

DRAFT
NOT TO BE QUOTED

Raffaella Campaner - PSE , Konstanz 2009

On Causal Explanation in the Health Sciences. Some Reflections on Epidemiologic Explanation (DRAFT – 12th September 2009)

I shall here focus on explanation, tackling what it is to causally explain within the health sciences. I shall consider how some hints from recent works into two of the main philosophical traditions on causation, namely those on, on the one hand, mechanistic causation as developed by Stuart Glennan and, on the other hand, manipulationist causation as developed by Jim Woodward, do when we look to a specific field within the health sciences, i.e. epidemiology. I shall refer to the wide and hot debate which has been taking place in epidemiology in the last decade which centrally involves the definition, status and methods of the discipline itself, and which has to do with what it is to explain a disease in epidemiological terms, as a complex and multilevel phenomenon. Such a debate provides some interesting suggestions and challenges as to what an adequate explanation should consider, and hence as to what a philosophical conception of explanation should account for.

1. Epidemiological paradigms and multilevel investigations

The debate on causal nexus and explanation of multilevel phenomena within epidemiology has been particularly vivid in the roughly the last decade. Various phases and paradigms can be identified in the history of modern epidemiology, during the 19th and 20th century. Each dominant paradigm centres in considerations on causal nexus, and affects public health practices differently:

- *sanitary statistics*, with the miasma paradigm (approximately 1840-1890): diseases are due to emanations from contaminated air, soil and water; interventions into urbanized societies are to be performed on sanitation and drainage;
- *infectious disease epidemiology*, with the advent of microbiology and the germ theory paradigm (established towards the end of the 19th century, lasted approximately from 1890 to 1950): diseases (such as tuberculosis, typhoid, diphtheria, infant diarrhoeas) are due to a single, specific

infectious agent (necessary and preferably sufficient), which has to be eradicated to interrupt transmission;

- *risk factor epidemiology*, with the theory of multiple causes, and an initial special focus on chronic diseases, (after World War II, approximately 1950-nowadays), also labelled “black box” paradigm¹: diseases are due to the exposure to a multiplicity of factors; and public health interventions should reduce individual risk. The specific-cause germ theory is substituted by a nonspecific-cause theory, and causes, which are denoted as “risk factors”, are taken to be unnecessary and insufficient. To evaluate what can be deemed risk factors for a disease, the risk factors are separated out of the web of causation, and the effects of exposures are isolated, and observed under simplified conditions.

This last paradigm, while presenting the advantage of acknowledging the webs of several causes underlying diseases, has been accused to have some serious drawbacks too:

a) a concentration on the *description* of the association risk factors/disease, vs. the *explanation* of causal processes: “the ideal is to create a state of all things being equal between exposed and unexposed populations. This staple of design and analysis manipulates study conditions to isolate the causal factors from those that are potentially confounding or irrelevant. At the same time, however, these simplified conditions obscure the antecedents of the risk factors under study. They also largely neglect the mediators linking the risk factors with the disease. Indeed, the controlled clinical trial – the best approximation of *ceteris paribus* and the model toward which other study designs were to strive – is designed for the *identification rather than the explanation* of causal factors” (Schwartz, Susser and Susser 1999, pp. 23-24, italics added). Causal relationships are isolated and analysed – the criticism goes – in so-to-speak “sterilized” conditions;

b) a strong focus on the *individual* level of organization: individuals are regarded as the preferred unit of interest over groups, and hence more proximate, biologic factors are favoured over more distal social, economic and environmental factors².

To overcome the limits of the black box paradigm, a further paradigm – which has been labelled “eco-epidemiology” - has been recently proposed. It promotes the study of multiple relations *across levels* and the reciprocal interpenetration of factors situated at different organization levels. “Ecologic epidemiology” aims to study data aggregated over groups rather than data on individuals, largely employs databases, provides disease mapping and detects geographic

¹ See Susser and Susser 1996a; on the “arc of epidemiology”, see also Susser, Schwartz, Morabia, Bromet 2006, ch. 2

² See Diez-Roux 1998.

anomalies³. Contrasting what it regards as too strong a focus on genetic factors - due to a growth in the last few decades in research on the genetic origins of diseases and their molecular mechanisms, and to the development of new technologies and screening tests⁴ - “eco-epidemiology” conceptualizes causes of pathologies as taking part into an interplay of factors at a number of different levels. For instance, “a genetic polymorphism may limit the ability of an individual to detoxify carcinogenic aromatic amines. However, only in an environment where this carcinogen is introduced by human economies does it become a potent risk factor for cancer” (Schwartz, Susser and Susser 1999, p. 28). Another example is given by recent studies on schizophrenia, and substantial variations in incidence of the pathology in different areas. Among the factors identified as causes of schizophrenia there are prenatal exposure to famine (specific historical moment), or, more in general, prenatal nutritional deficiency (specific period of development), paternal age at conception, genetic factors, but also – after observing a higher incidence of schizophrenia in urban areas – the timing and duration of exposure to the urban life (see March and Susser 2006).

Together with the recognition of the role of socio-economic and environmental factors and the reduction of the emphasis on the microlevel of molecular genetics, the emergence of the ecologic paradigm has promoted a shift of attention from risk factors’ effects on individuals, to populations. This in turn highlights the status of epidemiology as a discipline mainly oriented towards public health and prevention⁵. Such a different focus has been referred to by an epidemiologist as Paolo Vineis to draw a distinction between causes and mechanisms (see Vineis 2005). According to Vineis, causes and mechanisms have to be opposed as conceptual tools in a causal, epidemiologic analysis of diseases: on the one hand, when talking of “causes”, we are referring to *external* agents, which can be isolated analysed and separately from the organism; on the other hand, when talking of “mechanisms”, it is the *internal* functioning of the organism that we are thinking of. In so far as they are interested in public health, epidemiologists – Vineis states – are devoted to the former, namely to the study of “causes” in a probabilistic perspective, which allows them to formulate predictions on populations’ behaviour, whereas clinicians and researchers favour the search for “mechanisms”, in a deterministic perspective. Is it really the case?

2. Mechanistic and manipulability views

³ See for instance Wakefield 2008.

⁴ For some considerations on the “genetic paradigm” and its claims, see, for instance, Diez-Roux 1998 and Vineis 2005.

⁵ For recent reflections and commentaries over the status, role and future of epidemiology, see Susser and Susser 1996a and 1996b; Pearce 1996; Diez-Roux 1998.

Mechanistic knowledge is actually largely searched for, and especially invoked in order to overcome the limits of the black box paradigm, “with its focus on risk factor disease associations without sufficient consideration of the *downstream mechanisms* that allow to understand how the risk factors operates” (Susser, Schwartz, Morabia, Bromet 2006, p. 416, italics added). Instead of opposing “internal” and “external” factors as in Vineis’ analysis, a notion of mechanism should be adopted which allow to include both in one and the same account. Among contemporary, “neo-mechanistic” theories, I shall here consider Glennan’s, whose advocacy of the mechanistic approach to causation, and thus his contribution to the “revival” of this approach – which was started off by Wesley Salmon, and later promoted by such authors as Peter Machamer, Lindley Darden, Carl Craver, William Bechtel, Robert Richardson, Adele Abrahamsen, Jim Bogen – goes back to the Nineties. His “complex-systems account” (1996), revised in his (2002), centres in the following definition: “a mechanism for a behaviour is a complex system that produced that behaviour by the interaction of a number of parts, where the interactions between parts can be characterised by direct, invariant, change-relating generalizations” (Glennan 2002, p. S344)⁶. Glennan’s view of mechanistic causation is meant to be a theory of causal explanation too. Mechanisms are made up of parts, and events are claimed to be causally related when there is a mechanism that connects them; a good description of a mechanism is believed to provide an adequate causal explanation: “The description of the mechanism responsible for the production of [the] effect provides the explanation” (Glennan forthcoming, p. 9).

Glennan’s notion of mechanism is strongly linked to that of productive behaviour: a mechanism is identified by what it *does*. As in Salmon’s view, a central role is played by the notion of interaction, though this is not as precisely defined. According to Glennan, the sorts of allowable interactions that may take place between the parts of a mechanism simply depend upon the behaviour we are interested in explaining, and mechanisms must be such that their “‘internal’ parts interact to produce a system’s ‘external’ behaviour” (Glennan 1996, p. 49); no sharp distinction is drawn between “internal” as opposed to “external”, and no specific criterion is given regarding what can properly count as “parts” of a mechanism. They can easily be both what Vineis deems as “internal and “external”, i.e. the “mechanism” can be composed of parts that belong to both organisms and the environment they are in.

On the other hand, it seems that further features are called for to circumscribe “parts” and “interactions” in a causal sense, as something that makes a fundamental contribution to the correct

⁶ In his (1996) definition mechanisms are stated to work “according to direct causal laws” (p. 50).

functioning of a mechanisms as a whole. The main issue turns out thus to be that of providing some criterion of “relevance”, as recognised in Glennan’s latest work (forthcoming). The key-notion employed to identify a genuine causal mechanism is that of invariant generalization. As emerges from the key-definition given above, from his (2002), the interactions between parts of the mechanism which give rise to its behaviour are characterised by invariant generalizations, namely generalizations that would hold were a range of possible interventions to be performed. Already in his (1996) Glennan remarks that we are usually justified in asserting, for example, “if we were to turn the key, the car would start” because we know a mechanism exists which connects key-turning with car-starting. Likewise, we know that a given sort of circumstances exists in which “the counterfactual would turn out to be false, namely breakdown conditions for the mechanism which explains it. [...] Counterfactual generalizations can be understood in this way without appealing to unanalysed notions of cause, propensity, possible worlds, and the like” (1996, p. 63). No such thing as a counterfactual analysis of causation separated from the mechanistic one is put forward, and Glennan – whose position remains a genuinely mechanistic one – admits of counterfactuals only insofar as they stand in a close relation with mechanisms. According to him, a two-way relationship holds between invariant generalizations and mechanisms: “First, reliable behaviour of mechanisms depends upon the existence of invariant relations between their parts, and change-relating generalizations characterise these relations. Second, many such generalizations are mechanically explicable, in the sense that they are just generalizations about the behaviour of mechanisms. A single generalization can both be explained by a mechanism and characterise the interaction between parts of a larger mechanism” (Glennan 2005, pp. 445-446).

While widely discussed by Salmon, and Hitchcock’s works on Salmon’s view, relevance was not a major concern in Glennan’s former works on mechanistic causation. In his most recent paper, however, Glennan highlights the importance of indentifying causally relevant properties to explain why a cause brings about a given effect. In “Mechanisms, Causes and the Layered Model of the World” (forthcoming), he suggests that “causal claims are of two kinds – claims about the objects and events that *produce* effects and claims about the properties of or facts about these objects and events that are *relevant* to these effects” (p.2). In order to be explanatory, causal claims have to concern properties of the mechanism’s components that are relevant to the effect to be explained. The causally and explanatorily relevant properties are properties of the mechanism, its component parts, their interactions and organization (see Glennan forthcoming, p. 10). The identification of the *relevant* aspects in a hypothesized mechanism can be pursued through an interventionist-

counterfactual approach, given that “causal relevance is essentially a counterfactual notion” (Glennan forthcoming, p. 5). At the same time, Glennan states: “In contrast to claims about causal relevant properties, claims about productive events are not essentially counterfactual. To say that one event produced another is to say that *in fact* the causative event is connected to the effect via a continuous chain of causal processes. It matters not what might have happened had the productive event not occurred” (*ibid.*, pp. 5-6)⁷. Although productive events are not *essentially* counterfactual, counterfactuals are to be used, in some specific – as we shall see - “interventionist” sense, in order to identify *productive* mechanisms.

“Interventionist counterfactuals” with heuristic value can be regarded as compatible with a mechanistic account of causal explanation, as suggested by the appeal that Glennan himself makes in his (2002) to the notion of “invariant generalization”, explicitly borrowed from Jim Woodward, whose account is, instead, inspired by a manipulationist perspective on causation. Invariance is the fundamental notion on which his whole theory is grounded. Woodward defines invariance as “the key feature a relationship must possess if it is to count as causal or explanatory”, and believes a generalization is to be deemed as “invariant [...] across certain changes if it holds up to some appropriate levels of approximation across those changes” (Woodward 2003, p. 239). The invariance of the relationship between *X* and *Y* under at least some interventions on *X* is a necessary condition for the relationship between *X* and *Y* to be regarded as causal. As in any manipulability approach, a strong interest for controlling is expressed: “wiggling” on a given *X* that is a relatively invariant cause of *Y* gives one some control over whether *Y* obtains. “Invariance under intervention” is taken to stand for “invariance under some testing interventions on variables figuring in the generalization”. Causal generalizations are generalizations that are invariant under *some* (actual or ideal) interventions, and can be expressed in counterfactual terms: they are such that they *would have* continued to hold *if* various sorts of changes *had been made* to occur (“interventionist counterfactuals” or “active counterfactuals”). Invariant generalizations are the key to explanation. An explanation is stated to be an answer to a *what-if-things-had-been-different* question:., since information which is to be counted as relevant to causally explain an outcome involves the identification of factors such that, *if* manipulations of these factors *had been* possible, these manipulations *would have* proved a way to alter the phenomenon in question: “one ought to be able to associate with any successful explanation a hypothetical or counterfactual experiment: [...] the

⁷ Glennan states he accepts what he takes “to be the most commonly held view – that causation is in the first instance a relation between events, and that events are understood in terms of instances or occurrences or exemplifications of properties” (forthcoming, p. 3)

explanation must enable us to see what sort of difference it would have made for the explanandum if the factors cited in the explanans had been different in various possible ways. [...] Our interest in causal explanation represents a sort of generalization or extension of our interest in manipulation and control from cases in which manipulation is possible to cases in which it is not” (Woodward 2003, p. 11).

Commenting on another neo-mechanistic view, namely Machamer, Darden and Craver’s, Woodward states their account cannot “capture the idea that there is an overall productive relationship [...] without explicitly invoking the idea of counterfactual dependence” (Woodward 2000, p. 35). Counterfactual dependence shall be employed in order to identify *what* performs the production. It is in this respect that they are admitted in epidemiology too. According to Susser, Schwartz, Morabia and Bromet, actually “the counterfactual approach [...] has gained broad if not universal acceptance” (2006, p. 35) in epidemiology. Counterfactuals can be seen as having an important heuristic role with respect to the identification of mechanisms’ *relevant* components, for the identification – in epidemiological terms – of relevant risk factors. The application of a counterfactual approach leads epidemiologists “to ask [...] whether the removal of one component of the constellation of circumstances [...] would have prevented the outcome [...] from occurring in this particular instance. [...] The counterfactual has been adopted as a central tenet by many, though not all, epidemiologists (Kaufman and Poole 2000; Maldonado and Greenland 2002). The following definition of a cause consistent with a counterfactual approach is offered in a current textbook, *Modern Epidemiology*: ‘We can define a cause of a specific disease event as an antecedent event, condition or characteristic that was necessary for the occurrence of the disease at the moment it occurred, given that other conditions are fixed’ (Rothman and Greenland 1998, p. 8). [...] Under this concept of causation, an exposure is a cause if some of the exposed people who incurred the disease would not have incurred it without the exposure” (Susser, Schwartz, Morabia, Bromet 2006, p. 36 and p. 38). That is – we can rephrase – if an invariant generalization is shown to hold under some hypothetical interventions.

Can a manipulationist, counterfactual-interventionist theory fit such a field as epidemiology? On the one hand, as an account of causation it captures an essential aspect of the discipline, that is, its being strongly practice-oriented, with prevention as its main aim. Prevention can often be achieved even in the absence of mechanistic knowledge. Vineis has pointed out how the theoretical goal of understanding the mechanistic working of the disease and the practical goal of curing it do not necessarily go together. If, on the one hand, mechanistic knowledge can provide the premises

for the elaboration of an adequate therapy, on the other hand, in many cases the therapy itself has preceded the discovery of mechanistic details, and has done without it. Vineis has highlighted how the history of medicine is full of examples of cases in which the preventive measure was actually discovered much earlier (from a few to many decades) than the causal agent bringing about the disease (see Table below). “In the majority of historical cases many years passed between the identification of an effective preventive measure and the discovery of the ‘final’ cause or the mechanism of action. Actually, sometimes a therapeutic measure can prove effective in the absence of the slightest evidence of the biological causes or the mechanisms” (Vineis 2005, p. 117)⁸. Waiting for the mechanistic explanations of the diseases, with the descriptions of the productive behaviours of the causal agents, would have meant a serious delay in the promotion of those therapies and preventive strategies which have proved essential for reducing the incidence of these pathologies.

DISEASE	DISCOVERER AND DATE OF DISCOVERY OF THE PREVENTIVE MEASURE	DATE OF DISCOVERY OF THE CAUSE	CAUSAL AGENT
Scurvy	Lind, 1753	1928	Ascorbic acid deficiency
Pellagra	Casal, 1755	1924	Niacin deficiency
Cancer of the scrotum	Pott, 1775	1933	Benzopyrene
Smallpox	Jenner, 1798	1958	Orthopoxvirus
Puerperal fever	Semmelweiss, 1847	1879	Streptococcus
Cholera	Snow, 1849	1893	Vibrio Cholerae
Professional cancer of the bladder	Rehn, 1895	1938	2-naphthylamine
Yellow fever	Finlay, 1881	1928	Flavivirus
Cancer of the mouth (in tobacco chewers)	Abbe, 1915	1974	N-nitrosornicotine

(TABLE from Vineis 2005, p. 117)

⁸ According to Vineis, as a matter of fact, “epidemiologists appeal to causation mostly as to a basis for intervention” (Vineis 1991).

In various cases, therapeutic interventions hence are (and have to be) performed without an understanding of underlying mechanisms. In this sense, causation can be best conceived of in a manipulability perspective. At the same time, though, it appears it will not do, on its own, if a causal *explanation* is what we are looking for.

Both a mechanistic approach as Glennan's and an interventionist account as Woodward's provide crucial essential hints with respect to epidemiologic *explanation*, and neither would suffice on its own. Although it can be readily agreed that invariant generalizations play a role in explaining, and that in presenting an explanation one is committed to a set of counterfactual claims concerning what would have happened to the effect if the cause had been different, this is not to say that explanations consist just in exhibiting patterns of counterfactual dependence. It is one thing to say that its being invariant under intervention is what does the work of distinguishing a causal generalization from a non-causal claim, and another to say that only this very feature on its own is that which explains. Diseases under enquiry are organized, structured systems of interacting components, which we try to unravel for explanatory purposes; in order to uncover them, we shall appeal to interventionist counterfactuals. But invariant generalizations, telling us how a variable might vary were another to be changed by – actual or hypothetical – interventions, and correctly admitting of exceptions, will not suffice for explanatory purposes. “Causal claims say something different from: ‘the effect would not have occurred if the cause had not occurred’; they say something about *how* the effect has been brought about by the cause” (Lipton and Ødegaard 2005). What we want to know, in order for a causal explanation, and not simply a causal identification, to be elaborated, is what goes on *between* the exposure to the risk factors and the appearance of the symptoms, i.e.: we want to uncover what constitutes the pathology's *mechanistic working*. Only in this way shall we overcome the shortcomings of the black box paradigm. Explanations require “the specification of a complex mechanism consisting of many parts and interconnections” (Thagard 2003, p. 251). Specified mechanisms clarify the actions and effects of the risk factors and the organism's behaviour they start out; although not strictly necessary for curing, knowledge of mechanisms allows in turn more effective cures and prevention strategies. Woodward himself proposes a notion of mechanism, defined as a structured set of parts or components whose behaviour is described by invariant generalizations, and such that “the overall output of the mechanism will vary under manipulation of the input to each component and changes in the components themselves” (Woodward 2002, p. S375)⁹. To reconcile it with Glennan's claims, we

⁹ Woodward also acknowledges that “doing the experiment corresponding to the antecedents of [counterfactual claims] doesn't *make* [them] have the truth-values they do. Instead the experiments look like ways of *finding out* what the truth

can say that “the mechanism is doing the causal work”, and the invariant generalizations “simply summarize the behaviour of the mechanism” (Glennan forthcoming, p. 9).

Woodward and Christopher Hitchcock have recently claimed that “successful explanation has to do with the exhibition of patterns of counterfactual dependence describing how the system whose behaviour we wish to explain would change under various conditions” (Woodward and Hitchcock 2003a, p. 2). As a matter of fact, though, when having a closer look at scientific explanations, we do not find a long series of counterfactual, “what-if-things-had-been-different” claims; it is the behaviour of complex systems which is foremost presented, not how such behaviour varies, or, even less, how it would have varied if certain conditions, which did not obtain, had done so. Explanations provide the resources for answering what-if-things-had-been-different questions by making explicit *which* variables the explanandum depends upon, allow us to gain insights into properties we would like to control, to deal with matters such as control groups, to respond to why we chose some specific experimental strategy. Interventionist counterfactuals allow to discover *what is causally relevant*, while a mechanistic perspective shall be adopted to shed light on *how* relevant entities perform their productive activities, i.e. how causal relevance translates into productive causality¹⁰. If associated with interventions, as Woodward suggests, counterfactuals can play an essential heuristic role and yet leave all the explanatory power of mechanisms unaffected.

It is hence mechanistic knowledge which appears to be the ultimate target as far as explanation is concerned. For instance, with regard to schizophrenia, “we might attempt to identify prenatal viral infection as a risk factor, without necessarily understand how it combines with genetic vulnerability and adolescent cannabis use, and without understanding all the other pathways that can lead to schizophrenia. By identifying and eliminating this risk factor we could reduce the incidence of schizophrenia, even without understanding how the virus affects the brain of a developing foetus”, but then: “the knowledge that this exposure plays a role in causing the disease would help *direct research into causal mechanisms*” (Susser, Schwartz, Morabia, Bromet 2006, p. 35, italics added). Causal mechanistic explanations often provide the framework which allows to generalize the results of a given study beyond the specific instances that have been tested. “We want the knowledge generated by our studies to have meaning outside the confines of the study particulars. One way to accomplish this goal is to identify the mechanisms through which the exposure affects the disease, and the circumstances under which its effects are activated” (ibid., p. 423). For an adequate explanation to be elaborated, plausible mechanisms through which the

values of [the counterfactual claims] were all along” (2004, p. 46).

¹⁰ See Machamer (2004), p. 36.

exposure can work must be hypothesized, that are to be substantiated by “chains of causation” and “mediational processes” (*ibid.*, pp. 424-425). For instance, if we are to explain infant schizophrenia spectrum disorders and have identified maternal overweight as a possible cause, mechanisms shall be hypothesized through which maternal overweight influences foetal development. Different mechanisms can act. For example, the foetus can be affected by maternal overweight through gestational diabetes, or through the mother’s intake of amphetamine, which physicians prescribe in order to limit weight gain during pregnancy. Looking for more and more detailed mechanisms allows to reduce the range of possible explanations. “When we make our hypothesis about the data more specific by stipulating the active ingredients of the exposure, the mechanisms through which the exposure causes the disease, and the conditions under which the exposure has an effect, the number of plausible alternative explanations is decreased” (*ibid.*, p. 422). The number of possible alternatives is thus decreased because any explanation will have to account not only for the exposure-disease association, but also for the explanatory power of the mechanism that has been identified.

3. Causal explanation and multilevel phenomena

What further, specific issues are to be properly addressed for a satisfactory account of explanation in such a field as contemporary epidemiology to be drawn? As we’ve mentioned, phenomena at stake have a crucial multilevel character, with both higher level properties (for instance, living in a rich or poor neighbourhood) and lower level properties (for instance, genetic properties) playing an important role, and affecting each other. The former, i.e. socio-economic and environmental properties, have been increasingly identified as relevant to many pathologies, as properties which make a real difference and do not count as simple background conditions¹¹. Recent philosophical works in the mechanistic perspective have been highlighting the multilevel character of explanations. As far as Glennan (forthcoming) is concerned, his understanding of the relationships between properties at different levels rests on the idea that properties of things and causal relations obtaining between them depend on the mechanisms realizing such properties. No special issue arises as to how interactions occur between levels that are genuinely different, and not reducible to

¹¹ Susser and Susser 1996a, p. 668: “The focus on risk factors at the individual level [...] will no longer serve. We need to be concerned equally with causal pathways at the societal level and with pathogenesis and causality at the molecular level”.

one another. The issue is particularly relevant for epidemiologic analysis in the *ecologic* perspective¹². First of all, levels must be adequately defined, and relevant elements are to be placed at the most proper level they belong to. For instance: does a higher use of cannabis in urban areas as a causal factor of schizophrenia count as a high-level social factor – given its diffusion -, or as a low-level individual factor, with specific molecular pathways? (see March and Susser 2006). Or: are increased placental levels of corticotrophin releasing hormone (CRH), as a factor which favours pre-term delivery, an individual factor, with its specific chemical and physical features, or a socio-economic factor, given that such levels are higher in poorer women? (see Krieger 1999). The very identification of the levels relevant properties belong to is far from unproblematic and univocal. Furthermore, what may appear to be just one level, for instance, the social one, can be further subdivided, and – for instance – belonging to a family, neighbourhood, village, society may have different implications. Obviously, explanations may be pursued with different focuses and purposes. “The decision as to which levels to include should be based on the question at hand, the particular nature of the disease, and the pattern of disease rates” (Schwartz, Susser and Susser 1999, p. 26). If there’s a main interest for the *incidence* of a disease within a given population, the privileged level of investigation may be a high one, on which it may be easier to intervene and/or promote campaigns of prevention; if, instead, the focus is on *being a case* of a given pathology, i.e. on why certain individuals within a population get infected whereas others do not, the individual level may be what the enquiry concentrates on. Diseases occur always at the individual level, while prevention can be directed toward different levels. Social facts do not contribute to the occurrence of diseases in a disembodied way: they cause them “through mediating factors that, at some point in the causal chain, become biologic phenomena. Nonetheless, they are not reducible to individual-level phenomena: they may cause disease through a large number of interactive pathways that cannot be fully itemized. Although not reducible, social facts sometimes offer *the most useful* explanations for the incidence of the disease” (Susser, Schwartz, Morabia, Bromet 2006, p. 448, italics added)¹³. In all cases, analyses can be carried out at various degrees of abstraction. Descriptions of the ways things work may be more or less precise or detailed according to both

¹² A solution that has been put forward in the epidemiologic literature is the adoption of a multilevel analysis. I will not dwell on it here, and on the associated statistical methodology, but consider how the issue can challenge the philosophical approaches presented above.

¹³ For instance, “it is of course true that the availability of alcohol in and of itself cannot lead to alcoholism without working through the behaviour of individuals. The alcohol has to enter the body to make a difference. However, the availability of alcohol influences the alcoholism rate through many pathways and through interaction with numerous risk factors” (*ibidem*).

present knowledge or present specific purposes. Once the epidemiological investigation has analyzed determinants and outcomes at different levels of organization, the action that follows will address *the most efficacious levels*. Usefulness can be a criterion to decide on which level to focus, but it does not make an explanation “better” than another.

That talking of levels can be fraught with ambiguities and a source of confusion is recognized by Woodward (see Woodward 2008, note 1, p. 178), who tackles the issue as deserving deeper philosophical scrutiny. Woodward distinguishes between “upper-level”, or – he says - “coarse-grained”, and “lower-level”, or – he says - “fine-grained” causes. With “upper-level” he refers to more abstract and less physical in nature (for instance, social variables); with “lower levels” he refers to more physical and concrete causes (for instance, genetic factors). In his interventionist account no particular problem arises with respect to mixing variables belonging to different levels. Variables at high levels can be causes of variables at low levels, as long as “the right sort of stable manipulability relationships are present. [...] Relatively coarse-grained environmental events [...] can causally influence fine-grained patterns of gene expression, which in turn can influence more macroscopic neural processes [...] which in turn alter macroscopic mental or behavioural patterns” (Woodward 2008a, p. 146). According to Woodward, who has developed this point together with Christopher Hitchcock (see Woodward and Hitchcock 2003a and 2003b), the interventionist theory of explanation has among its virtues over other views the capability of making sense of the intuition that some explanations are *deeper* than others. Invariance is not presented as an all-or-nothing matter, but, rather, as admitting degrees: most generalizations that are invariant under some interventions are not invariant under others, and a generalization is regarded as more invariant than another if it is invariant under a wider range of interventions. If the class of changes under which a relationship R_1 is invariant is a subset of the class of changes under which R_2 is invariant, then R_2 is claimed to be more invariant than R_1 . The more invariant the generalization included in the causal explanation, the deeper the explanation in which it figures: “an explanation is deeper insofar as makes use of a generalization that is *more* general”, where the generality they are thinking of is “generality with respect to *other possible* properties of the very object or system that is the focus of explanation” (Woodward and Hitchcock 2003b, pp. 181-182). It is to be stressed that generality is to be conceived here in the proper way, in the light of the overall theory Woodward and Hitchcock put forward, that is, as generality with respect to hypothetical changes in the system under study. For instance, in the field at hand, risk factors may exist that operate in only a specific context, but have a very strong impact there, and risk factors that are much weaker but whose effects may

extend over many contexts. It is hence crucial to distinguish between the scope and the stability of a generalization, the former having to do with how broadly the generalization applies, the latter with the range of variations under which it holds. A very stable generalization can have a narrow scope, and a very broadly applying generalization can be invariant under a restricted range of interventions. Upper-levels claims may capture a wider range of dependency relationships than lower-level causal claims, but they may also, on the contrary, be less invariant¹⁴.

As far as epidemiology is concerned, on the one hand, epidemiologic explanation in the ecologic perspective does not privilege any level, neither low or high, over the other, and has actually this aspect as one of its peculiar aims. Higher levels are not reduced to lower ones, nor are lower levels explanations regarded as superior to upper level ones, the idea being that it is from an interplay of variables at different levels that diseases originate. The emphasis is not so much on stability as on “completeness”, an explanation being more complete or comprehensive the greater the range of relevant variables from different levels it manages to put together. “Fine-grainness” can be hence considered in a different sense, as the degree of specification and detail that is reached in the analysis of the levels involved. On the other hand, insofar as a more stable, hence “deeper” in Woodward and Hitchcock’s terms, explanation is an explanation that provides the resources for answering a wider range of what-if-things-had-been-different, it can provide the resources for more extensive manipulation, and hence, for epidemiologic purposes, for planning interventions and reach larger control. A “deeper explanation” in Woodward and Hitchcock’s sense can prove as a *more useful* explanation, an explanation which allows to develop more efficacious interventions. In this sense, explanations which focus on different levels of the same phenomenon could be regarded as “better” or “worse” explanations by different epidemiologic perspectives and paradigms, emphasizing, for instance, either the genetic or the social or the environmental factors, with corresponding different views on what interventions should be directed to. The ecologic paradigm is explicitly meant to overcome such privileging one level over the others, putting, on the contrary, “things back together” (Diez-Roux 1998, p. 1028).

Not only are different levels to be integrated, but time dimension too shall be taken into account, both in the sense of the influence of historical periods in the development and spread of a pathology and in the sense of the life-course dimension. Examining the trajectory of a disease over the life course can lead to include long-deferred effects of in-utero factors, early childhood and adolescence experiences, and cumulative effects of long-terms exposures. In order to represent the

¹⁴ See Woodward 2008, pp. 172-173.

network of interactions building up the disease, a mechanistic approach looks as the most viable option. If a “what-if-things-had-been-different” investigation allows to determine whether or not the exposures under investigation have a causal effect on the health outcome, the intricate net of interactions and trajectories in time to be reconstructed, within and across levels, will much more naturally and adequately be expressed in terms of mechanisms, rather than in terms of – even a long list of – invariant generalizations. Furthermore, contemporary epidemiology is devoting increasing attention also to the relationship between the individual and the group into which he/she is included. “The challenge to epidemiology today is to reconsider dimensions of populations or societies which we may have lost in our examination of the individual-level causes of disease”. Individual-level explanations need to be integrated “into broader models incorporating interactions between individuals, as well as group-level or society-level determinants (which may modify or interact with individual-level properties)” (*ibidem*). Recent studies have highlighted how groups may have non-additive properties: population system epidemiology has stressed how populations cannot be simply defined by linear combinations of individuals, and how deeper investigations are to be performed on the relation between causal connections at the individual and at the group level, while the growth of interest in ecologic determinants of health promoted by eco-epidemiology has been accompanied by an interest in the patterns of individuals within groups. Efforts have been directed towards an understanding of those aspects regarding the health of populations which cannot just be seen as the sum of effects on individuals composing those populations. Population patterns of exposure, and not simply numbers of individuals exposed to a certain disease, are relevant with respect to population health; for instance, changing patterns of connection between exposed and unexposed individuals is relevant with respect to infection levels in a population, and the level of infection in a segment of a population can affect the risk of infection for other population segments. Differences made by *arrangements* of elements which cannot be understood dealing with just a heap of individuals have been highlighted. Instead of considering joint effects of multiple exposures in individuals, in population systems modeling “models of nonlinear population processes are needed that define how time-varying patterns of connections among individuals affect population level outcomes” (Koopman & Lynch 1999, p. 1170). Transmission models incorporating interactions between individuals and how they are linked to a population network are thus more and more broadly considered. In *Making Things Happen*, Woodward states: “The truth of a claim such as (S) ‘smoking causes lung cancer’ depends on relationships that do or would obtain (under appropriate manipulations) at the level of particular individuals. [...] the claim (S) would be true even if no one

were to smoke, as long as it is the case [...] that manipulating whether some particular human being [...] smokes will change whether they develop [...] lung cancer” (Woodward 2003, p. 40). In many cases this perspective will not suffice for explanatory purposes, since accounts shall be provided for cases in which individuals play different roles within the population network. Individuals with very low risk of infection, for instance, can be key individuals in the transmission of the infection at the population level. Such things as contact patterns and joint effects of multiple exposures need to be incorporated. As rightly suggested by Glennan, the concept of interaction is then to be assumed as a key-concept, to go beyond the identification of risk factors, “into the realm of explaining causal processes” (Susser, Schwartz, Morabia, Bromet 2006, p. 39).

It is with respect to these and related issues that epidemiology has been rethinking its aims and methods. To overcome the black box paradigm – “‘black box’ being the general metaphor for a self-contained unit whose inner processes are hidden from the viewer” (Susser and Susser 1996a, p. 670) – epidemiology is striving for insights into multiple levels causes and their dynamic interplay, into connections patterns and mediators in the causal chains between exposures and outcomes, to get models closer to a “video” than to a “snapshot” (Susser, Schwartz, Morabia, Bromet 2006, p. 465). “Epidemiologists aim not only to identify causes, but also to explain the *causal processes* that lead to disease. Causal explanation requires us to elaborate our causal ideas through the specification and examination of alternative explanations, antecedents, mediators, and causal partners. [...] The elucidation of *causal pathways* also helps to locate points for public health intervention” (*ibid.*, p. 71, italics added). Adequate explanations of the patterns of interactions between explanatorily relevant properties will be elaborated in mechanistic terms, the relevant properties being obtained as answers to what-if-things-had-been-different questions.

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