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Case Review

Mind the Gaps: Investigating Collective Health Aggression

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Abstract

Whenever one suspects some intoxication, infective epidemics or other collective health harm, it is paramount first to define and localise its source – especially if it is an event hitting big numbers of patients, with high severity and quick development of symptoms [23,24]. An outbreak investigation routine must be early established, with a comprising strategy and pragmatical objectives oriented towards precise diagnosis. Those will grant a realistic assessing of risks for the community, curative measures needed towards the ill and prevention directed to future cases.

Healthcare professionals must have great attention towards novel aggressions to men's health and their clinical manifestations; a careful analysis of the available data is needed, in order to avoid being misled by some false assumption that may impair the accuracy of the diagnoses and might delay the needful curative and preventive courses directed towards the population [25].

The determinants of emerging diseases and unusual behaviour of the known microorganisms, health-aggressive mediums and artefacts are multiple; therefore, epidemiologists must consider every item of evidence for each upsurge, including the ecology and environmental issues [1,2]. Some useful guide towards the determination of causality is the investigation of etiology, along with simple mapping strategies and statistical instruments that begin with the use of simple statistics and methods.

This paper reviews some of the measures to be taken in such cases, with particular emphasis on the actions related to healthcare professionals and the clinical laboratory.

Keywords: Health Aggression; Investigating Collective

Introduction

Investigating outbreaks and epidemics is somewhat like detective work. Only, the stakeholders here are the healthcare professionals, research and industries. The leading detectives are Doctors and Nurses, who testify diseases every day. They must observe that some sickness or condition is on the rise – and therefore report them to their superiors, so that the information will eventually reach the defence and prosecution lawyers (the local and national Epidemiologic Centres and Regulation Authorities) to determine and decide about causality, liabilities, and how to deal with the new evidence. Only after that must we thoroughly evaluate the events, and conclude as to the accountable people for the events. The definitive management of future occurencies, including surveillance and notification, must follow and be integrated into public policies.

Nevertheless, sometimes events develop so quickly that something must be done at a base level too, even before a considerable surge of death and sickness takes place, or significant outcomes

harm the current victims. Often-times the investigation of a new aggressive agent must start at an individual diagnostic level.

Crime and punishment: from the murder castle to the murder cook

Historians claim the first known serial killer of America was H.H. Holmes (1861 - 1896) [5]. However, there may be some medical grounds to dispute that. At about the same time, a fierce – and perhaps initially unwitting – female serial killer might have been the first perpetrator. Mary Mallon, (23/09/1869-11/11/1938), was born in Ireland and then immigrated to the US. Though her first documented murderous activities have taken place in New York (1900 - 1907), nobody knows when it started. After having arrived as a refugee, and have been responsible for many deaths, she reputedly killed about 25 people, and made more than a hundred sick or intoxicated, having been engaged as a cook despite admonishing against that. Her weapon – of which she might be at first unknowing – was the Typhoid fever [3,4].

The detective that discovered her was the sanitary engineer named George Soper [6,22,31-33] – sometimes mentioned as George Sober – of which not much remains but his name and several published papers. In the investigative process he became the first man to describe the possibility of someone – unwillingly – harvesting some infectious microorganism (namely, *Salmonella typhi)* and thereby becoming a so-called healthy carrier – unwitting answerable for several disease cases.

Sober would have first investigated all environmental sources and concluded they were clean before he associated many local cases of the disease to the presence and actions of Mary [4] – thus determining that the outbreak must have had a human source. Mary's real crimes? Being an asymptomatic carrier (at a time when there were no Penicillin), cooking, and – simultaneously – not properly washing her hands. It was only the combination of the three that might have matched a criminal action – at a time when vaccination, efficient soaps and antibiotics were not readily available. For that, she became known as "Typhoid Mary" [4,6,7] even though Typhoid was everywhere.

H.H. Holmes, on the other hands, practised numerous kinds of scam and fraud, until he eventually built his murder castle. There, he built a series of secret passages and corridors, which he would use to trap his victims and disguise several murder cases. Upon discovery of his last crime (the murder of Benjamin Pitezel and his two daughters, in intend to pursue an insurance claim) he was convicted and executed by hanging (May 7, 1896). While he was in jail, his castle mysteriously burned. The total numbers of his victims are still unknown. His grave stays in Philadelphia, Pennsylvania [5].

Mary Mallon was at first subject to a three-year quarantine. She was then released, and – by then not so unwittingly – worked as a cook at different places under assumed names, changing jobs and names as the Typhoid followed her. Eventually, she died on the Riverside Hospital where she had been taken care of during about six years, after the stroke she had suffered while on her second forced quarantine at North Brother Island. Her body was quickly buried in a grave (specifically at St. Raymond's Cemetery, in the Bronx). It is questionable if an autopsy was accomplished, but some historians say that her secret murder weapon was cultivated as a strain of *S. typhi* she kept in her gallstones – for whom she had in the past refused an operation. Her liability to some deaths, the total number of victims, or the fairness of her punishment is still subject of debate.

The people and even medical authorities at that time had been utterly unaware of the phenomenon of the healthy carrier – and indeed, that might be part of the reasons why Typhoid was a highly endemic disease. Eventually, after Mary's episode and quarantine, other carriers were discovered. However, no other example of a quarantine such as hers was ever registered: Mary's ultimate punishment was a total of 29 years in forced isolation, where she regularly received fresh ingredients to cook her foods, and ushered to offer regular samples for biological investigation. She complained of isolation and that her friends would not wish to eat her cooking.

Even today, some clinicians and students of Medical Ethics still condone or question that practice. To be sure, In modern times, equally innocent patients have and will be subject to similar treatment, in the name of "avoiding dissemination of dangerous organisms". As for Typhoid, a vaccination is nowadays available, and the disease is currently not anymore as deadly as it once was [9-11].

Establishing causal links – Human nurture versus environment nature.

A single event is seldom enough to produce a common health ailment, epidemic or adverse reaction [18]. A considerable num-

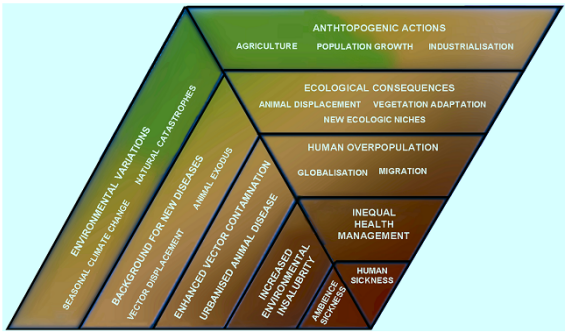

Figure 1: The path to disease is complicated. Does it start with men or with nature? Both intervene, as we gradually evolve from a relatively healthy (green) stage to a final state of the sickness of both (red). Adapted from [18].

ber of (unnoticed until too late) events is what it takes for a new pathogen to be present and proliferate, or for a new epidemic to be manifest. Adverse events in healthcare happen after opportunities offered by numerous sources – be it from humans themselves, from the environment and other animals and living beings. In the times of the Plague, rats or other animals were involved in a pandemic; that undoubtedly originated from the fact humans that provided them food. The environment indeed offered the right humidity, temperature and other conditions for both the mouse and its flea to develop; those fleas fed both on rat's and human's blood thus spreading the disease [15,16]. Forces like numeric human population, human actions toward the ambient, and even therapeutic use of drugs have been in action – and will go on – for long periods. While the new epidemics appear to be sudden, one must always consider as evidence some ecologic factors and gradually changing relationships as determinants [2] whenever investigating a new illness.

We can only improve Health safety by minimising the gaps in that hypothetical Swiss Cheese [36] so the probability of similar unfavourable events or infections will lower in the future. That means not only strengthening the system of knowledge and skills of providers, but also the system and processes of care of the collective, either in the workplaces, ecosystems or home environments.

Although such health preventive actions further to some — perhaps even more complex — causal theory, patients, healthcare professionals, Government Agencies and Industries can effectively prevent most sickness and contagion if they have appropriate hygienic information. That is because the praxis of some simple hygienic actions would in itself be sufficient to minimise the transmission of most infective agents actively. Individual measures such as handwashing, correct garbage collection, food conservation and proper destination of human stool and residua would result in a cleaner adjacent, local and world environment. Collective measures such as vector combat, vaccination and hygiene keeping in public and vacant land would be a significant contribution against the escalating of pathogens in the environment. A lesser number of pathogens interacting with animals and men would give less opportunity for those thriving microorganisms to interact in predictable and unpredictable ways. Prudent use of chemicals and antimicrobials in the Industry and environment, preventing the contamination of animals and humans, would avoid intoxication. Less use of antimicrobials in cattle, domestic animals and human therapy would minimise the evolutionary pressure imposed on germs. Better control of insects might mean fewer disease vectors.

Unfortunately, not all communities and citizens follow such measures effectively

We are reaching the rounded number of 7,760,000,000 human beings as of now [34]. A fierce globalisation process means that people, insects, domestic animals and – inside them – pathogenic agents can quickly travel around the world and infect new hosts populations. The risk of emergent diseases grows [18]. Population growth is not accompanied or even proportional to people's income, [35] and the access of people to health prevention and food. [26-30]. Meanwhile, the diseases tend to cluster around those who are more susceptible: the elderly, the children, the immunosuppressed, those already sick and undernourished (Figure 2).

New disease identification – filling some gaps

We should regard every unexpected incident, no matter how unpleasant or minor, as an opportunity to learn and to improve our techniques against the infective and intoxicating agents.

Figure 2: Beyond a simple direct consideration, the pathogenesis of old and new sickness can be considered multi-causal. Adapted from open-source images from the Wikipedia and http://www.kindpng.com

What we learn from Mallon's story is that anytime that given disease clusters in the same region or place, going far beyond the usual percentages, a collective causative agent must be present. If we are to keep general citizens safe from potential harm, we must deal with those in a way that prevents their repeated action. What we might learn from talking with George Soper is that sometimes simple techniques are enough to handle what appear to be complex situations.

Collecting epidemiological data must be a routine at every centre. When unusual symptoms appear to escalate in a given area, city, or country, it is imperative to attempt to map those and to alert epidemiological authorities – in a proportional intervention to the identified numbers, intensity and severity of real and anticipated harm. Data collecting must start early, or else one risks losing connection to "patient zero", link to teratogenicity, or opportunity to detect a chemical cause. One must start to collect some data even before higher health authorities are aware that something is wrong (Figure 3).

Unfortunately, we also deal with diseases that sometimes have remarkably similar (or confounding) symptoms. Most virus, and even several bacteria, enter their human victims by air; the first symptoms are often a flu-like syndrome. Food poisoning, and other sicknesses, both infective and toxic-driven, can have multiple causes – but being admitted into the human system by oral route often-times means the first symptoms hit the gastrointestinal system. Besides the uncertain probability of being some criminal deploy of a deadly manufactured virus [14], the possibility of some new or old infecting agent, newly transformed, is always at stake. Therefore, all healthcare providers should be continuously attentive to the possibility of new diseases or a new manifestation of old diseases. Should any suspicion arise, prompt collection of data about the events, and the patients that suffer from similar illnesses, should follow.

Figure 3: Collecting epidemiologic data may require prestidigitation. The clock is ticking, and one must aptly collect numerous data and summarise those into an appropriate map. Image edited from an epidemiologic investigation from a "mystery disease" in Brazil and free clipart at http://clipart-library.com, https://www.clipartkey.com/, and https://www.clipart.email.

When those symptoms occur in a given centre, the healthcare professionals tend to direct their attention to parties, restaurant, needy neighbourhoods or any place where people cluster. Nevertheless, that may be of little help if the disease is bound to an insect vector – with hundreds of meter of flight wingspan; to a group of flying bats, mammals or wandering animals; or to some unknown

asymptomatic carrier that flying around the world. Indeed, nowadays, the possibility that a new disease strikes as multiple simultaneous cases around the world almost simultaneously seem at least very feasible.

Healthcare professionals must be able to balance the importance of the symptoms they observe; the events some patients do (or not) say; the possibility of emerging of significant epidemics of important morbidities to future patients. Even some extra information available – such as environmental breaking, inundation, intoxication, new cultural habits that spread and even iatrogenic (unintended) harm – is to consider.

What we can learn from some examples

From July to August 2019, a series of patients presenting with specific lung disease emerged in hospitals in North Carolina. Patients presented with abdominal symptoms (emesis and abdominal disease dyspnoea, and fever. The clinical picture developed with fever, leucocytosis, and eosinophilia. By September 6, 2019, the MMWR posted a release about new pneumonia cases – which coincided to a new habit of some consumers that started using cannabis-derived oily additives. The disease is the so-called E-cigarette Vaping Associated Lipoid Pneumonia (EVALI) [12]. E-cigarettes have been in use since about the '60s when the first dispositive were created and fabricated. The legal skirmish among the FDA, consumers and producers has been going on ever since [8]. So, why did EVALI not rise until 2019? Or did healthcare professionals misdiagnose it, unsuspecting of patients, who were probably reluctant to report the use of an illegal substance?.

On 30/12/2019, a Hospital of the state of Minas Gerais (Brazil) notified a specific case of Renal Failure and severe neurologic impairment. The first symptoms were, sequentially, general gastrointestinal symptoms, followed by Renal Failure and progressive neurologic impairment, happening in the period of a few days. Other cases followed, reaching about 20 known patients as of today. Eventually, the denominated "nephron-neural syndrome" was causally linked to some specific brands of local beers, all produced by the same Fabricant. The presence of Ethylene Glycol was determined in the blood of some of the patients, and the chemicals were found on some lots of beer. The case is not yet closed: the Fabricant's procedures is still under revision and there are the possibilities of sabotage and contamination from their supplier of antifreeze. However, why weren't all consumers intoxicated, and why did some patients deny ever having drunk? Ethanol inhibits the metabolism of Ethylene Glycol, therefore delaying the toxic effects, masking intoxications and allowing for a higher intake of the substance before toxaemia is manifest; Meanwhile, the contamination of beer, albeit not desirable, showed small content. Some consumers, of course, may have exceeded in alcohol consumption or even been drunken drivers (Any amount of alcohol detected in drivers in Brazil is considered illegal) What ultimately raised the alarm was the high anion gap acidosis most patients presented [17].

On 1947, a routine investigation about the Yellow Fever in Uganda uncovered a new tropical virus, later identified on the mosquito vector *Aedes africanus*. The victims were captive sentinel Rhesus monkeys. The first documented cases of human diseases appeared in Uganda and Tanzania as soon as 1952. By 1983 the epidemics had spread to Asia, and at 2007 a massive outbreak happened on Micronesia. Between 2013 and 2014, the virus had hit the Pacific Islands and French Polynesia. After it hit Brazil in 2015 – where simultaneous clusters of Guillain-Barré's syndrome and subsequently Microcephaly (in babies born from infected mothers) occurred – the virus was declared it a Public health Emergency of International Concern (PHEIC). Testing for the virus was developed in a hurry. After some time the Microcephaly Epidemics wore out before robust studies could either confirm or deny the association [19-21] and on November 18, the WHO did not consider it a PHEIS anymore. [23,33] What had gone wrong? Did the virus suffer successive mutations? Did it somehow interact with the many other tropical virus's endemic in the region? None of the above? All of them? Perhaps the answers will have to wait for the next outbreak.

What can we do about the potential and real epidemics?

Perhaps the first action to take is to define the problem: that includes analysing the clinical picture, deciding if it is an actual epidemic, ascertaining if it is local or if it has potential to generalise, before taking further actions. While the risk of some pathogen taking global proportions is always present, on the other hand raising an untrue alarm may mean several untoward consequences: the people may panic, unintendedly spending resources on relatively harmless situations, and people and institutions may be discredited.

We must simultaneously be able to define what are positive cases, probable cases, unlikely cases and excluded cases. That may

require an agreement between specialists and ascertainment with straightforward methodological and statistic evaluation. The correct, unequivocal and agreed definition of cases is at the root of future investigation since it will avoid misdiagnosis and confounding factors.

Once that is done, a comprehensive and confidential interview with the patients is of interest. Once the individual risks are known, one can use simple statistics (Figure 4). From there, it will be possible to direct further investigations towards the most probable causes.

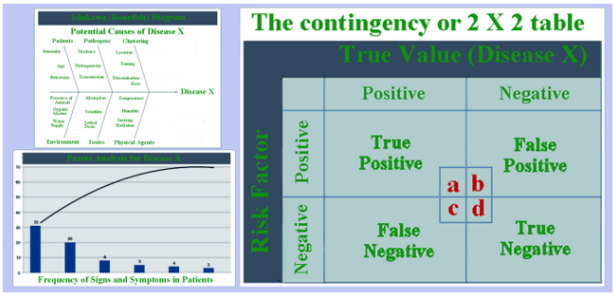

Figure 4: Some simple statistic and Methodologic tools may be very helpful for the initial investigation of a disease outbreak. Simulated graphics.

Notification is paramount. It must be decided how comprehensive it will be – from local authorities to national ones, and even global.

Since the press is to be involved, it is essential to grant the best possible information so that the population is at the same time aware of the risks and how to avoid those, able to decide when to go to hospitals for consultation (and thus avoid overcrowding) and avoid panic-driven actions.

Meanwhile, as new cases arise, they shall integrate the protocol.

The early determination of infection or toxic origin of the epidemic prompts the directed actions: the cleaning of a source of food or environment contamination; isolation measures toward infected and non-infected cases; or initiating vector control may be necessary. Alternatively, it may be merely the case of dealing with some consumer habit. In some cases, one must make a balance between personal and collective rights and dues.

It is not an easy task, and it may have to involve administrative as well as all health-related personnel.

The laboratory: how to bridge some more gaps

Whenever a disease needs diagnosis, Laboratory exams will be needed. That is not different in epidemics. However, in cases of a new or unrecognised disease, health professionals are deprived of some crucial data: that is, the epidemiology or sickness is not yet known. It is impossible, therefore, to know its frequency, severity, or morbid mortality in the population. Thus, we cannot estimate the prevalence from clinical data, and the Negative and Positive Predictive Values are not reliable. We need the most specific and sensitive exams we can have. The fact is, however, that they are not always readily available. As we deal with a new virus, specific tests might take time to develop, and they will ultimately derive from the clinical cases – the very people we are willing to treat. Besides, some other virus may be evident as interference and source of false positives. If one is going to use a toxic substance panel, it is vital to decide on which substance to focus, in the face of data such as probable exposures and associated symptoms.

Some general exams might be essential to the diagnosis. Nevertheless, caution is necessary. In the case of a Leucocytosis, even the stress associated with the primary disease can be the cause. It is useful to evaluate further if there is lymphocytosis (which may imply specific bacterial, viral and chronic condition), Neutrophilia (Generally, but not always, attributed to some acute bacterial infections) or Eosinoplylia (whose causes may be parasites or any other kind of toxic reaction). Clinical chemistry is mandatory for all cases, to evaluate electrolyte balance, blood oxygenation, glucose levels, and renal function. Those may not point to specific sickness, but sometimes they mean a clue to some condition. It may be challenging to select which from a sizeable available number of toxic agents to determine in the patient's blood or urine, but sometimes a general exam may point to a specific chemical determination one should order.

Immunologic assays can determine a high number of viral agents. The choice of those is to be determined needs clinical and epidemiologic data. Most emergent viral epidemics must wait until more sensitive and specific exams are available; some bacterial agents are of fastidious growing and have specific requirements for isolation not routinely used. All those factors highlight the impor-

tance of the proper leading of the first phases of clinical evaluation and epidemiological data.

Conclusion

We live in a globalising world, and precisely nowadays we are living some epidemics that might be harmful to the planet, such as the now emerging coronavirus from China [Perlman, S.] At the Year of the Rat (Figure 2) both healthcare personnel and patients must understand that health is not a straightforward mathematical equation. Accurate information must be collected and processed, and we must not forget that the cat (Figure 5) may also have its place. Meanwhile, all people may be held responsible for the dissemination of pathogens or the intoxication of communities.

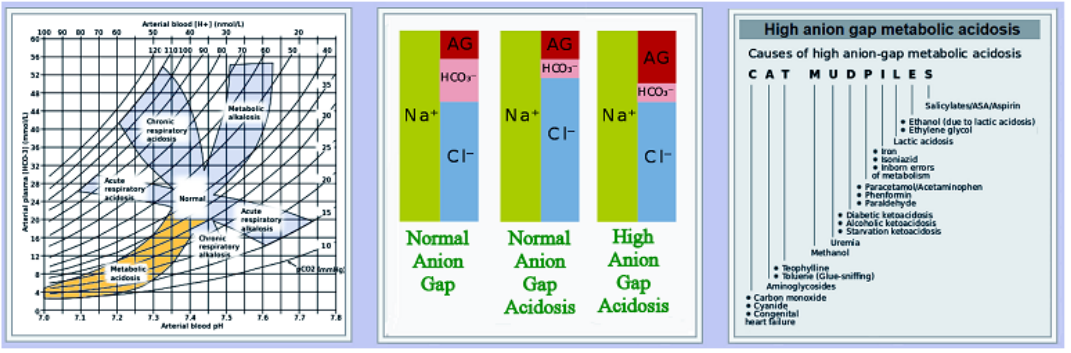

Figure 5: The correct analysis of Arterial Blood Gases showing a high Anion Gap Metabolic Acidosis may uncover a handful of causes of intoxication. Adapted from Open Source clipart from Wikipedia [13] as the now emerging coronavirus from China [24].

Bibliography

1. Andrews Paul. Typhoid Mary Mallon – Villain or Victim? (2019).
2. Araujo VL. "Ecology: Is it Part of the Evidence?". *Acta Scientific Microbiology* 2.9 (2019): 01-03.
3. ATA. American Thoracic Society. Vaping Associated Pulmonary Illness (2010).
4. Bender R. College of Literature Science and The Arts. University of Michigan. The Military Surgeon, Soper, P. George Soper on Mary Mallon. Original Articles Typhoid Mary (1919).
5. Biography.com H.H. Holmes Biography. Murderer (2017): 1861-1896.
6. Britannica. George Soper. American Sanitary Engineer.
7. Britannica. Typhoid Mary. Historical Figure.
8. CASAA. Consumer Advocateds For Smoke Free Association. A Historical Timeline of Electronic Cigarette.
9. CDC. Vaccine Information Statement.
10. Chelsea. A question for Typhoid Mary.
11. CMPA. The Canadian Medical Protective Association. What is "Systems Thinking".
12. Davidson K., *et al.* "Outbreak of Electronic-Cigarette–Associated Acute Lipoid Pneumonia -North Carolina". *Morbidity and Mortality Weekly Report* 68 (2019): 784-786.
13. Deeranged Physiology, Anion Gaps: Its Mmerits and Demerits.
14. IMDB. International Movies Database. Inferno (2016).
15. JMVH. The History of the Plague – Part 1. The Three Great Pandemics.
16. JMVH. The Journal of Military and Veterans' Health. The History of The Plague.
17. Latus J., *et al*. "Ethylene glycol poisoning: a rare but life-threatening cause of metabolic acidosis-a single-centre experience Joerg Latus". *Clin Kidney J* (2012) 5: 120-123.

18. Lindahl J and Grace D. "The consequences of human actions on risks for infectious diseases: a review". *Infection Ecology and Epidemiology* (2015): 3.0048.

19. Marini F., *et al*. "Mary Mallon (1869-1938) and the history of typhoid fever". *Annals of Gastroenterology* (2013): 26.

20. Matias DS., *et al.* "The value of Uncertainty: The Zika and Microcefalia link". *Journal of Evidence-Based Healthcare* (2019).

21. MG, BRAZIL. Minas Gerais State, Brazil. Investigação dos casos de insuficiência renal e alterações neurológicas (SES-MG, 08/01).

22. OCLC. WorldCat Identities. Soper, George A. (George Albert) 1870-1948.

23. Oostvogels R., *et al.* "The importance of the osmolality gap in ethylene glycol intoxication – In patients with very high lactate levels, calculate the osmolality gap, as ethylene glycol poisoning may falsely elevate lactate levels". *BMJ* 347 (2013): f6904.

24. Perlman S. "Another Decade, Another Coronavirus". *The New England Journal of Medicine* (2020).

25. Perneger J. "The Swiss cheese model of safety incidents: are there holes in the metaphor?" *BMC Health Services Research* 5 (2005): 71.

26. Population Action International. Why Population Matters to Infectious Diseases and HIV/AIDS.

27. Ross E. Burning 'Inferno' Question: How Fast Can A Deadly Virus Spread? (2016).

28. Shiel WC. Medical Definition of Koch's postulates. Medicine Net.

29. United Nations. Department of Economic and Social Affairs. Population Dynamics. World Population Prospects (2019).

30. VIAF. Virtual International Authority File. George Soper U.S. sanitation engineer, discoverer of Typhoid Mary.

31. VIAF. Virtul International Authority File.

32. WHO. Fifth meeting of the Emergency Committee under the International Health Regulations regarding microcephaly, other neurological disorders and Zika virus (2005).

33. WHO. The history of Zika Virus.

34. Worldometer. World Population.

35. Worldpppoplaton review. World Population (2020): 739.

36. Reason, J. "Human error. Models and management". *Western Journal of Medicine* 172.6 (2000): 393–396.