Correspondence

Hepatitis C virus genotype 1 NS5A variants in Japanese patients

I read with interest the Article by Masashi Mizokami and colleagues,1 which described the results of treating Japanese patients with hepatitis C virus (HCV) genotype 1 with the NS5A inhibitor ledipasvir and NS5B nucleoside inhibitor sofosbuvir with or without ribavirin. The authors showed that 76 (22%) of 341 patients had NS5A resistance-associated variants at baseline, however, they did not provide the frequency of specific NS5A variants detected at baseline. This is a limitation for a proper assessment of patients receiving ledipasvir and sofosbuvir, and therefore their study results cannot be compared with those of other studies in the specialty.

In Japan, 70% of patients with HCV seropositivity have genotype 1b, and the NS5A variants L31M/V and Y93H in HCV genotype 1b have been shown to decrease activity of the NS5A inhibitor daclastavir in Japanese patients.1–4 The frequency of these NS5A resistance-variants has been reported in about 2–5% and 8–25% of patients with Japanese HCV genotype 1b.1–4 In an analysis of patients who received ledipasvir and sofosbuvir in phase 3 trials in the USA and Europe, 37 (29 with genotype 1a and eight with genotype 1b) had virological failure.2 Of the eight patients with genotype 1b and virological failures, seven (88%) had virus with NS5A resistance-associated substitutions L31V/M/I or Y93H at the time of virological failure. Additionally, three (43%) of these seven patients with HCV genotype 1b had baseline NS5A resistance-associated variants. These data suggested a potential effect of NS5A-resistant variants on the activity of ledipasvir. In Mizokami and colleagues’ study,1 a patient who had a relapse after receiving 12 weeks of ledipasvir and sofosbuvir with ribavirin had HCV genotype 1b with the NS5A resistant-associated variant Y93H at baseline and time of relapse.

In view of the reported frequency of NS5A variants L31M/V and Y93H in HCV genotype 1b in Japan, and that ledipasvir has a similar potency and resistance profile to that of daclastavir,1 Mizokami and colleagues should also report the frequency of baseline L31M/V and Y93H variants as part of the disease characteristics of patients with HCV genotype 1b who are treated with ledipasvir and sofosbuvir in Japan, because this will enable an important assessment of the antiviral activity of this promising interferon-free regimen to progress. I was an employee of AbbVie and held stock options during my employment.

Regis A Vilchez
regis.vilchez@alumni.bcm.edu
Department of Molecular Virology and Microbiology, Baylor College of Medicine, Houston, TX, USA


Schistosomiasis in Corsica and the pivotal role of travellers

We read with interest the Comment by Jérôme Boissier and colleagues regarding the detection of urinary schistosomiasis acquired in Corsica.2 They suggest that snail-borne helminthiasis, including schistosomiasis, should be considered an emerging public health threat as a result of climate change. Although we do agree with this concept, we would like to emphasise the pivotal part played by travellers in this evolving situation. We have identified cases of schistosomiasis in tourists from Germany, Belgium, and Canada through the GeoSentinel and EuroTravNet networks,3 and colleagues have reported cases in Italian tourists.2 Among the 141 cases reported so far, most occurred in visitors from outside Corsica, with only a few cases among locals (n=19). The population of the touristic area of Porto Vecchio where patients were exposed to the parasite increases by ten times during the summer season, driven by a large influx of tourists from mainly France but also from Europe (especially Italy, Germany, and Switzerland), and North America.2 The first cases of schistosomiasis acquired in Corsica were identified in January, 2014, in a German family from Dusseldorf exposed during the...
summer of 2013 before any case was identified in the French population.\(^2\) Because tourists outnumber residents,\(^3\) surveillance of schistosomiasis originating in Corsica must include national and international travellers.

Most cases in travellers up to now have been identified by the screening of asymptomatic individuals who spontaneously came for assessment after the large media attention; clinicians, including general practitioners, therefore need to be alert to the risk of acquiring schistosomiasis in Corsican rivers.\(^2,3\) Diagnosis is challenging—in both acute and chronic infections in travellers, the sensitivity of microscopic examination of urine to detect eggs is notoriously poor and the performance of serology is far from optimum. Most reference travel clinics therefore use conventional microscopy that is systematically combined with two different serological tests. The sensitivity of this approach (diagnosis of infection if two serological tests are positive) has been estimated at more than 78% for chronic schistosomiasis.\(^1\) Alternatively, the use of a western blot method using Schistosoma haematobium antigen can be considered.\(^3\)

Travel has always been a factor in the dissemination of parasites. Paleoparasitological analyses have identified S haematobium eggs dated to the 15th century in a latrine in Montbéliard, France that were attributed to importation from Africa.\(^5\) The intensive scale of global travel and immigration in the 21st century is a pivotal factor in the carriage of pathogens and their introduction into susceptible areas. At best, surveillance should even be expanded to other Mediterranean areas with similar suitable ecology.

We declare no competing interests.

*Philippe Gautret, Frank P Mockenhaupt, Emmanuel Bottieau, Philippe Parola, Patricia Schlagenhauf philippe.gautret@club-internet.fr

Institut Hospitalo-Universitaire Méditerranée Infection, 13005 Marseille, France (PG, PP); Aix Marseille Université, Marseille, France (PG, PP); Institute of Tropical Medicine and International Health, Charité – Universitätsmedizin Berlin, Berlin, Germany (FPM); Department of Clinical Sciences, Institute of Tropical Medicine, Antwerp, Belgium (EB); and University of Zurich Centre for Travel Medicine, WHO Collaborating Centre for Travellers’ Health, Institute for Epidemiology, Biostatistics and Prevention, Zürich, Switzerland (PS).


Mission Indradhanush and the counterfeit drug trade in India

In Lancet Infectious Diseases, Sanjeeet Bagchi’s report on Mission Indradhanush summarises India’s initiative to provide children protection against diphtheria, whooping cough, tetanus, poliomyelitis, tuberculosis, measles, and hepatitis B.\(^1\) However, one of the key questions that hasn’t been addressed either in the report or in the published views of India’s health minister and health officials is what measures are being undertaken by the Indian Health Ministry to guarantee the availability of genuine vaccines at centres associated with Mission Indradhanush?

According to the Pharmaceutical Security Institute, of 2177 reported cases of incidents involving counterfeit drugs in 2014, 875 cases (around 40%) were from Asia.\(^3\) In Asia, India and China are the key players in the manufacture, distribution, and sale of counterfeit drugs.\(^4\) Both the manufacture and sale of counterfeit drugs is very high throughout India, which is a major obstacle to the success of Mission Indradhanush. Additionally, India is one of major hubs for the export of counterfeit drugs, especially through Dubai (United Arab Emirates), which has threatened health care in southeast Asian and sub-Saharan African countries. One of the direct global effects of the Indian counterfeit drug trade is the development of artemisinin-resistant Plasmodium falciparum in southeast Asian and sub-Saharan African countries, because India is one of the largest exporters of antimalarial drugs to these nations.\(^5\) Additionally, reports from key Indian newspapers in 2014–15 alone reveal several incidents related to the counterfeit drug trade.

<table>
<thead>
<tr>
<th>Year</th>
<th>Region</th>
<th>Report</th>
<th>Source</th>
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</thead>
<tbody>
<tr>
<td>2015</td>
<td>Ludhiana, Punjab</td>
<td>Illegal manufacture of dietary supplements and</td>
<td>Times of India</td>
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<td></td>
<td></td>
<td>their sale as imported products</td>
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<tr>
<td>2015</td>
<td>Chandigarh, Punjab</td>
<td>Manufacture of hydroxyprogesterone caproate</td>
<td>Chandigarh Tribune</td>
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<td></td>
<td></td>
<td>injection without any active ingredient</td>
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<tr>
<td>2015</td>
<td>Berhampur, Orissa</td>
<td>Stolen government drugs consisting of antibiotics recovered from a private clinic</td>
<td>Times of India</td>
</tr>
<tr>
<td>2015</td>
<td>Panchkula, Haryana</td>
<td>Sale of expired medicines</td>
<td>The Tribune</td>
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<tr>
<td>2015</td>
<td>New Delhi</td>
<td>Three people arrested for the manufacture and</td>
<td>The Indian Express</td>
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<td></td>
<td></td>
<td>sale of spurious drugs</td>
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<tr>
<td>2014</td>
<td>Bhubaneswar, Orissa</td>
<td>Sale of fake pentavalent vaccines</td>
<td>Times of India</td>
</tr>
</tbody>
</table>

Table: Some incidents related to counterfeit drugs in India, 2014–15

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