LETTERS TO THE EDITOR

Exposures, mutations and the history of causality

EDITOR,— The editorial by Paolo Vineis is an interesting attempt to clarify various interpretations of causality in the medical literature. The following remarks are to be taken as a mere running commentary of the excellent paper by Vineis.

Causation is a conditional relation such as: if C then D. Ventricular standstill causes death: if the ventricles fail to contract, the patient dies.

What binds causes to their effect? Counterfactual conditionals (or counterfactuals) introduce some sort of necessity in a causal relation. Counterfactuals have the following structure: Assuming that (1) if C then D and (2) C and D occur.

Then we have: if C had not occurred (though it did), D would not have occurred. The counterfactual conditionals are of the form of the facts as the first part of the conditional “if C had not occurred” is false. Counterfactuals translate into predictions and introduce some support of necessity that allows to separate statements that are accidentally true from those which are regularly true: in the second case, our knowledge extends to the counterfactual cases.

Incidentally, I have serious reservations about the usefulness of Hempel's or Popper's hypothetico-deductive models because there are no such things as general laws in medicine: medical explanation is not deductive.

Vineis distinguishes five major interpretations of causality in medicine. After discussing an earlier broad Aristotelian one he brings in a second stream, springing from the success of bacteriology and according to which causality is analysed in terms of agency: a cause is a single, necessary factor of which causality is analysed. In a second stream, springing from the success of bacteriology and according to which causality is analysed in terms of agency: a cause is a single, necessary factor of which causality is analysed. In a second stream, springing from the success of bacteriology and according to which causality is analysed in terms of agency: a cause is a single, necessary factor of which causality is analysed.

The third stream, a cause is a sine qua non determinant on which the effect depends; it usually involves a cause-effect relation of some mixed nature, at once empirical and semantic. Necessary factors depend on the way we carve the universe; a point highlighted by MacMahon. According to the third stream, a cause is a sine qua non determinant on which the effect depends; it usually involves a cause-effect relation of some mixed nature, at once empirical and semantic. Necessary factors depend on the way we carve the universe; a point highlighted by MacMahon.

Vineis distinguishes five major interpretations of causality in medicine. After discussing an earlier broad Aristotelian one he brings in a second stream, springing from the success of bacteriology and according to which causality is analysed in terms of agency: a cause is a single, necessary factor of which causality is analysed. In a second stream, springing from the success of bacteriology and according to which causality is analysed in terms of agency: a cause is a single, necessary factor of which causality is analysed. In a second stream, springing from the success of bacteriology and according to which causality is analysed in terms of agency: a cause is a single, necessary factor of which causality is analysed. In a second stream, springing from the success of bacteriology and according to which causality is analysed in terms of agency: a cause is a single, necessary factor of which causality is analysed. In a second stream, springing from the success of bacteriology and according to which causality is analysed in terms of agency: a cause is a single, necessary factor of which causality is analysed.

For Mackie, a cause is part of some sufficient conditions—that is, a INSUS condition. Exposed attributable fraction (or Cole's attributable proportion) is the INUS element namely Mackie's necessary causal component of a sufficient set; it estimates how necessary the exposure is for the occurrence of the disease. Cotter et al., counterfactually, what is the probability that the disease would not have occurred among the non-exposed, given that exposure and disease actually occurred. Yet, there is, as it were, no known example in medical science of a condition sufficient for its effect so that when this deterministic model broke down a fourth stream emerged as the ideas of sufficient and necessary causes were being traded away for a probabilistic model.


Table 1

<table>
<thead>
<tr>
<th>Disease manifestations</th>
<th>Polytetnic</th>
<th>Monothetic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuberculosis</td>
<td>Monothetic</td>
<td>Polytetnic</td>
</tr>
<tr>
<td>Smallpox</td>
<td>Polytetnic</td>
<td>Monothetic</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>Polytetnic</td>
<td>Monothetic</td>
</tr>
<tr>
<td>Cancer</td>
<td>Polytetnic</td>
<td>Monothetic</td>
</tr>
</tbody>
</table>

Author's reply

EDITOR,— I thank Dr Karhausen for his clear comments to my paper on causality in epidemiology. In addition to a summary of the different models of causation that have been used in medical reasoning, he gives some suggestions that deserve further theoretical development.

According to Bayes's theorem, the probability of disease given exposure is: $P(D|E) = \frac{P(E|D)P(D)}{P(E)}$.

This is the probability of developing the disease, conditional on exposure, is given by the product of the a priori (unconditional) probability of disease by the likelihood of exposure among the cases, divided by the prior probability of exposure. If disease is sufficient, $P(non-D|E) = 0$ (none of the exposed is healthy), while if the cause is necessary, $P(non-E|D) = 0$ (no diseased person is unexposed).

In addition, while it is clear that causes are rarely sufficient and/or necessary, also in case definition we have to face blurred borders among diseases. Let us consider the following scenario (see table 1).

For groups I and II the causal agent is single and well known (a virus for smallpox, a bacterium for tuberculosis). However, even in such cases of monoycausal, disease manifestations can be polythetic—that is, based on
more than one criterion; in the case of tuberculosis, the disease is not always univocally recognisable, and complex clinical and immunological criteria have to be used. In other words, while for smallpox clinical diagnosis is unequivocal, tuberculosis is a complex constellation from a symptomatological point of view, and the only way to recognise its different manifestations as belonging to a single entity is to refer to the causal agent. For many infectious diseases (another example is syphilis), the complex and polythetic clinical features can be unified in a single entity only because the causal agent can be identified or its presence can be inferred by immunological means. A univocally defined disease (on the basis of histology) such as lung cancer has several causes. Lung cancer cases have a certain histological appearance in common, but they cannot be unified on the basis of their aetiology. Finally, many psychiatric diseases are polythetic, both clinically and aetiologically. For example, bulimia cannot be univocally distinguished from other conditions characterised by compulsive eating or obesity. As for causal hypotheses, they are still extremely vague and apparently at the border between psychiatry, genetics and social medicine.

It should be emphasised that situations such as smallpox are an exception, while the rule is represented by “blurred” borders among different diseases, both on the side of symptoms and on the side of causal pathways.

Authors’ reply: Thinking about interactions and mechanisms

EDITOR,—We enjoyed the comments offered by Dr Karhausen on our two papers, as they discuss several causal issues that may be particularly relevant for research on mechanisms of carcinogenesis, and for the biological, clinical and epidemiological analyses of oncogene-environment interactions. We are not sure we totally agree with his (perhaps too clear cut) distinction between the roles of epidemiology and “experimental medicine” in analysing mechanistic interactions, and between processes, factors and events. None the less, at this time we have little to add to the aetiological and aetiological considerations we made in our previous papers, in this journal and elsewhere.

When new integrative studies are designed, and as new empirical evidence is accrued on the environmental causes of oncogene activation, we hope the proposals of Karhausen will again be thought out.

MIQUEL PORTA
LAURA RUIZ
MANUEL JARIOD
ALFREDO CARRATO
NURIA MALATS
Institut Municipal d’Investigació Mèdica (IMIM), Universitat Autònoma de Barcelona and Universitat Pompeu Fabra, Carrer del Dr Aiguader 80, E-08003 Barcelona, Spain

Correspondence to: Professor Porta
(e-mail: mporta@imim.es)


