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Follow up after a family based genetic screening programme for familial hypercholesterolaemia: is screening alone enough?

Merel C van Maarle, Marlies E A Stouthard, Perla J Marang-van de Mheen, Niek S Klazinga and Gouke J Bonsel

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Notes
HSV-1 was found in 751 (70%) of all positive swabs in women <25 years, 141 (41%) in men <25 years, 413 (49%) in women ≥25 years, and 182 (25%) in men ≥25 years. In 1986-8, 33% (187) of all positive swabs were due to HSV-1, rising progressively to 56% (548) in 1998-2000 (P<0.0001). A significant rise (P<0.0001, 1986 v 2000) in the proportion of isolates attributable to HSV-1 occurred in each of the four age and sex subgroups (P<0.0001) (figure).

Comment
Both the number and percentage of genital HSV-1 infections have risen. Genital infection with HSV-1 is strongly associated with being young (aged <25 years) and being female.

Explanations include changing host susceptibility and changing sexual behaviour of the population. The population seroprevalence of HSV-1 is falling; increasing numbers of young adults are susceptible to HSV-1 infection.3 As genital tract reactivation of latent HSV-1 infection is infrequent, most new cases of genital HSV-1 infection are likely to be due to orogenital transmission, but there is no evidence suggesting that oral sex practices have changed substantially.4 The occurrence of HSV-1 infection in women, seen consistently in other studies,5 is unexplained.

These results have three important implications for management. Firstly, patients should be counselled about the more favourable clinical course of genital HSV-1 than of HSV-2 infection; recurrences are generally milder and infrequent. Secondly, subclinical shedding of HSV-1 is less common; this has a direct bearing on the likelihood of transmission.7 Thirdly, preventive strategies for genital herpes should focus on the risk of unprotected orogenital intercourse, which is frequently perceived as “safe” in the context of sexually transmitted infections.

We thank Geoffrey Clements, previously director of the West of Scotland Specialist Virology Centre.

Participants, methods, and results

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Familial hypercholesterolaemia is an autosomal dominant disorder of lipoprotein metabolism, with an estimated frequency of 1 in 500 in Western countries; it results in excess mortality from coronary artery disease.1 Now that the genetic defects can be detected and statins are available to lower lipids effectively, genetic screening has been considered.2 3 In 1994 a family based genetic screening programme for familial hypercholesterolaemia started in the Netherlands. The programme's effectiveness rests on the evidence based treatment of newly identified patients. We therefore assessed the subsequent preventive care and short term clinical outcome in people testing positive for familial hypercholesterolaemia as a proxy for the expected long term level of coronary artery disease.4

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Quality of treatment and clinical outcome in people testing positive for familial hypercholesterolaemia. Values are numbers (percentages)

<table>
<thead>
<tr>
<th>Follow up</th>
<th>Newly identified cases (n=41)</th>
<th>Confirmed cases (n=125)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>At screening</td>
<td>At follow up</td>
</tr>
<tr>
<td>Cholesterol checked</td>
<td>17 (41)*</td>
<td>29 (71)*</td>
</tr>
<tr>
<td>Use of drugs</td>
<td>0*</td>
<td>14 (34)*</td>
</tr>
<tr>
<td>Use of statin</td>
<td>0*</td>
<td>14 (34)*</td>
</tr>
<tr>
<td>Diet</td>
<td>5 (12)*</td>
<td>19 (46)*</td>
</tr>
<tr>
<td>Lifestyle advice</td>
<td>0*</td>
<td>34 (83)*</td>
</tr>
<tr>
<td>Quality of treatment:†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>10 (24)</td>
<td>20 (48)</td>
</tr>
<tr>
<td>Moderate</td>
<td>0</td>
<td>4 (10)</td>
</tr>
<tr>
<td>Unsatisfactory</td>
<td>31 (76)</td>
<td>16 (39)</td>
</tr>
<tr>
<td>Missing</td>
<td>0</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Known hypercholesterolaemia</td>
<td>0*</td>
<td>10 (24)*</td>
</tr>
<tr>
<td>Cholesterol unknown</td>
<td>31 (76)*</td>
<td>9 (22)*</td>
</tr>
<tr>
<td>Smoking</td>
<td>14 (34)</td>
<td>12 (29)</td>
</tr>
<tr>
<td>Body mass index &gt;27 kg/m²</td>
<td>3 (7)</td>
<td>4 (10)</td>
</tr>
<tr>
<td>Quality of clinical outcome:‡</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>5 (12)</td>
<td>15 (37)</td>
</tr>
<tr>
<td>Moderate</td>
<td>5 (12)</td>
<td>6 (15)</td>
</tr>
<tr>
<td>Unsatisfactory</td>
<td>31 (76)</td>
<td>19 (46)</td>
</tr>
<tr>
<td>Missing</td>
<td>0</td>
<td>1 (2)</td>
</tr>
</tbody>
</table>

NR—not relevant.
†Significant difference in time (P<0.05).
‡Use of statin (depending on cholesterol level), adherence to diet, and advice to quit smoking and lose weight if necessary; moderate-use of statin, without diet or appropriate lifestyle advice; unsatisfactory—no drugs while hypercholesterolaemic, or using cholesterol lowering drugs other than statins.
§Cholesterol <6.5 mmol/l and body mass index <27 kg/m², and non-smoker; moderate—cholesterol <6.5 mmol/l and body mass index >27 kg/m², smoker, or both; unsatisfactory—cholesterol ≥6.5 mmol/l or unknown, regardless of body mass index or smoking status.

We divided the people testing positive into two categories: those with an unknown cholesterol concentration or with normal cholesterol without treatment at the time of screening (“newly identified cases”) and those known to have hypercholesterolaemia (cholesterol ≥6.5 mmol/l) or being treated for this condition (“confirmed cases”).

One hundred and sixty six (77%) participants filled out all three questionnaires. Respondents and people lost to follow up differed in only one characteristic—use of statin (57% v 39%, P < 0.05).

Seventy three (44%) respondents were men, 41 (25%) were newly identified, and 125 (75%) were confirmed cases. The confirmed cases were older (48.2 v 38.9 years), had higher cholesterol concentrations (10.7 v 6.0 mmol/l), if known, and were more likely to have at least one first degree relative with cardiovascular disease (62 (50%) v 13 (32%)) or one premature cardiovascular death in the family (26 (21%) v 2 (5%)) (P < 0.05 for all comparisons).

Although the quality of treatment and clinical outcome improved substantially over time in both groups (table), people testing positive for familial hypercholesterolaemia did not attain an optimal level of care. Quality of treatment was still unsatisfactory in 33 (20%) cases, and quality of clinical outcome was still insufficient in 75 (45%). Fifty eight (35%) participants were hypercholesterolaemic at follow up, nine (16%) of those with hypercholesterolaemia did not take statins, and 40 (24%) participants smoked.

Comment

Both confirmed and newly identified patients benefit from screening for familial hypercholesterolaemia, as their risk status improves and cholesterol lowering treatment is instituted, but in almost half of all cases the achieved level of care does not keep up with current guidelines. Opportunities for improvement towards current guidelines include physician education, better implementation of guidelines, and, especially, an intensification of the link between diagnosis and follow up care in the screening process.

We thank the respondents for their enthusiasm and Marina Umans-Eckenhausen and the genetic field workers of the foundation for tracing hereditary hypercholesterolaemia for their support and help with inclusion of the study population.

Contributors: All authors conceived the study, and MCvM and MEAS collected the data. MCvM, MEAS, and JGB contributed to the analysis and interpretation of the data, and all authors contributed to the preparation of the paper. MCvM is the guarantor.

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Competing interests: None declared.


One hundred years ago
The hygienic spittoon question in France

At a recent meeting of the Paris Académie de Médecine M. Périé presented a report on the utilisation of spittoons in the Gare du Nord. The Académie some time ago made an appeal to the railway companies of France to place spittoons in their stations so that persons who felt inclined to expectorate might do so without danger to their fellows. The Nord Company at once placed spittoons of the pattern recommended by the Académie in its Paris terminus, and engaged trained male nurses to look after them. The spittoons have been available for about a year, but they have been very little used. Some time ago the Académie drew up a code of recommendations for the prophylaxis of tuberculosus, in which naturally the question of expectoration occupied a prominent place. A receptacle of a convenient pattern, which could be carried in the pocket and used without exciting much attention, was recommended. It was expected that the issue of this sanitary charge—for such it was intended to be—would be followed by an immediate abatement of the spitting nuisance, and that the pocket spittoon would quickly come into general use.

It is令人惊讶的是，没有需求。 （Spitting for example）...