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Hepatitis C: an emerging concern

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ABSTRACT: Hepatitis C has surfaced worldwide as a formidable concern to public health. Recent developments have sharpened methods of serological detectability, epidemiological study and patient treatment. In the light of the global situation, this article briefly presents known local epidemiology about hepatitis C derived from routine data and personal communication from some key workers. The occurrence of a serious, potentially progressive, transmissible condition in a young population will incur high-costs to patients, contacts and care services. The article concludes by highlighting the areas offering greatest scope to check this condition through prevention and patient management.

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A global overview

After many years of doubt about non-A, non-B hepatitis (NANBH), these last eight years have seen major advances in the characterisation of the hepatitis C virus (HCV) and substantial progress in the methodology of detection and disease management.

Recent developments have underlined the main areas of risk associated with transmission of bloodborne viruses. The recent history of hepatitis C has overlapped with that of hepatitis B virus and HIV, with which it shares several characteristics.

Hepatitis C is a cosmopolitan infection, varying in frequency by region (Table 1)[1,2]. Many HCV-infected individuals in the West are either intravenous drug users (IDUs), or recipients of blood products which, in the past, had not been screened for anti-HCV[3]. Before the introduction of blood donor screening and virus inactivation methods for plasma products, infection of haemophiliacs was widespread owing to contamination of pooled clotting factor concentrates[4].

Other parenteral risks include tattooing, and needle-stick injuries among health care workers. Needle-stick injuries from HCV-viraemic patients lead to transmission in 3-10% of cases, a risk lying between that for hepatitis B virus and HIV[3]. Care workers acquiring bloodborne viruses may subsequently pose a risk of infecting patients. At least one episode of carer-to-patient transmission of hepatitis C infection is documented to have followed cardiac surgery in UK in 1994[5].

The first known transmission of HCV from tattooing occurred in 1989[6]. Some cases of hepatitis C, without evident history of previous parenteral exposure, may have resulted from use of improperly sterilised surgical instruments, or by blood admixture in folk medicine[3].

Table1 - Inter-country comparison of anti-HCV seroprevalence in blood donors

Country	% donors ELISA-1 positive	Year publishrd
Taiwan	0.28%	1991
Turkey	0.31%	1991
Australia	0.45%	1992
USA	0.5%	1990
Finland	0.51%	1992
UK	0.6%	1992
Netherlands	0.7%	1990
Cuba	0.8%	1992
Guadeloupe	0.8%	1992
Malta*	1.01%	1993
Italy (South)	1.37%	1989
Spain	1.5%	1990

* ELISA-2 screening; confirmed 0.04%

Intrafamilial spread by social contact has not been proven, but mother-to-infant transmission occurs in some 10% of seropositive mothers, commonly when the mother is co-infected with HIV, and when HCV titres are high[7,8].

Sexual transmission is probably negligible or rare (Table 2): two studies in low prevalence areas showed no evidence of transmission[9,10].

Diagnosis and screening

As serological tests for hepatitis A and hepatitis B

Table 2 - Co-prevalence of anti-HCV in spouses of HCV-positive cases[1]

Country	HCV-positive spouses / index case	Year of publication
USA	0/40	1990
Spain	5/71	1990
Finland	0/30	1991
USA (multicentre)	5/194	1991
Japan	14/176	1992
Taiwan	5/25	1992
Italy	13/83	1992
USA/Italy/ Australia	3/106	1992
Netherlands	0/50	1993

became commercially available by the mid-seventies[11], non-A non-B hepatitis remained essentially a diagnosis of exclusion until 1990 when the first specific test for anti-HCV antibodies (ELISA-1) was introduced[12]. With time, test sensitivity[11] and specificity[13] were improved, and supplementary tests using recombinant immunoblot assay technology were developed[11]. The move from ELISA-1 to ELISA-2 shifted detectibility for anti-HCV from 90% to close to 100%[14]. The first reports on alpha interferon treatment for NANBH appeared in 1986[15], and the RNA genome of hepatitis C first described in 1989[16]. Hepatitis C virus is associated with 90% of non-A non-B hepatitis[3].

The Maltese perspective

As in the rest of the world, commercial blood testing for hepatitis C only became available in Malta in the early nineteen-nineties. Epidemiological description has been problematic due to the high frequency of asymptomatic infections, and practical difficulties in investigating infection with connotations of socially undesirable activity.

Data collection

The term 'serum hepatitis' used in statutory notification of hepatitis in Malta[17] does not distinguish between hepatitis B and C. Time trends derived from official figures of notified disease[18] (Table 3) may suffer from substantial artefactual variation due to inconsistent notification practices amongst clinicians over the years.

While anonymity may encourage more persons at risk to test, it limits the possibility for epidemiological surveillance. The codification used for anonymous testing is non-standard and so repeat testing cannot be easily differentiated from fresh testing by surveying laboratory records alone.

Virology laboratory, St. Luke's Hospital

Diagnostic anti-HCV testing became available at the Malta state health services in 1992[19]. The tests employed recombinant antigens which overcame initial problems of low sensitivity and specificity of earlier tests. ELISA-3 has been introduced very recently at the Virology Laboratory. Supplemental tests, including recombinant immunoblot assays (RIBA), are also performed. Common reasons for testing include IDU, sexual exposure, investigation of jaundice, deranged liver function, post-transfusion and pre-dialysis. From January 1994 to April 1997, 431 individuals are known to have reacted positive for HCV at Virology Laboratory, SLH. 80% were males and the main identified risk factor is IDU[19].

Blood transfusion & organ donation

In Malta, ELISA-2 is used by the Blood Transfusion Department for anti-HCV screening: initial positives are subjected to 3-8 further tests to minimise false positives[2]. Anti-HCV screening of blood products started in March 1992. HCV antibodies were detected in 2.9-4.7 per 10,000 donations over the period 1992-1994. As blood is nowadays fractioned into several products, screening for hepatitis C helped avert an estimated 4 to 24 primary infections per year over this period.

Intravenous drug use

The size of the local IDU population is undetermined. A total of 1074 users have been registered with the Detoxification Unit, SLH[20]. IDUs started being screened for anti-HCV in December 1993. 316 were tested by August 1996: 48% were anti-HCV positive. 65% of 104 users testing through the anti-drug NGO CARITAS were also anti-HCV positive[21]. In contrast, only 3% of newly admitted drug addicts tested at Detoxification Centre, Malta over 1992-93 were HBsAg positive[22].

Users of formal drug rehabilitation programmes are almost certainly a non-representative fraction of the underlying IDU population: grapevine reports hint at unreached pockets of users, circumscribed by age, location (eg. newly built areas) and social status (both extremes)[23].

Anecdotal reports (to the author) indicate HCV transmission in Malta going back at least to the mid-1980s, and occurring as recent as 1996, and presumably extending also to the present.

Prisons

Prisoners may be at risk of hepatitis through injecting drugs, skin piercing and sexual activity. Prison

Table 3 - Notified cases of serum hepatitis and AIDS, Maltese residents, 1988-96

	1988	1989	1990	1991	1992	1993	1994	1995	1996
NANBH	-	3	3	1	1	6	7	5	2
HBV	10	9	10	18	13	14	8	5	2
AIDS	8	0	1	7	4	3	5	3	4

authorities worldwide differ in their efforts to prevent bloodborne infections, but in most countries, persons in prison are afforded less protection against infection than those outside[24] (Table 4).

Table 4 - Prison health policies in Malta and around the world [24,25]

	Methadone treatment	Condom provision	Needle exchange	Education	Segregation ofHIV+ves	Voluntary testing
Australia	✔	✔	●	✔	✘	✔
England	✔	✘	✘	✔	✘	✔
France	✔	✔	✘	n/a	✘	✔
Germany	✔	✔	n/a	✔	✔	✔
India	n/a	✘	✘	✔	✔	✘
Israel	✔	✘	✘	✔	✔	✔
Malta	✔	✘	✘	✔	n/a	✔
Netherlands	✔	✔	✔	✔	n/a	✔
Scotland	✔	✘	●	✔	✘	✔
Thailand	✘	✘	✘	n/a	✔	✔
US	✔	✔	✘	✔	n/a	✔

✔ Yes/Some n/a Notapplicable/available

✘ No ● Cleaning facilities in some

Anti-HCV testing was introduced in Malta's Corradino Correctional Facilities in 1994. Testing is voluntary and coupled with incentives of free basic routine immunisation and inclusion in drug rehabilitation programmes[25]. In February 1997, 46% of 251 inmates were anti-HCV positive[26]. The raised HCV seroprevalence noted in this setting is confounded by a high proportion of inmates with past or concurrent history of IDU.

Other risk areas

There is no data available on occupational and iatrogenic transmission of hepatitis C in Malta. Ad hoc studies in this area are not prioritised given no standard eradicative treatment as yet for asymptomatic carriage.

There is also risk of infection from skin instrumentation at tattooing, cosmesis, electrolysis, bodypiercing and acupuncture. Skin instrumentation has not been independently linked to HCV infection in Maltese seropositives.

Although mother-to-child transmission has yet to be documented in Malta, the likelihood of its occurrence may increase as more of our females with a history of intravenous drug use bear children, mirroring the experience in vertical HIV-1 transmission in countries where IDU is an important component of HIV transmission. Local experience in paediatric hepatitis C is limited.

Clinical perspective

In Malta, patients with hepatitis C coming to treatment are picked up largely through screening of IDUs and prison inmates, or from follow-up investigations for abnormal liver function tests. Most are asymptomatic with only minimally raised transaminases indicative of ongoing hepatitis. This is in contrast with other forms of hepatitis which present with classical features in the acute or subacute stage.

Following current recommendations, in Malta, patients with deranged liver function and histological proof of active hepatitis are considered for alpha interferon treatment. Treatment guidelines have been formulated and are, at present, being piloted. Apart from disease criteria, for inclusion, patients with a history of drug use have to be clean of abuse for at least six months before start of treatment. The regimen currently adopted locally uses three mega Units of alpha interferon by sub-cutaneous injection three times a week. Duration of treatment is generally 12 months: however this may be extended, as recent studies suggest that outcomes can improve with regimens spread out longer[27]. Optimisation stands to be determined. Quantitative measurement of HCV RNA, though costly, is a useful tool in determining prognosis or evaluating response to therapy[14].

Alpha interferon treatment has its drawbacks: apart from the cost (thrice weekly injection for 12 months tops Lm1,000 in medicinal costs alone[28]), adverse effects are quite common. These include flu-like symptoms, depression and neutropenia[29]. A full evaluation of response to treatment (which would include key quality of life measures) is in order for patients undergoing care.

Conclusion

In conclusion, a case is made for prioritising hepatitis C in Malta as a formidable emerging concern, which will have a significant impact on health resources. The following summary recommendations are being made based on greatest scope for action.

1. Safe practices at transfusion and organ donation.
It is essential to ring-fence this priority area given that:

- efficiency of infection via this route is high
- fractioning of blood products means one infected donation can affect several recipients
- infection acquired post-donation has become highly unacceptable more so for conditions which can be detected

2. Preventive action in other risk areas.
Efforts should be directed at educating IDUs on safe practice, and risks of needle sharing. The policy of distributing syringes freely should be upheld. The management of correctional facilities will increasingly have to face in-prison transmission of bloodborne conditions, and pressures to stream inmates by crime category or serostatus.

Preventive action is labour-intensive, involving contact tracing, pre- and post-test counselling, testing and referral. Given the occurrence of associated risk locally (IDU, sexual exposure), there is sufficient scope to customise services towards preventive action coupled with AIDS education, and in conjunction with other sectors outside the formal health services.

Regulatory functions remain necessary to uphold sterile practice in areas like dentistry, other surgery, tattooing and beauty therapy.

3. Occupational risk management

Workers occupationally exposed to blood and blood products may be at increased risk of acquiring hepatitis through their work. An infected worker can then transmit infection to patients treated. If the litiginous setting stands to intensify, this would have to be addressed. Infected workers will have to be suspended from performing interventions with high risk of viral transmission, with attendant loss of hard-gained expertise. Universal precautions in risky patient-worker interactions remains important.

4. Epidemiological survey and analysis

There is clear scope for focusing studies in specific risk areas. Such might include seroprevalence surveys of those multiply-transfused in the pre-screening era and offspring of women at risk or with confirmed HCV. Known associated conditions which may be of local relevance and amenable to study include subjects with thalassaemia, haemophilia, and on dialysis[14].

Serial testing of comparable populations over time (eg blood donors, IDUs or antenatal females) could be a useful indicator of extension of infection over time. Unlinked anonymous studies would help estimate seroprevalence in various at-risk subgroups not generally in contact with the health services.

5. Patient care

Dedicating care services through a centralised liver clinic is expected to concentrate expertise, ensure better adherence to evaluated protocols and enhance academic pursuit. This should promote uniform eligibility and management modalities based on evidence rather than idiosyncrasy and routine habit. The possible stigma connotations of a 'liver clinic' have to be recognised. Therapy with new and expensive chemotherapy has also to be viewed in the light of its 'transplant-sparing' effect, as these interventions incur very high costs to patients and services.

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