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The value of vaccines

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Abstract

Today, we have the technology to make vaccines against most infectious diseases and in theory we could free mankind from most of them. In spite of the great progress of science and technology, vaccines are an endangered species and there are increasing non-technological barriers to their development. Indeed, we have no mechanisms for developing vaccines needed only in developing countries, and in developed countries they are not a priority. Industry is walking away from vaccines and even the existing ones are in jeopardy. The reasons for the low interest in vaccines lie in the high risk and low profitability of the vaccine business. A story about the consequences that an infectious disease had on the economic development of the city of Siena in 1348 is used to show that our society is not calculating the intangible values deriving from vaccination. The failure of assigning the right value to vaccines and preventive medicine is a major risk of today's world that, having the opportunity of improving the proportion of healthy population, may have made the choice of increasing the number of chronically sick people.

Keywords: Vaccination; Siena; Economic development

1. Vaccines, an endangered species

The new technologies provide many new opportunities to fight infectious diseases by vaccination, and in theory we have almost no more technological limits to develop vaccines against infectious diseases (some are still difficult as HIV teaches us). However, vaccines are not easier to develop. Fig. 1 shows that the technological revolutions of the last 25 years (recombinant DNA, conjugate vaccines, DNA vaccination, genomics, and the impressive developments of immunology) have shortened the path of discovery of new vaccines from approximately 5–15 to 2–5 years in the year 2000. In many cases, the new technologies made doable vaccines that were impossible before. Fig. 1 also shows that while the discovery phase of vaccines is much shorter in the year 2000, the development path is much longer than in 1980. The increased development times are due in part to a justified increase in GMP and clinical trials standards, but in large part to emotional requests which do not add scientifically solid data. Keeping in mind that the costs per year of development are approximately 10-fold those of discovery, we can easily imagine how the investment for vaccine development soared. The process and the costs of vaccine development have become similar to those of pharmaceuticals. Recently, it has been calculated that licensing of a new pharmaceutical product requires an investment of 850 million dollars [1]. The significant increase in development costs is one of the reasons why vaccines are not a priority for industry. The other and perhaps major reason for the low interest of industry in vaccines is the low profitability of the business. In fact, the economic value associated with vaccines is negligible when measured up with that of pharmaceuticals. Worldwide, vaccine sales are estimated to be approximately US$ 6.5 billion, which represents only about 2% of the global pharmaceutical market [2], an amount roughly equivalent to the sales of one successful drug. During the last 40 years, most pharmaceutical manufacturers have not considered vaccines an attractive business opportunity because of their low return on investment and their the exposure to legal liability. Since 1967, the number of companies producing vaccines in the United States dropped from 37 to 10. Similar figures apply to Europe. Therefore, today the economics of vaccines have become the major obstacle to vaccine development.

The economic value of vaccines is usually calculated by cost-effectiveness studies. So far, experts have calculated that vaccines are cost-effective because their cost is lower than the cumulative cost of treatment, hospitalisation, lost working days, etc. For instance, it has been calculated that for every single US$ spent on mumps–measles–rubella (MMR) vaccine, more than US$ 21 are saved in direct medical care cost, while the diphtheria, tetanus and acellular

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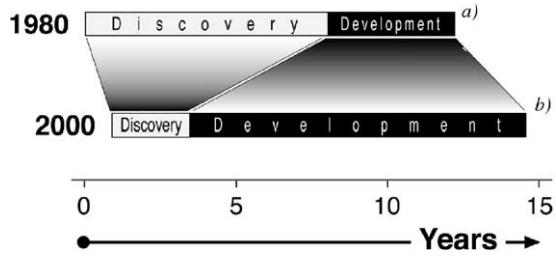

Fig. 1. The path of vaccine discovery and development. The technological revolutions of the last 25 years shortened the path of discovery of new vaccines. However, while the discovery phase of vaccines is much shorter, today the development path, which costs approximately 10-fold than discovery, is much longer than in the past. (a) Vaccine discovery and development path in 1980; (b) vaccine discovery and development path in 2000.

pertussis (DTaP) vaccine saves US$ 24 for every single US$ spent; for every single US$ spent on Hib vaccine, more than US$ 2 are saved [3]. More recent studies have calculated that the Hib vaccination in USA had a net present value of 0.95 billion for direct costs and US$ 2.09 billion for societal costs [4]. Although the above are unequivocal numbers, and there is consensus that vaccines are vastly cost-effective, they are not impressive enough to justify more public and private investments. The question is whether this is the right approach to calculate the costs saved by preventing infectious diseases.

We believe that the benefits of vaccines go far beyond the cost saved to treat the diseases. What is the value of being alive? What is the value of being healthy? What is the value of the lost opportunity for economic growth? An example of a value which is not captured by the present cost–benefit analysis is the following: if we had an insurance company that could guarantee life-long protection from the 10 diseases that today can be fully prevented by vaccination, in a developed country parents would easily spend US$ 7500 for insurance (approximately US$ 100 per year for an average life-span of 75 years) to buy health for their children. Instead, we face the complaint from policy-makers that the cost of complete vaccination of approximately US$ 500 is prohibitive (this is only US$ 6.6 per year for an average life-span of 75 years!). A second uncalculated benefit of health is the increased economic growth potential of a population free from major diseases. Gallup and Sachs report that countries with severe malaria grow at 0.4% per year compared to the 2.3% growth rate of similar countries without malaria, and also end up with half their income level. They conclude that the economic cost of malaria in Africa is far greater than the direct cost of illness estimated by WHO and limits the chances of these countries to escape poverty [5]. HIV in Africa provides another dramatic example of how the economy of developing nations can be totally devastated by a non-preventable and locally uncontrollable epidemic disease.

If the above intangible values were included in a cost–benefit analysis, we would find the present cost/benefit ratio to be underestimated by a factor between 10 and 100. Such calculation would provide the rationale to invest in vaccine development for developed and developing countries, and would improve the global quality of life.

2. The 1348 plague in Siena destroyed a flourishing economy and left the largest monument to infectious diseases

There are many examples that can be quoted to assess the consequences of infectious diseases on the economic development of societies. Among them, one of the most impressive is the story of the city of Siena in 1348. We will take this as a case study because it happened long-time ago, and therefore is far from emotional waves, and also because the symposium reported in this issue of Vaccine was held in Siena 654 years later. In the 14th century, Siena, a city located on the way from Rome to France and northern Europe, had one of the most powerful economies of its time. It had wealth, and a population of 100,000 inhabitants (to have an idea of dimensions, Paris had only 70,000 at that time). In modern terms, we could imagine Siena at that time as being the California of the year 2000. Economy, culture and art were rallying, people wanted to move there. In that atmosphere, the inhabitants had a dream: to build the largest cathedral in history. The cathedral was designed, and in 1338 construction started. Unfortunately, after only 11 years, in 1347 the plague (also called “the Black Death”) appeared in northern Europe and killed 30% of the European population. In May 1348, the epidemic spread to Siena.

According to the *Chronica Senese* of Agnolo di Tura, 80,000 people died from May to October 1348. Di Tura reported, “And I, Agnolo di Tura, carried with my own hands my five little sons to the pit; and what I did many others did likewise”. By July 1348, “you could hardly find a person . . . ”, wrote one of the reporters of the time. The expanding economy of the city was checked and the deaths of many painters, among them the brothers Pietro and Ambrogio Lorenzetti, ended the development of the first Sienese school [6]. Famine and two subsequent waves of plague in 1363 and 1374 did the rest. By the beginning of 1400, the cathedral was too big for the remaining population, and those that knew how to built the cathedral had died.

The social and economic structure of the Republic of Siena was drastically and irretrievably changed. Today Siena’s population is 55,000. Development of the city has been frozen since 1348. And, thanks to the plague, the city now is a beautiful living museum surrounded by the hills of Tuscany. Siena does have a cathedral, but not the one that had been planned. The unfinished original construction can be considered a “monument to infectious diseases” (Fig. 2).

In 1300, vaccines were not available, and Siena did not have the choice of preventing the plague by investing in vaccination. However, today we do have that choice and we can use the Sienese example to model both the short

Fig. 2. The original front of the Siena cathedral, as it is nowadays. The front wall of the cathedral of Siena, the construction of which was interrupted by the plague in 1348. The plague wiped out over 70% of the population. The wall, with its gaping, monumental windows, stands 654 years after the plague as a reminder of how devastating infectious diseases can be and represents the largest "monument to infectious disease" ever built by mankind.

and long-term consequences of devastating infectious diseases. What was the cost of the 1348 plague to Siena? Nobody has yet calculated the cost of this infectious disease to the economy of Siena. Perhaps no number can describe the opportunities lost for many centuries. Still we can hypothesize that, without the plague, Siena would have grown 10-fold, to one million people. If so, the cost of the missed opportunity would be US$ >10 billion per year, every year, even today!

If in the cost–benefit analysis, we include only a small fraction of the real costs of infectious diseases (for example the cost of the plague to the economic development of Siena, the recent costs of BSE and foot and mouth disease to the economy of Europe, the costs of HIV, and the costs of not having safe and effective vaccines against bioterrorism agents), economists, policy-makers and politicians, both in developed and developing countries, would inevitably consider vaccines as having much higher priority. The end result would be more investment in the development, manufacturing and commercialisation of new vaccines, and the population of both developed and developing countries would enjoy a healthier life, which inevitably translates also into a better economy.

3. The increase of chronic diseases is a consequence of ignoring the intangible value of vaccination and prevention

On 26 October 2002, the British Medical Journal made the frightening prediction that by 2020, we will see a major increase of chronic diseases and schematically represented the dramatic situation in the cover page [7]. A modified version of the figure is shown in Fig. 3.

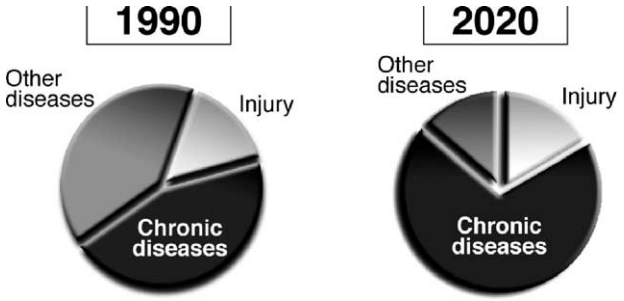

Fig. 3. Increase of chronic diseases in the global burden of diseases. Based on data from Harvard Public School of Health's project on the global burden of disease, the incidence of different diseases in 1990 is compared to the perspective incidence in 2020. The burden of chronic diseases in the developing world is compared to the burden from injuries, and to the burden from other diseases (infectious, maternal and perinatal, and nutritional diseases).

The increase in chronic diseases derives from the progress of modern medicine that, with the help of several waves of revolutionary technologies, is becoming able to provide an acceptable quality of life to people affected by diseases that in the past led to death in shorter periods of time. Since we are willing to pay very expensive therapies to be cured, pharmaceutical companies are making huge investments to find new therapies, and we can be confident that the quality of life of chronically sick people will continue to improve.

Given the power of the new technologies, similar investments could lead to the prevention of many diseases and to a society with a much higher proportion of healthy people, and less chronically sick people. Regrettably, these investments are not encouraged and therefore the prediction of the increase of chronic diseases is likely to be correct. Why are we not investing in keeping people healthy and instead we invest only in curing them once they are sick, or in stabilising their chronic diseases? The answer is very simple. There is little money to be made in keeping people healthy and therefore investments are made only to cure diseases.

We believe that we could build a healthier society, instead of a society of chronically sick people, by assigning more economic value to disease prevention. For instance, vaccines which could prevent many infectious diseases leading to chronic infections, and preventive medicine in general, are not prioritised by policy-makers because we fail to associate the appropriate economic value to them [8,9].

In conclusion, the increase in chronic diseases is our choice, not an inevitable fate. This means that we may be able to prevent this from happening, or make it happen to a lesser extent, if society is ready to take the appropriate measures.

4. Conclusions

Under the present conditions, industry (pharmaceutical companies) has no choice other than to prioritise therapy, because only this strategy provides the best return to investors. They will continue to do so until another strategy is shown to be as profitable. The current investment in therapy that does not prevent disease to start with will inevitably promote the development of more and more and, very likely, better remedies to cure people once they become sick. We believe that this abandonment of prevention as a strategy is the antithesis of medicine and, ultimately, does not seem to be in the best interest for mankind. Given a choice, most people would certainly prefer to remain healthy rather than to get sick so that they can be cured. However, this is not going to happen unless we change the rules of the game.

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