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Forensic epidemiology in Italy: principles and applications

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Summary. Forensic epidemiology (FE) implies the use of epidemiological data in the processes and the involvement of epidemiologists in judicial proceedings. FE is essential for the assessment of causal association between the exposure to specific agents and the occurrence of diseases. In this paper we describe FE principles and applications in the Italian context as in recent years FE emerged increasingly as well as the need of experienced and trained epidemiological experts able to navigate legal proceedings. In the literature, the principles of FE have been widely described by different authors, among them: Kennet Rothman who introduced the definition of cause, Sir Austin Bradford Hill who proposed an analytic framework to assess the causal association, and recently by Sana Loue who described the actual legislation and application of FE in the United States. Despite the legislation varies among different countries epidemiological methods and theories represent the foundation for the application of FE we illustrate in this paper. The association between environmental pollution and disease, mobile phones and cancer, vaccines and autism, asbestos and pleural mesothelioma are all situations that underscore the need for FE investigations in criminal acts. Causal association is a complex process: in real life only in limited cases causal associations are assessed by gathering robust scientific evidence, while cases with doubts and situations where different approaches to questions may lead to discordant arguments to questions may lead to discordant arguments are more frequent. Therefore, during the assessment of causation in civil and criminal matters the choice the epidemiological expert - with his knowledge and expertise - and the evidence from well-designed studies are crucial to fill the gaps between clinical and epidemiological data and the low. (www.actabiomedica.it)

Key words: Forensic epidemiology, epidemiological methods, causation, causality, environmental and occupational epidemiology, vaccines, judicial proceedings

I. Principles of Forensic Epidemiology

More and more in recent years, the role of epidemiology has emerged as crucial to inform judicial processes where causal connections between the exposure to specific agents and disease or harm are alleged (1), including: the association between environmental pollution and disease, mobile phones and cancer, vaccines and autism, asbestos and pleural mesothelioma. These situations need to be managed with both legal and epidemiological expertise.

Epidemiology is defined as: "the study of the distribution and determinants of health-related states or events (including disease), and the application of this study to the control of diseases and other health problems" (2). The term: "Forensics" derives from *Forum*, the assembly of ancient Rome where processes took place and today it refers to everything that concerns an investigation or a judicial issue. The two terms have been combined in: "Forensic science", which indicates all those practices and methods applicable to a case resolution (1). In 1999 these two concepts were integrat-ed into the term "forensic epidemiology", referring to the use of epidemiological data in the processes and the involvement of epidemiologists in judicial proceedings (1, 3).

The concept of *cause* is subject of continuous discussion in epidemiology - as in other scientific disciplines - there is no single definition of cause. In 1976 Kennet Rothman - Professor of epidemiology at the Boston University - proposed and analytic framework for cause: "A cause is an act or event or a state of nature which initiates or permits, alone or in conjunction with other causes, a sequence of events resulting in an effect" (4, 5).

A cause is defined sufficient when it inevitably produces or initiates an event and necessary if an event cannot develop in its absence (6). The causality of certain diseases can be related to singular factors, also defined "mono-factorial diseases" - as infectious diseases, but more frequently the disease is the result of an interaction between genetic, individual and environmental factors, where the environment is understood as any biological, chemical, physical, psychological or other factor that can have an effect on health. Four types of factors - predisposing, activating, precipitating and reinforcing factors - are involved in causality of the disease (6). Epidemiological tools measure: i) the contribution of each risk factor in developing the disease and ii) the eventual reduction of the disease if eliminating the risk factors.

This is a very complex process because it is often necessary to consider the interaction of multiple causes. In fact, the effect of two or more causes that interact is often higher than would be expected on the basis of summing the individual effects (6-8).

A systematic approach to determine the causal nature of an association was developed by Sir Austin Bradford Hill - Professor Emeritus of Medical Statistics at the University of London - in 1965 in the manuscript entitled "The environment and disease: association or causation?". Professor A.B. Hill proposed a list of key elements - Table 1 - to be assessed when analysing a possible causal association.

A.B. Hill stated: "None of my nine viewpoints can bring indisputable evidence for or against the cause and effect hypothesis and none can be required *as a sine qua non*" (8). Moreover, it is not necessary that all the criteria are verified, but without doubt the possibility to verify the criteria as much as possible allows considerable evidence to an etiological hypothesis.

Subsequently K.J. Rothman introduced the concept on the connection between the results of epidemiological studies and their application at the individual level. According to the author, epidemiology is a discipline that produces results applicable at the population level but also at individual level, in fact, it is likely that the individual has the same characteristics of the population examined through an epidemiological study (4, 5),

Table 1. The nine principles of Sir Austin Bradford Hill

1. **strength of the association:** Which is the strength of the association between the cause and the effect? (Relative risk) - Is the incidence of the disease among the exposed higher than the corresponding one in the reference population?
2. **Consistency:** Have other studies identified similar results? Is the observation similar in different populations, places, times and circumstances?
3. **Specificity**: Does the association concern a specific exposure and a specific disease?
4. **Temporality/Dose-response relationship:** Does that exposure precede the effect?
5. **Biological gradient**: Does the effect/event increase by increasing the exposure? Does the removal of a possible cause lead to reduction of disease?;
6. **Plausibility**: Is the causation we suspect biologically plausible with the actual evidence?
7. **Coherence:** Is the association coherent with the natural history of the disease?
8. **Experiment**: Is the association confirmed by experimental or quasi-experimental evidence?
9. **Analogy:** Analogous reasoning.

Adapted from A.B. Hill "The environment and disease: association or causation?" Proceedings of the Royal Society of Medicine 19656; 58: 295-300 (9).

II. Applications of Forensic Epidemiology

These theories on forensic epidemiology are still applied into practice and they represent the foundations of the forensic epidemiology nowadays. For instance A.B. Hill criteria previously mentioned are the basis of the methodology adopted by the International Agency for Research on Cancer (IARC) in assessing the carcinogenic risk from epidemiological studies (10).

In recent years, forensic epidemiological principles and knowledge are also required in many civil and criminal litigations in which epidemiologists have been asked to express their expertise in in order to verify the possible causal relationships between the exposure to risk factors and the development of a disease (11). For examples, this includes forensic epidemiological investigations on:

environmental disasters, the occupational epidemiology that focuses on illnesses and injuries related to the workplace environment and immunization safety.

Environmental and occupational epidemiology

In 1970s the United States was the first country, which faced legal proceedings with compensation to victims for massive damage from exposure to toxic substances. The country, however, opted for the civil process for assessing the causal imputation of harmful events related to exposure to toxic substances, while in the Italian system these events are managed in the context of criminal process (12).

However, the standards of proof for criminal liability (Italy) or civil liability (United States) are different: on the one hand, "beyond any reasonable doubt" (criminal liability), on the other the "most likely" (civil liability) (13).

The epidemiological assessment "Beyond all reasonable doubt" is different from the one which verifies if the causal nature of an association is "most likely". In the criminal liability processes - as those which take place in Italy - is required to evaluate each subject, "beyond any reasonable doubt" on the possible causal nature of an association, but in the case of multifactorial pathologies it is difficult to determine if subjects would not be ill without exposure (14).

In Italy, epidemiologists - have been involved especially in environmental disasters including the processes of: i) the Eternit case in Turin (Piedmont region) where the Italian company "Eternit" exposed around 3000 people to asbestos; ii) the case of Ilva steel-plant in Taranto (Apulia region); iii) the Tirreno Power in Savona (Liguria region) where the death of a hundred of people was attributed to the emissions of the power plant; iv) the Enel Spa of Porto Tolle a coal-fired central in the Veneto region and v) the shipyards of Porto Marghera in Venice (in the Veneto region) that poured into the atmosphere toxic fumes and into the sea carcinogenic substances (14).

It is relevant to make reference to the epidemiological report carried out in 2010 in the Eternit Process: the Cozzini Cassation judgment represented an epidemiological assessment to be taken as example for its completeness (15). In the last section of the judgement it is explained the complex epidemiological assessment entitled: "knowledge of asbestos hazard and asbestos-related pathologies". The hazard of asbestos on the populations involved in the investigation for the Eternit case is based on the results of several epidemiological studies. From these cohorts and case-control studies emerged a statistically significant correlation between the exposure to asbestos and the cases of asbestosis, lung cancer and mesothelioma (16). The case Eternit has been one of the first public safety crimes in Italy - which has been widely disseminated by media - in which the epidemiological evidence has been largely motivated and detailed.

Also in Taranto (Apulia region) the Ilva case has been widely reported by media. The Ilva enterprise is one of the largest steelworks in Europe, but epidemiological investigations assessed an increased incidence of different diseases in the populations adjacent to the huge industrial pole and therefore particularly exposed to emissions. The epidemiological assessment (16) in 2012 signed by well-known Italian epidemiologists states: "the continued exposure to pollutants in the atmosphere emitted by the steel plant caused and still cause in the population degenerative phenomena in different organs that result in disease and death. The methodologies adopted allowed to quantify the risks of disease and the morbidity caused both by recent and past exposures and allowed to exclude the role of confusion due to possible external factors. The environment and the health of the population must be continuously monitored in order to better assess temporal changes and to ensure prevention and adequate health care" (16).

The Tirreno Power case in Savona - a power station - in the Liguria region is similar: the death of a hundred of people from 2000 to 2007 was attributed to the emissions of the power plant. And in 2014 through the epidemiological investigation the magistrate in charge of preliminary investigations decided to confiscate the company and to interrupt of a substantial part of the productive activity, for the same causes against the public safety hypothesized in Turin and in Taranto (15).

Occupational epidemiology

Another example of the application of epidemiology in judicial disputes comes from the Tribunal of

Ivrea (Piedmont region): in April 2017 the court acknowledged the vitality to a worker who developed brain cancer (acoustic neuroma) due to the excessive use of the mobile phone. Although the carcinogenic effect of electromagnetic waves of the cell phone had already been recognised in 2013 among probable carcinogens for humans (Class 2B) by the International Agency for Research on Cancer (17) this judgement met many criticisms and doubts from the scientific community.

With a great media attention, after a few days from Ivrea's judgment also the Florence court (Tuscany region) recognized a case similar to a worker who spent more than 10 years 2-3 hours a day on the telephone and developed cancer.

The case of vaccines

In recent years it has been hypothesized that vaccinations are cause of serious illnesses: these not evidence based information caused great alarmism - especially among parents - and media scandal, resulting in an increase of the vaccine hesitancy and in a decrease in immunisations (15, 18-23).

- In Rimini (Emilia-Romagna region), in 2012, the court sentenced the Ministry of Health to the compensation - as expected by the article 210/92 of the Italian low - for a link between the MMR trivalent vaccine (measles - mumps - rubella) and the occurrence of autism in a child vaccinated in 2002. This first judgement was defined as "historical" and used as a point of reference in many civil cases for damages possibly associated to vaccinations initiated later. Nevertheless in 2015 the court of Bologna overturned the Rimini judgment: by defining "scientifically irrelevant" the reasons of that judgment. According to the consultant it is also to be considered that "in the clinical history of the child there is no realistic temporal correlation between the progressive appearance of autistic occurrence and the MMR vaccine".
- In Genoa (Liguria region) a parent appeal was initiated to ascertain whether the encephalopathy related to autism syndrome in his child had been caused by vaccine against MMR in 2003. In April 2013, the Court of di Genoa rejected the request of the two parents to be reimbursed for lack of evidence and casualty between the pathology and vaccination".
- In 2014 in Milan (Lombardy region) recognised the autistic disease occurred in a child after the hexavalent vaccine, but it is still awaiting the appeal process requested by the Ministry.
- In the influenza season 2014-2015 in the whole Italian country 35 deaths were reported through the National Network of Pharmacovigilance as having occurred after Fluad administration and deemed to be associated with it. EMA's Pharmacovigilance Risk Assessment Committee and (PRAC) concluded that there was no evidence of a causal relationship between the fatal events and the administration of the vaccine and reassured other countries about the safety of the influenza vaccine (24).
- Similarly, in 2015 in Caserta (Campania region) some vaccinations were blamed to be associated with "serious psychotic motor impairment" including anti-polio, anti-diphtheria-tetanus pertussis, anti-hemophilus b, Anti-hepatitis B and finally anti-MMR but the claim was rejected as any epidemiological evidence was retrieved.
- In the same year, the Regional Administrative Court of Sicily required the Ministry of Health to compensate an autistic child who in 2000 received the tetravalent vaccine (anti-diphtheria-tetanus-pertussis-hepatitis B). The cause-effect link was recognized in 2014 and the family had been awarded a compensation of 250.000 euros, never paid by the Ministry.
- Recently, in July 2017, in Salerno - Campania region - The Supreme Court rejected the request to a father to be compensated for the autistic son. The parent's thesis was that the child was affected by encephalopathy with post-vaccination autism syndrome. According to the Court, there is no connection between the disease and the Sabin anti-polio vaccine administered to the minor.

The forensic epidemiology investigations demonstrated the absence of any causal link between vaccines and the attributed events, in particular any causal link between vaccines and autism has never been demonstrated. As stressed by the WHO (25) these disorders

have other etiologies, but they are certainly not caused by vaccinations.

Conclusions

Concluding, the choice the epidemiological expert - to express his knowledge and expertise - is a crucial moment: for the technical abilities and for past experience and scientific orientation on certain scientific controversies as well. Further more, evidence can be controversial: it is necessary to give the various types of evidence the right meaning. Evidence from well-designed studies is particularly relevant, especially the likelihood of a causal association increases when many and different types of studies - lead to the same conclusion.

Concerning this, in real life only in limited cases causal associations are assessed by gathering robust scientific evidence, while cases with doubts and situations where different approaches to questions may lead to discordant arguments, are more common. Causal association is a complex process that implies the evaluation of the etiological hypothesis in its entirety in order to compose the most appropriate image of the phenomenon under examination.

References

1. Loue S. Forensic Epidemiology: Integrating Public Health and Law Enforcement: Jones & Bartlett Learning; 2010.
2. Last J. A dictionary ofepidemiology, 2" ed Oxford, Oxford University Press, 1988.
3. Loue S. Forensic Epidemiology: A Comprehensive Guide for Legal and Epidemiology Professionals: Southern Illinois University Press; 1999.
4. Rothman KJ. Causes. 1976. American journal of epidemiology 1995; 141(2): 90-5; discussion 89.
5. Rothman KJ, Greenland S. Causation and causal inference in epidemiology. American journal of public health 2005; 95 Suppl 1: S144-50.
6. Beaglehole R. Epidemiologia di base / R. Beaglehole, R. Bonita, T. Kjellstrm; edizione italiana a cura di G. Aggazzotti. Casalnoceto: F. Folini; 1997.
7. Signorelli C. Elementi di metodologia epidemiologica. Roma. Società Editrice Universo, 2011.
8. Signorelli C. Igiene e Sanità Pubblica. Secrets domande & risposte. Roma: Società Editrice Universo (SEU), 2017.
9. Hill A. The environment and disease: association or causation? Proceedings of the Royal Society of Medicine 1965; 58: 295-300.
10. World Health Organization International Agency for Research on Cancer. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. 2006; Preamble. Lyon, France.
11. Renga G, Signorelli C. Epidemiology in Italy: contributions from the specialists in hygiene and preventive medicine, current state and future prospects. Epidemiol Prev 2005 Mar-Apr; 29(2): 116-23. Review. Italian.PubMed PMID: 16124746.
12. Zirulia S. Esposizione a sostanze tossiche e imputazione causale. Nuovi scenari del diritto penale della modernità. Aracne editrice Edizione, 2015.
13. Masera L. Evidenza epidemiologica di un aumento di mortalità e responsabilità. Diritto penale e contemporaneo, 2014.
14. Terracini B. Ruolo e affidabilità dei periti in tribunale. Epidemiol Prev 2011; 35 (1 EPdiMezzo): 4-4.
15. Signorelli C. Vaccines: building on scientific excellence and dispelling false myths. Epidemiol Prev 2015; 39(3): 198-201.
16. Biggeri A, Triassi M, Forastiere F. Conclusioni perizia epidemiologica sull'ILVA di Taranto, 2012.
17. International Agency for Research on Cancer (IARC). List of Classifications, Volumes 1-118.
18. Odone A, Chiesa V, Ciorba V, Cella P, Pasquarella C, Signorelli C. Influenza and immunization: a quantitative study of media coverage in the season of the "Fluad case". Epidemiol Prev 2015; 39(4 Suppl 1): 139-45.
19. Odone A, Signorelli C. When vaccine hesitancy makes headlines. Vaccine 2017; 35(9): 1209-10.
20. Bonanni P, Ferro A, Guerra R, et al. Vaccine coverage in Italy and assessment of the 2012-2014 National Immunization Prevention Plan. Epidemiol Prev 2015; 39(4 Suppl 1): 146-58.
21. Odone A, Signorelli C. What are we told? A news media monitoring model for public health and the case of vaccines. European journal of public health 2016; 26(4): 533-4.
22. Ferro A, Odone A, Siddu A, et al. Monitoring the web to support vaccine coverage: results of two years of the portal VaccinarSi. Epidemiol Prev 2015; 39(4 Suppl 1): 88-93.
23. Signorelli C, Odone A, Cella P, Iannazzo S, D'Ancona F, Guerra R. Infant immunization coverage in Italy (2000-2016). Ann Ist Super Sanità 2017; 53(3): 231-7.
24. Signorelli C, Odone A, Conversano M, Bonanni P. Deaths after Fluad flu vaccine and the epidemic of panic in Italy. BMJ 2015; 350: h116.
25. World Health Organization. Questions and answers about autism spectrum disorders (ASD). Online Q&A, 2016.

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