Causal Attribution and Crossing over Between Probabilities in Clinical Diagnosis

Pierdaniele Giaretta

Daniele Chiffi

1. The Framework

When speaking of abduction, Ingvar Johansson and Niels Lynøe say that “all the physicians who every working day (based on some known disease–symptom correlation) diagnose patients as having known diseases are making *abductions to known (disease) kinds*” (Johansson & Lynøe 2008:125). In fact, physicians usually base their diagnostic work and therapeutic decisions on the available medical knowledge.

Some Italian and Polish methodologists and philosophers of medicine put great emphasis on the distinction between the research activity made to extend medical knowledge, which might lead to the identification of new diseases or the discovery of new biomedical processes, and the research activity consisting of recognizing the disease or the pathological process affecting a particular individual.¹

Augusto Murri (1841–1932) argued that the increasingly rapid progress of theoretical knowledge in medicine has led to a split in clinical activity and pathological research. It seemed to him that the activity of the clinician was very different from that of the pathologist: While the latter looks for new ideas to solve open problems, tries to identify new relationships between phenomena, and ends up by considering diseases as abstract entities, the former only needs to re-cognize (*ri-conoscere*, in Italian) the disease; that is, to place the phenomena occurring in a patient within the context of the already codified knowledge. Murri was convinced that the re-cognizing of the clinician may be an even more difficult task than that of the researcher: While the latter, in fact, can isolate a problem from contour factors, and tackle the problem with the help of an experiment, the clinician has to consider and dissect the entire set of phenomena that is present in his (her) patient.

¹ See Murri (1972, 2004); Antiseri (1981); Scandellari & Federspil (1985); Federspil (2004, 2010); Scandellari (2010); and Löwy (1991).

Taking up Murri's thesis, according to which the diagnosis involves not knowing, but re-cognizing (not *conoscere*, but *ri-conoscere*), Dario Antiseri (1940–) argues that diagnosing is recognizing a pathological situation; that is, the way in which many events have become connected to each other, leading to a known morbid phenomenon. The recognizing by the clinician is therefore very different from the knowing of the scientist, so that “*one can know and be simultaneously unable to recognize*” (Antiseri 1981:98).

Likewise, Giovanni Federspil (1938–2010) and Cesare Scandellari (1933–) endorse Murri's distinction of the two main medical fields: the pathological and the clinical. They further argue that the objectives and methods of pathological research are different from those of clinical activity, but do not claim at all that the biomedical knowledge of the pathologist is irrelevant to the solution of clinical problems.

Within the Polish School of Philosophy of Medicine, its founder, Tytus Chalubinski (1820–1889), and Edmund Biernacki (1866–1911) argued that the clinical method must be based on a holistic approach and be oriented to the care of the symptoms. According to Biernacki, the work of the clinician does not require a thorough understanding of the phenomena that occur in the human body. He distinguishes the knowledge, often only partial, of the disease from its recognition, and admits that the progress in the understanding of diseases has refined the diagnostic possibilities, but believes that “knowledge about the diseases and therapeutics are independent of one another, and in fact, they exist in the doctor's mind as two different kinds of knowledge” (Biernacki 1991: 57). Contrary to what most doctors believe, a diagnosis is not necessary for the treatment of diseases. However, Wladyslaw Bieganski (1857–1917), another member of the same school, believes that the clinician cannot renounce establishing what the nature of the disease affecting the patient is and that the therapeutic indications should be grounded on this judgment.

In the following, we will adopt the point of view of the above-mentioned Italian methodologists and philosophers of medicine, according to which, clinical activity has its own methods, and does not intend to increase the knowledge of pathological science, even if it presupposes

the codified knowledge of this science in order to make the correct diagnosis and then proceed to therapeutic indications.¹

In particular, we will assume that in certain cases, the clinician avails himself (herself) of the already established causal knowledge, sometimes expressed by means of sentences such as, for example, sentences of the type, ‘the phenomena X may be caused by Y’, or ‘the phenomena X are sometimes/often/always caused by Y’. We also assume, as is implicitly assumed in clinical practice, that there is nothing wrong in talking about the probability that the phenomena X are caused by Y. Such talk merely needs to be clarified.

The knowledge of the causes constitutes a part of the pathogenetic knowledge and certainly contributes towards justifying the diagnosis. However, this knowledge is not always available. Johansson and Lynøe distinguish between the knowledge of the mechanisms “that explain how a certain event can give rise to a certain effect” (Johansson & Lynøe 2008:179) and the correlation knowledge that provides “statistical associations between diseases and variables such as age, sex, profession, home environment, lifestyle, exposure to chemicals, etc.” (Johansson & Lynøe 2008:181). The two types of knowledge are connected to one another in the following way:

A statistically significant association tells us in itself nothing about causal relations. It does neither exclude nor prove causality, but given some presuppositions it might be an indicator of causality. [...] improved correlation knowledge can give rise to improved mechanism knowledge. And vice versa, knowledge about new mechanisms can give rise to the introduction of new variables into purely statistical research. In this manner, *mechanism knowledge and correlation knowledge cannot only complement each other, but also interact in a way that makes both of them grow faster than they would on their own.* (Johansson & Lynøe 2008:181–182)

¹ The Polish Bieganski, who also argues for the need for providing a diagnosis, and who connects diagnosis and therapy, appears more concerned with emphasizing the unity of medicine rather than the diversity of tasks pertaining to both pathology and clinical medicine.

We believe that, when appropriately “improved”, as hinted at by Johansson and Lynøe, even correlation knowledge can be useful in order to reach a diagnostic judgment.

Whatever type of knowledge the clinician refers to, it is unavoidable for him (her) to make probabilistic assessments. Additionally, it is unrealistic to expect that his (her) assessments do not represent a personal opinion. It is reasonable, instead, to expect and to require that the clinician takes into account the relevant statistical probabilities. When doing so, the clinician may draw inferences — called ‘cross-over probabilistic inferences’ by Johansson and Lynøe — in which “the premises are frequency-objective (ontological) statements and the conclusion is a subjective (epistemological) probability statement” (Johansson & Lynøe 2008: 139–140). We agree, but we also believe that the cross over between different kinds of probabilities does not only have an inferential form. We will consider this in a more general way.

Both causal attribution and the cross over between probabilities may occur in clinical diagnosis. We will deal with a hypothetical, but quite realistic clinical case and will go through various idealized ways in which the case can be framed. The possibility of causal attributions will gradually fade and the role of the probabilistic evaluations will change. In some of the ways in which the case will be framed, special requirements need to be satisfied by the partition that provides the point of reference for the diagnostic research. The cross over between probabilities occurs in these framings as an important, not negligible aspect.

2. The Case: First Version

Suppose we know that a given pathogen g rarely causes disease f . Doctors often express themselves in this way, without providing any general and precise analysis about what it means to say that something never/rarely/.../often/always causes something else. Let us call G the exposure to g and F the patient coming down with the disease f . As many doctors would do, we assume, moreover, that the fact that g rarely causes f implies that, with respect to the reference population, the statistical probability $P(F/G)$ is low or very low. How can one nevertheless say that, in certain specific circumstances, the event F is due to the event G ? If a is the individual in question, how can one, in other words,

say that in the given circumstances *Fa* took place¹ because of *Ga*? Both *Fa* and *Ga* took place, but obviously this is not enough to justify the assertion '*Fa* because *Ga*', where the 'why' has causal meaning. May we think that in the circumstances in which the event *Fa* has taken place, that include the previous occurrence of *Ga*, the probability of *Fa* given *Ga*, understood as a non-statistical probability, is much higher than $P(F/G)$? Do we thus have an example of a cross-over probability of the type pointed out by Johansson and Lynøe?

Consider the following case. We know that the probability of a person who has eaten shellfish developing a glottal oedema is low and we also know that James has eaten shellfish. We observe that James has developed a glottal oedema. The glottal oedema is "a pathological rare condition, allergic in nature that occurs shortly after the contact between an allergen and a sensitive subject, and admits only a few possible causes among which there is certainly the ingestion of shellfish" (Federspil 2005:76). Knowing that in the few hours before the onset of the glottal oedema James had not come into contact with other possible allergens, a clinician would conclude that, with high probability, James developed an oedema of the glottis due to the ingestion of shellfish.

From the logical point of view, the clinician makes an inference based on premises, which he recognizes as true, and the inference leads him to recognize the truth of the conclusion that is inferred. What are the premises of the inference? If we include among them the general relevant knowledge concerning the glottal oedema, we have:

- (A) The probability that a person who has eaten shellfish shortly afterwards develops a glottal oedema is low.
- (B) James has eaten shellfish.
- (B₁) James has a glottal oedema.
- (B₂) The glottal oedema has an allergic cause.
- (B₃) After the ingestion of shellfish, and before the onset of the glottal oedema, James did not come into contact with known allergens other than shellfish and a possible previous contact with a known allergen could not have caused the oedema.

¹ Here and in the following we adopt this shorter way of speaking instead of referring, more correctly, to the event the sentence is about.

(B₄) The glottal oedema appeared shortly after the ingestion of shellfish.

The conclusion that is considered as being very likely is the following:

(C) The cause of James' glottal oedema was the ingestion of shellfish.

The conclusion (C) actually appears very likely, despite the premise (A). Consequently, one might have the impression that an event, James' glottal oedema, which according to the statistical law (A) is unlikely given the ingestion of shellfish, appears certainly, or almost certainly to be due to the ingestion of shellfish. Do we have a transition from a low statistical probability to a high probability of another kind?

We cannot answer fully without first observing that the ingestion of shellfish, which is given in (A) as the condition of a conditional probability, is alleged as something that happened to James and then is integrated with other information, including a specific example of the type of conditioned event; that is, James' glottal oedema. If we keep on talking in terms of conditional probability, we might be tempted to say that the statistical probability $P(F/G)$ has given way to the probability of Fa given Ga and other information. There seemed to be a transition from a statistical probability into a different kind of probability and it should be noted that the transition is made while changing the content of the conditional probability.

The probabilistic analysis of the inference should be carried out in detail, but before doing so, it should be noted that this type of analysis could be avoided, or carried out in a special way, if, after all the assumptions are made explicit, the inference ends up to be of a deductive nature.

Suppose it is considered obvious that

(C₁) The absence of contact with allergens other than shellfish necessarily implies that none of them can have caused James' oedema.

So the falsity of the conclusion (C), despite the truth of the premises (B)–(B₄), is only possible if one admits the possibility that James' oedema depends on an allergen that is not known to us, but which he came into contact with. In fact, from (B₁) and (B₂) it follows that the oedema of the glottis is only due to the action of an allergen, (B₃) states that shellfish are the only known allergen with which James had contact

that could have caused the oedema, and (B4), which states that the time between the ingestion of shellfish and the appearance of the glottal oedema was short, seems to exclude, with high probability, but presumably in a way that is difficult to determine, that James could have come into contact with an unknown allergen such as to cause the oedema of his glottis. If this possibility is ruled out, (A) does not seem to have any role in the justification of (C); thus, we can share Federspil's statement that "the conclusion is not based on the probability inherent in the law invoked" (Federspil 2005:76).¹ We can point out that assuming that

(C₂) James did not come into contact with any unknown allergen

the piece of reasoning that was implicitly carried out appears to be deductive in nature.²

Of course, being able to reach a diagnostic conclusion by deductive inference does not guarantee the certainty of the conclusion. The conclusion of a deductive inference is certain if all of its premises are certain. Since it is not always the case that all the premises are certain, neither is the conclusion always certain that is gained through deductive reasoning. The case of premises not all being certain is quite common, but we do not always notice the non-certainty of some premise. For example, it may be difficult to notice that in the deductive inference from (B)–(B3) and (C1)–(C2) to (C). Consider, in particular, the premises (B2), (B3) and (C2). (B2) is a general statement concerning the cases of glottal oedema. Unless it is a part of the definition of a glottal oedema that its only possible causes are allergens, it cannot be excluded that there might be cases of this disease that do not have an allergic cause. As concerns (B3), its reliability depends, among other things, on an investigation based on indirect observations, not made by the clinician but reported to him, which might be insufficient to exclude contact with other known allergens. (C2) appears to be plausible, given

¹ There is a clear similarity between the case described by Federspil and the famous case of paresis due to syphilis adduced by Scriven (1959) to show that the causal attribution does not presuppose the high predictability of the caused effect.

² Note that (C2) can be suggested, of course not justified, by (B4), and bereaves (B4) of any role from the deductive point of view.

the breadth of available knowledge about the possible allergens, but obviously it cannot be taken as being certain.

If the uncertainty of a sentence s is defined as $1-\text{prob}(s)$, where ‘prob’ is an appropriate notion of the probability for sentences, we know that the uncertainty of a deductive conclusion does not exceed the total uncertainty of the premises, given by the sum of the uncertainties of the individual premises. In short, the uncertainty does not increase when validly inferring the conclusion. It can remain the same if the premises are consistent and all of them are essential for the validity of the deductive conclusion (Adams 1975, 1998; Hájek 2001). Consequently, in general, a deductive conclusion is less uncertain (more reliable) the less uncertain (the more certain) its premises are. It follows that assumptions that are more or less plausible, but not certain, and that are taken too superficially for granted, may transmit to the conclusion a degree of uncertainty that is too low compared to what is reasonably required for a clinical diagnosis and a choice of therapy.

However, is it adequate to define the uncertainty of a sentence s as $1-\text{prob}(s)$? For the sake of argument, assume that it is, although in the case under consideration, the probability concerns (also) sentences stating relations of causation, and it is known that the account of causation is a complex and controversial issue. We grant that the way in which it is possible to assign a probabilistic value to a statement of causation such as (C) is not entirely clear. An objective sense can be suggested by the fact that an allergen acts only under certain conditions, so that one might think to look for the percentage of the cases where such conditions are satisfied among the cases of contact with the allergen. On the other hand, the fact that these conditions are generally not known, or cannot be ascertained, seems to give room for the application of a subjective-epistemic notion of probability.

At any rate, it has to be kept in mind that the clinician has to express himself about particular cases on the basis of what he (she) believes, and what he (she) believes depends on his (her) expertise and scientific background. So it appears natural, perhaps even unavoidable, to interpret the probabilistic assessments of the clinician about a particular case in an epistemic-subjective sense, as degrees of confidence based on his (her) opinions and knowledge. This raises the question of how the clinician *should* be influenced by the available ‘objective’ scientific and statistical

knowledge. It is a difficult and complex problem, which we will try to deal with in the next sections.

3. The Case: Second Version

Suppose that the clinician does not have any doubt about the allergic nature of the glottal oedema, hence he (she) accepts (B_2), but he (she) is not willing to hold (B_3) (after the ingestion of shellfish, and before the onset of the glottal oedema, James did not come into contact with known allergens other than shellfish, and a possible previous contact with a known allergen could not have caused the oedema) because he (she) is not sure of the reliability of the investigation that was carried out to establish (B_3). The deduction of (C) is no longer possible and so the possibility of evaluating the probability of (C) based on the way in which the uncertainty of the premises is transmitted to the conclusion through deductions is no longer available.

Can the clinician calculate the probability of (C) in a different way? Let us observe at the outset that the problem is not to determine how high the conditional probability is that James will have an oedema of the glottis given that he has ingested shellfish. If it is identified with the statistical probability of a glottal oedema given the ingestion of shellfish, this probability is low and, in any case, could not in itself adequately represent a relation of causation. If, on the other hand, from a Bayesian point of view, it is taken into account that both James' glottal oedema and his previous ingestion of shellfish are acquired, entirely certain information, the probability of each of these two events is to be updated to 1 and, therefore, even the conditional probability of the former event given the latter is to be updated to 1.

One might think of giving up any understanding of the relation of causation and may simply say that the statement (C) is justified to the extent that the oedema event is predictable from the ingestion of shellfish, according to the classical approach of the 'received view' in the philosophy of science. However, if we rely solely on the statistical probability of the glottal oedema given the ingestion of shellfish, the absence of an oedema, rather than its appearance, is predictable. Additionally, the absence of an oedema would have been predictable with even higher probability, if one were able to verify with certainty that James did not come into contact with any other (known or unknown) allergen. Perhaps the knowledge of certain physiological features of James would have

allowed the clinician to make a reliable prediction of the appearance of the glottal oedema, but such knowledge was not, and is not available.

We assume that the relation of causation cannot be eliminated, or reduced to other notions and we will consider how it is possible to assign a probabilistic value to the causal statement (C). Note that the clinician already knows that James has a glottal oedema. His (her) final objective is not to ascertain what the degree of probability is that James has developed the oedema after the ingestion of shellfish. He (she) is interested in treating the oedema and it may be useful to know what has caused the oedema in order to remove it. The etiological knowledge may also be useful for preventing future oedemas and this could be an additional motivation for the search of the cause.

Since the clinician cannot fully ascertain the cause with complete certainty, he (she) can try to ascertain what the probabilities of the single possible alternative known causes are; that is, for each possible cause, the clinician can assess the conditional probability of the oedema given the cause and the other relevant information. Knowing these probabilities, he (she) can easily see which holds the highest rank.

In this research, the clinician is faced with two problems. In the first place, the conditional statistical probability of a possible cause given the morbid phenomenon is not often immediately available. Secondly, he (she) must take into account what he (she) knows about James. Regarding the first problem, the inverse probabilities of the morbid phenomenon given the possible cause and the initial probabilities can be more readily known. Suppose that, in fact, these probabilities are known, and therefore the requested conditional probabilities may be indirectly reconstructed from them. In order to take into account the special features of James — this is the other problem to deal with — the clinician could transform these probabilities into subjective-epistemic probabilities. Using a basic idea of Salmon and applying Bayesianism, the clinician may proceed as follows.

We refer to as large as possible a population R of individuals who came into contact with at least one known allergen and we call A the property of having a glottal oedema. For each set of known allergens, consider the property of having come into contact with the allergens of the set. For the sake of simplicity, we assume that there are only two allergens, c_1 and c_2 , corresponding to the C_1 property of having been in

contact with c_1 and the C_2 property of having been in contact with c_2 . The properties to be considered are therefore $C_1 \wedge \neg C_2$, $C_2 \wedge \neg C_1$ and $C_1 \wedge C_2$. Call, respectively, K_1 , K_2 and K_3 , their restrictions to R^1 and suppose that the statistical probabilities $P(A/R)$ and $P(A/K_i)$, $1 \leq i \leq 3$, are known. Suppose also that $P(A/K_i) \neq P(A/R)$ for all i . It follows that every property K_i is *statistically relevant* for A within R according to the definition Salmon gave of this notion. According to the way in which K_i has been introduced, and based on the shared scientific knowledge, K_i , $i \leq 3$, can have causal efficacy for A ; namely, having the property K_i may causally determine having the property A , since c_1 or c_2 can cause the oedema of the glottis. The causal role of K_3 may be due to the causal efficacy of only c_1 , or of only c_2 or of both c_1 and c_2 . Assume that for the cases of oedema in K_3 there is no possibility of identifying which of these possibilities took place.

Let us wonder whether, based on the already acquired knowledge — that is, the scientific knowledge s and evidence e — we know certain conditions F , also endowed with causal efficacy for A , such that $P(A/K_i \wedge F) > P(A/K_i)$. If the answer is negative, we say that the class described by K_i is epistemically and causally homogeneous with respect to A , s and e . If, for each i , the class described by K_i is epistemically and causally homogeneous with respect to A , s and e , the partition K of R in K_1 , K_2 and K_3 is epistemically and causally homogeneous with respect to A , s and e .

The main difference of this notion of homogeneity compared to that of Salmon concerns the restriction of the quantification to the conditions that have a causal role for the *explanandum*. Of course, speaking of a causal role introduces some lack of clarity that the context may eliminate partially, but not completely. On the other hand, it now seems to be a widely shared conviction that it is not possible to provide an eliminative reduction of the relation of causation. Furthermore, because of the irreflexivity of the causation relation, speaking of a condition F endowed with causal efficacy for the *explanandum* A has the advantage of excluding immediately that A itself may be regarded as one of the conditions F by which to assess the homogeneity of the classes of the considered partition.

¹ A , K_1 , K_2 and K_3 isolate certain classes to which we refer in the same manner.

Is the concept of epistemic causal homogeneity useful to the clinician dealing with James' case? K_i is epistemically and causally homogeneous with respect to A , if any further causal specification of the possible cause represented by K_i is not known such as to make A more likely. The idea that we want to capture is that having the property K_i is known as causally contributing to having A , and just now, there is nothing more that one can know about it.

If James has the property K_i , if K_i is epistemically and causally homogeneous with respect to A , and if that is known as a part of the total available evidence, it is reasonable to require that the clinician assigns to James a probability of developing a glottal oedema that depends on the statistical probability $P(A/K_i)$. More precisely, if James is called j , it is natural to require and to assume that the subjective probability p of the clinician and the evidence e available to him (her) are such that:

$$(i) \quad p(A_j/e) = p(A_j/K_j \wedge P(A/K_i)=q)$$

that is, the subjective probability that the clinician assigns to A_j given e is determined by the subjective probability of A_j given both K_j and $P(A/K_i)=q$, where $P(A/K_i)$ is the statistical probability of A in K_i , and in addition:

$$(ii) \quad p(A_j/K_j \wedge P(A/K_i)=q) = q$$

that is, the subjective probability of A_j given K_j and $P(A/K_i)=q$ has the same value q as the statistical probability $P(A/K_i)$.¹

If we already know that James had a glottal oedema and that, in addition, he belongs to a specific K_i , the knowledge of the causal role of K_i justifies the corresponding attribution of causality, even if $P(A/K_i)$ is low. In this case, the value of the statistical probability $P(A/K_i)$ does not have any significant role, as it happens to lie within the deductive reconstruction of the argument.

However, we are now considering the case in which the clinician does not accept (B_3) and therefore does not know that James belongs to a specific subclass K_i . For each subclass K_i , the clinician may have uncer-

¹ Cf. Festa (2004: 60, 64). Of course, it is assumed that the statistical probabilities have been correctly determined.

tain evidence concerning James' belonging to K_i . Suppose, for example, that his (her) subjective evaluations are the following:

$$p(K_{1j}) = 0.4$$

$$p(K_{2j}) = 0.5$$

$$p(K_{3j}) = 0.1$$

In general, the subjective evaluations of the clinician can vary within a very wide range, but they should be compatible with a correct use of the available information. In particular, the clinician should not assess James' belonging to a specific K_i as more likely for the reason, through example, that the oedema of the glottis would be statistically more likely in K_i . The incorrectness of such an assessment should be intuitively evident if we consider the case that K_i has very few elements. The possible higher level of probability of A in K_i could not clearly be a reason for considering James' belonging to K_i as more likely.

Concerning the conditional probabilities of the type $p(A_j/K_{ij})$, let us continue to assume that the total evidence available to the clinician is not such as to make $p(A_j/K_{ij})$ different from $P(A/K_i)$, even if K_{ij} is not known. For purely illustrative purposes, we can suppose that the clinician endorses the following, completely hypothetical, conditional probabilities:

$$p(A_j/K_{1j}) = 0.2$$

$$p(A_j/K_{2j}) = 0.1$$

$$p(A_j/K_{3j}) = 0.3$$

From Bayes' theorem, it follows that:

$$p(K_{1j}/A_j) = (0.4 \times 0.2) / (0.4 \times 0.2 + 0.5 \times 0.1 + 0.1 \times 0.3) = 0.08 / (0.08 + 0.05 + 0.03) = 0.08 / 0.16 = 0.5$$

$$p(K_{2j}/A_j) = (0.5 \times 0.1) / 0.16 = 0.05 / 0.16 = 0.31$$

$$p(K_{3j}/A_j) = (0.1 \times 0.3) / 0.16 = 0.03 / 0.16 = 0.18$$

Hence, the probability of belonging to the class K_1 given the glottal oedema is greater than the other conditional probabilities of the same type. Given the causal significance of K_1 with respect to A , it seems reasonable to conclude that the probability that James' oedema was caused by c_1 is the highest, because the probability of James' belonging to K_1 , given his oedema, is the highest.

5. The Case: Fourth Version

How should one proceed when one observes a glottal oedema in the case — entirely fictional — in which no possible cause is known? Suppose that the clinician knows only that certain conditions favour the appearance of the oedema; namely, that the oedema is more frequent among those who satisfy at least one of certain conditions. In epidemiological terms, we can say that we only know some risk factors for the oedema of the glottis. Risk factors cannot be considered as causes and their knowledge might have no utility in terms of diagnosis and treatment. Suppose, however, that certain conditions are useful in determining the type of oedema, the prognosis and possibly the treatment. In this case, it is natural to try to determine what the condition was that favoured James' oedema, as it would be useful information from the clinical point of view, even if it was not sufficient to identify a cause with certainty and precision.

What kind of conditions might be taken into consideration? The clinician should draw information from his (her) pathological and epidemiological knowledge, but he (she) should also be guided by some methodological principles that are justified by general epistemological considerations. In particular, although in the case imagined it is not possible to speak of causes, but only of favourable conditions, it is natural to rule out those conditions that do not satisfy some formal properties of the causes. In particular, D can be a cause of E neither if it takes place after E, nor if both D and E are direct effects of a third event C (a conjunctive fork).

Here we will only mention some basic ideas that were proposed by Hans Reichenbach and Patrick Suppes, without thinking that the line of research they have opened up leads eventually to a satisfactory notion of probabilistic causality. Reichenbach's and Suppes' proposals mainly concern the problem of distinguishing between correlations and causality, and the problem of recovering an asymmetrical probabilistic causal relation such that the probabilistic cause precedes the probabilistic effect.

The first problem concerns the conjunctive fork, which is defined by Reichenbach as follows:

1. $0 < P(C) < 1$
2. $(D \wedge E/C) = P(D/C) P(E/C)$

3. $P(D \wedge E / \neg C) = P(D / \neg C) P(E / \neg C)$
4. $P(D / C) > P(D / \neg C)$
5. $P(E / C) > P(E / \neg C)$

Condition 1 states that the probability of the event C is in the open interval $(0,1)$, conditions 2 and 3 state that D and E are probabilistically independent with respect to C and to $\neg C$, while conditions 4 and 5 state that C is positively relevant for both D and E . It is often said that C and $\neg C$ screen off D from E . Conditions 1–5 entail 6:

6. $P(D \wedge E) > P(D)P(E)$; namely, there is a positive correlation between D and E , but this is due to the common ‘cause’ C .

Thus, if there is a positive correlation between D and E and there is an event C which satisfies 1–5, then C is a (probabilistic) cause for both D and E and this fact explains the lack of independency between D and E (Reichenbach 1956).¹

As concerns the second problem mentioned above, Suppes assumes, as a primitive fact, that a cause temporally precedes its effects. On this basis, he introduces the idea of a *prima facie* ‘cause’ such that when it occurs, it increases the probability of the effects (Suppes 1970). Suppes states that C is a *prima facie* ‘cause’ of E if and only if:

- $t' < t$
- $P(C_{t'}) > 0$
- $P(E_t / C_{t'}) > P(E_t)$, which holds only in cases where $P(E_t / C_{t'}) > P(E_t / \neg C_{t'})$ holds.

Afterwards, he defines a strong notion of a spurious cause as follows: $C_{t'}$ is a spurious ‘cause’ of the event E_t if and only if $C_{t'}$ is a *prima facie* ‘cause’ of E_t and there is a partition $\{K_{1,t''}, K_{2,t''}, \dots, K_{n,t''}\}$ such that

- $t'' < t'$
- $P(E_t / C_{t'} \wedge K_{i,t''}) = P(E_t / K_{i,t''})$, where i is a natural number belonging to $[1, n]$.

A genuine cause is a non-spurious *prima facie* ‘cause’.

¹ It has been observed that when more events screen off D from E , the notion of the conjunctive fork is not sufficient to individuate a common cause (Uffink 1999), but we will not go into this issue herein.

The search for a satisfactory notion of probabilistic causality¹ continued and attempts were made to face the many paradoxes that were more or less associated with it (the Simpson Paradox, the Lindrey–Jeffrey Paradox, etc.). In the following, we merely hint at a simple way in which the basic idea of screening off — which was already tacitly applied — might be slightly modified by adding a temporal reference and is then used for diagnostic purposes in the new imaginary version of our case, where no proper causal knowledge is assumed to be available.

The reference class is made up of a population R , which we assume to be divided on the basis of the conditions C_1 and C_2 in such a way that the properties $C_1 \wedge \neg C_2$, $C_2 \wedge \neg C_1$, $C_1 \wedge C_2$ and $\neg C_1 \wedge \neg C_2$ determine a partition K in the corresponding classes K_1 , K_2 , K_3 and K_4 . Let K_i be the class of the instances of K_i at t and $A_{t'}$ the class of instances of A at t' , where $t < t'$. We can request that $K_{i,t}$ should be considered as a condition that favours $A_{t'}$ only if² there is no known condition C_{t*} , defined on R , where $t^* < t$, such that C_{t*} screens off $K_{i,t}$ from $A_{t'}$. Then, the diagnostic process may proceed as above, transforming statistical probabilities of the form $P(/)$ into a subjective-epistemic probability of the form $p(/)$ with the aim of seeking for which $K_{i,t} p(K_{i,j}/A_{t,j})$ is the highest.

It is important to point out that other requirements also, formulated in the search for a satisfactory concept of probabilistic causality, may, or should be used to bound and guide the search for an informative condition about the pathological problem of a patient, when its origin and evolution are broadly unknown.

6. A Final, but not Minor Problem

The classes into which the reference population is divided correspond to as many hypotheses about the cause or condition that has favoured James' oedema. The assignment of James into any of these classes has an initial plausibility that the clinician can quantify by means of probabilistic values representing the extent of his (or her) initial confidence in their truth. As emphasized above, these values should be used as the

¹ The original motivation for this line of research was a reductionist one. See Salmon (1980) for a critique of such motivation, which is now generally abandoned.

² What follows 'only if' is proposed as a necessary condition that is open to further specification.

basis by which to calculate the probability of James' belonging to each class, given the oedema.

As stated by Johansson and Lynøe, "it is difficult, not to say impossible, to ascribe numerical values to epistemic statements" (Johansson & Lynøe 2008:134). However, there are procedures that may help the clinician explicitly and soundly to assess the epistemic initial probabilities.

The clinician's assessment of the initial probability of an event might turn out to be inconsistent. The so-called expert elicitation can be applied to individuate and eliminate the possible inconsistencies. Many techniques of eliciting probabilities are available (cf. Slottje, van der Sluijs & Knol 2008). According to one of these techniques, the expert is asked to evaluate whether the actual value of a quantity is higher or lower than a certain number. This can be carried out, for instance, by means of graphical tools such as probabilistic wheels. Alternatively, the expert is asked to fix the value of a quantity such that the probability of higher or lower values turns out to be some specific amount. We do not go into the analysis of these techniques. What is important for our discussion is that the clinician should be aware of the possibility of incurring inconsistencies and also of the availability of some methods for avoiding these.

Moreover, even if clinician's assessments of the probabilities relevant to specific clinical problem comply with the rules of the probability calculus, nonetheless they might turn out to be arbitrary, at least to a certain extent. Arbitrariness should be limited and, in fact, can be reduced by taking into account the epidemiological information. Of course, epidemiological data is not always *relevant* when dealing with a clinical case. It seems reasonable to hold that it may be relevant for the analysis of a clinical case when some of the following conditions are fulfilled (cf. Lagiou, Adami & Trichopoulos 2005):

1. The exposure to risk factors is also an established cause of the disease;
2. The exposure of the individual is similar (as regarding duration, intensity, latency) to the exposure causing the disease;
3. The disease of the individual must be similar to that which is etiologically associated with the exposure;
4. The individual has not to be exposed to other risk factors; and

5. The relative risk (RR) — namely, the ratio of the probability of the disease in the exposed population to that in the unexposed population — must be greater than 2. If the RR is lower than 2, then the association between the exposure to the risk factor and the population needs to be carefully analysed and methodologically motivated, since a weak association does not rule out the possibility of the clinical relevance of such an association.

The above conditions do not need to be interpreted as strong criteria for the relevance of epidemiologic data in the clinical context, but as possible constraints that might guide the integration of epidemiological evidence in clinical practice. It is worth noting that clinical guidelines can help the clinician's decision-making process. Of course, the clinician can break away from the guidelines if there is a reasonable motivation for a different judgment. Nevertheless, such subjective judgment, even when it is formally consistent, cannot be arbitrary but should be methodologically constrained and explicitly justifiable based on the theoretical and empirical knowledge available given the specific situation.

7. Concluding Remarks

We discussed the role of causality and probability assignments in relation to a case that seemed to us to be quite significant. The analysis was made within the framework provided by some theses about the nature of the physician's diagnostic activity. Initially, we endorsed the idea that clinical diagnosis is based on pathological knowledge that has already been acquired and that it is not intended to extend this knowledge, although it might unintentionally lead to the acquisition of information that is useful for its extension. Secondly, we observed that the presupposed knowledge can be both causal knowledge and correlation knowledge. Causal knowledge concerns both events that trigger disease processes and mechanisms by which these processes evolve. Based on recent research concerning the notion of cause, we hold that this concept is not completely reducible to other concepts, and that a primitive idea of causal relationship may tacitly underlie the research of correlations that are relevant for medical knowledge.

We emphasized that the role of probability is crucial. It is even crucial to assess the confidence to be accorded to conclusions obtained deductively from not entirely certain premises. In our opinion, it is unavoidable to assume that the assignment of probability values that a clinician is

willing to make is the result of a personal evaluation. Therefore, probabilities are to be taken as subjective. However, it is natural to request that they are not arbitrary and that they are linked as much as possible to appropriate and reliable statistical probabilities.

It seems to us that in clinical diagnosis, initial probabilities are more difficult to connect with statistical data. That is not surprising and, to a certain extent, is as it should be. There is, however, a problem in assuring the consistency and limiting the arbitrariness of the clinician's evaluations. We hinted at some indications, taken from the literature, which might be useful for this purpose. Some conditional probabilities are instead more easily identifiable with suitable statistical frequencies. The identification requires a high degree of normative idealization and we derived from the literature some indications about the ideal way in which this identification can be pursued. In a less idealizing approach, one might look for some other general justified ways in which the clinician may transform the conditional statistical probabilities into subjective conditional probabilities regarding the patient he is taking care of.

At the end of this contribution, we would like to highlight how some distinctions and fundamental problems formulated by Johansson and Lynøe formed the starting point for the perspective outlined here.

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