona (31) to 15.2% in 2015 in Sicily (32), with a national prevalence of 4.0–5.6%. In this study on newly arrived immigrants the prevalence was 3.9%; the patients were mainly Asians, especially Pakistani (5.3%), while among Africans the rate was lower (2.7%).

Such differences, as deduced from the reported risk factors, seem to be related to intravenous drug addiction, more common among the screened Asians than the Africans (9). Another risk factor was the high percentage of sexually transmitted infections (33), since all the screened HCV-positive Africans were infected via this route. An additional risk factor could have been infection via blood transfusion, blood derivative products or following invasive procedures (surgery, endoscopic tests, etc.) performed with inadequately sterilized instruments (34,35). These events are not infrequent in some Asian countries, where, although public health care systems

are accessible, they are not always at a level to prevent nosocomial infections. In contrast, in many parts of Africa, mainly in Sub-Saharan Africa, due to an almost total absence of a health care system, the possibility of carrying out invasive procedures or blood transfusions is very small. Consequently, although such a situation impedes the provision of adequate health care to people, it certainly generates comparatively lower rates of diffusion of hepatitis C virus (11,34,35).

Screening for HIV is systematically recommended in individuals coming from countries and communities where HIV prevalence is $\geq 0.1\%$, such as immigrants from Sub-Saharan African and Asian countries. In fact, in these populations the risk of HIV-infection is greater than in the native population and in particular, the incidence of new HIV diagnoses in Italy is estimated to be 8 times higher in immigrants than in Italians (21). However, in our screened population, the overall prevalence of HIV-infection was 1.0%, which is quite low considering that the rate of HIV-infections in the majority of the native countries of the immigrants is much higher than in Western countries, including Italy. These data confirm, after many years, previous findings from our research group that highlighted that newly arrived immigrants (< 2 months) had a 1.5% prevalence of HIV-infection (36).

This low rate could possibly be explained by the statistical bias known as the “healthy migrant effect,” for which immigrants are “positively selected” from among their original population as individuals more apt to embark on such a strenuous migratory project. These migrant health advantages, however, tend to vanish over time due to high-risk behaviours. Regarding HIV-infection, the preponderance of young, sexually active males is already a risk factor, enhanced by contacts between parties belonging to the same ethnic group. Therefore, despite the high incidence of infection in immigrants resident in the country reported in previous studies, the low prevalence of HIV infection in our cohort of recently arrived individuals seems to suggest that HIV-infection is more often acquired during their stay in the host country rather than imported from the country of origin (37–39).

Active tuberculosis (TB) is an increasing problem among immigrants living in Western countries (40). It may be the clinical expression of a new infection acquired in the host country or more often the reactivation of a latent form (LTBI) brought from their country of origin (40,41). Also, in Italy it has been shown that, in recent years, > 50% of new cases of TB affect immigrant subjects (41,42). This LTBI represents a state of equilibrium in which the host can control the infection, but cannot completely eradicate the bacteria. This is related to a persistent

immune response to stimulation by Mycobacterium tuberculosis antigens; therefore, infected individuals can be entirely asymptomatic. The greatest danger is in reactivation (active TB after remote infection) cases and the subsequent silent spread to close contacts. Therefore, patients with LTBI are the largest reservoir for potential transmission.

A high prevalence of LTBI with rates of 52–72%, and elevated risk for TB reactivation with rates of 7.8%, was observed in immigrants within the first 2–5 years of arrival (43,44), making tuberculosis the most relevant infectious disease currently. This is predominantly among immigrants from highly endemic areas such as Sub-Saharan Africa and the Indian subcontinent. The peculiar aspect of this study is the population screened, consisting of recent immigrants residing in Italy for no longer than 3 months. Only a minority of screened immigrants (82/238) volunteered for the TST, and 11 of those (13.4%) did not turn up to be checked, perhaps for fear of expulsion. The prevalence of positivity for TST was of 29.6%, a rate lower than what has been observed in other studies (43,44). This low rate of positivity could be due to errors in the administration and reading of TST as the technique was performed “in the field” and not in a hospital setting, and subjectivity is one of the main limitations for the TST, even though it was performed by trained personnel. The presence of immunosuppression could also influence TST results, even if only a few studies are available (44). Our results were not influenced by HIV-related immunosuppression because only 1 patient was HIV positive, with a low viral load; but other causes of immunodeficiency such as malnutrition and fatigue cannot be excluded for the most recently arrived subjects due to the hardships of their migratory journey.

Conclusions

Most immigrants are healthy people, but they can also constitute a population at risk because they might be asymptomatic carriers of infections that might be activated at a later time. It is important to determine the presence of pathologies for the immigrants themselves and for the potential public health implications. Therefore, every country that welcomes immigrants must implement affordable and cost-effective screening protocols. These programmes should be characterized by the principles of equality and respect for the immigrants, and be aimed at both the health of the individual and that of the host community. Such programmes could follow the example of Italy, where many public health facilities have voluntarily opened outpatient clinics dedicated to immigrants.

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Dépistage de maladies infectieuses chez les immigrants asymptomatiques nouvellement arrivés en Italie du Sud

Résumé

Contexte : Le dépistage de maladies infectieuses chez les immigrants asymptomatiques est actuellement effectué lors de l'accueil de nouveaux arrivants.

Objectifs : La présente étude a pour objectif de décrire la fréquence des infections dans une cohorte d'immigrants asymptomatiques nouvellement arrivés en Italie du Sud.

Méthodes : Nous avons étudié une cohorte de 238 hommes originaires d'Afrique subsaharienne et d'Asie hébergés dans un centre d'accueil (CARA) à Foggia, entre janvier et décembre 2015. Le test cutané à la tuberculine permettant de diagnostiquer l'infection tuberculeuse latente ainsi que le test sérologique/virologique pour l'infection par le VHB, le VHC et le VIH ont été réalisés.

Résultats : Dans cette cohorte, seuls 205 individus ont accepté de se soumettre aux tests de recherche des marqueurs sérologiques/virologiques, tandis que 82 autres ont choisi de réaliser seulement le test de dépistage de l'infection tuberculeuse latente ; 49 personnes ont accepté les deux tests. Parmi les hommes ayant fait le dépistage des marqueurs virologiques, 23 sur 205 (11,2 %) étaient positifs à l'AgHBs ; 12 sur 23 (52,2 %) avaient une hépatite active chronique ; 77 sur 205 (37,6 %) étaient uniquement positifs pour l'anticorps anti-HBc. Sur les 205 individus, 8 (3,9 %) présentaient une infection par le VHC et une infection chronique par le VHC n'a été diagnostiquée que chez deux personnes. Seuls deux (1,0 %) individus sur 205 étaient positifs au test anti-VIH et à l'ARN du VIH. Une infection tuberculeuse latente a été détectée chez 29,6 % des personnes ayant effectué le test de dépistage de la tuberculose.

Conclusions : Les immigrants asymptomatiques présentent un risque accru face à certaines infections, principalement l'hépatite C et la tuberculose.

فحص المهاجرين الجدد عديمي الأعراض للتحقق من الإصابة بالأمراض المعدية في جنوب إيطاليا

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الخلاصة

الخلفية: يجري حالياً فحص المهاجرين عديمي الأعراض للتحقق من إصابتهم بالأمراض المعدية لدى قدومهم.

الأهداف: وصف معدل تكرار الإصابة بالعدوى لدى مجموعة من المهاجرين عديمي الأعراض القادمين حديثاً في جنوب إيطاليا.

طرق البحث: قمنا بدراسة مجموعة مكونة من 238 رجلاً آسيوياً ومن أفريقيا جنوب الصحراء الكبرى الذين وصلوا إلى مركز استقبال (كارا) في مدينة فوجيا، في الفترة بين يناير/ كانون الثاني وديسمبر/ كانون الأول 2015. وأجري اختبار التوبركولين الجلدي لتشخيص عدوى السل الخافي، والاختبار المصلي/ الفيروسي لفيروس التهاب الكبد B و C وفيروس نقص المناعة البشرية.

النتائج: وافق 205 شخصاً من هذه المجموعة على الخضوع لفحص العلامات المصلية/ الفيروسية فقط، بينما وافق 82 آخرون على خضوعهم لفحص عدوى السل الخافي فقط؛ ووافق 49 آخرين على الخضوع لكلا الاختبارين. ومن بين الأشخاص الذين خضعوا لفحص العلامات الفيروسية، كانت نتيجة 23 شخصاً من أصل 205 (11,2 %) موجبة في فحص الجلوبيولين المناعي لالتهاب الكبد (HBsAg) (B)؛ بينما تأكدت إصابة 12 شخصاً من أصل 23 (52,2 %) بالتهاب الكبد المزمن النشط؛ أما 77 شخصاً من أصل 205 (37,6 %) كان نتيجتهم موجبة فقط في فحص ضد المستضد اللبني لالتهاب الكبد B. وتأكدت إصابة 8 أشخاص من أصل 205 (3,9 %) بفيروس التهاب الكبد C، وشخص فردين فقط بالتهاب الكبد C المزمن. وكانت نتيجة شخصين فقط من أصل 205 (1,0 %) موجبة في فحص الأجسام المضادة لفيروس نقص المناعة البشرية وحض الـ RNA لفيروس نقص المناعة البشرية. كما وجدنا عدوى السل الخافي في 29,6 % من الأشخاص الذين خضعوا لفحص السل.

الاستنتاجات: يُعدُّ المهاجرون الذين لا تبدو عليهم أعراض المرض في خطر متزايد للإصابة ببعض حالات العدوى، لا سيما فيروس التهاب الكبد B والسل.

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