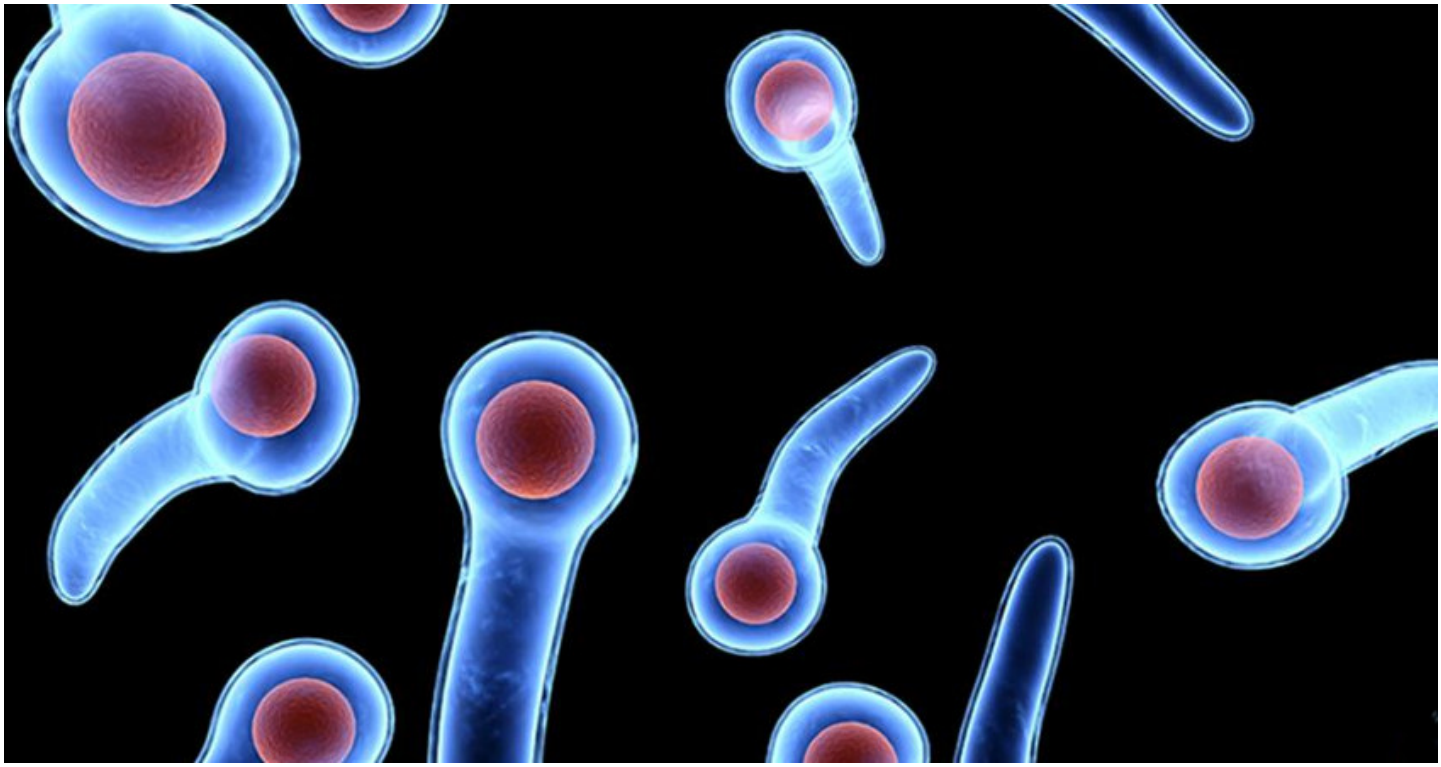
Vaccines, a proven protection against pathogens in our environment

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07-05-2019



This article offers a series of reflections on an increasingly critical society with regard to vaccines. Vaccines, which are one of the most beautiful scientific discoveries in the history of mankind, are now causing controversy in developed countries. "Prophylactic" vaccination is an essential means of prevention against a number of infectious diseases. Some of these diseases can be strictly human (hepatitis B, measles, bacterial meningitis), others originate in the environment: tetanus (soil contaminated with excrement) - see above image- or poliomyelitis (contamination with water and food contaminated with water). Even diseases as common as influenza can have an environmental origin (pandemic influenza strains come from avian and swine strains). We present here the history of these oppositions and resistances to vaccination, which were born with the first public health measures in the 19th century in England where they took violent forms. Then we analyze the current controversies over vaccines. Finally, we analyse the consequences of the decline in vaccination, before looking at how the balance between mandatory and recommended vaccines is struck.

Vaccination killed four doctors in a Pakistani province one morning in November 2014. These precious health workers did not die from the **vaccine**, but under bullets of Kalashnikovs from the Taliban who had sentenced them to death for the "crime of spreading a non-Islamic vaccine". The small group of vaccinators had just arrived on board 4x4s in this small border village as part of the WHO **polio** eradication programme. These doctors went around the countryside, knocking on doors, begging mothers to let them approach their children to make them drink a few drops of the precious vaccine. Pakistan remains one of the last three countries in which polio is still prevalent along with Nigeria (in which vaccinators have also been murdered). Pakistan accounts for 85% of the unfortunate cases of poliomyelitis, a viral disease that causes muscle paralysis and can kill by respiratory paralysis. This disease should no longer affect a single child, as there are several effective vaccines.

This bloody fact illustrates by its radicality and violence the problems and oppositions that vaccines have caused since the beginning of their history. These Pakistani doctors are not the first victims of obscurantist revolts in the short history of vaccines. Vaccination campaigns have generated conflicts and resistance since their inception. Not all oppositions are as radical or completely unfounded, but they are rooted in the same societal sources.

But the result of vaccination resistance is always the same, and the victims are most often children. Thus, measles reappeared in France in epidemic form between 2008 and 2012. It killed 10 people, caused 23,000 (reported) cases and more than 5,000 patients had to be hospitalized for complications. Three cases of severe **tetanus** have been reported since 2012 in children in France. In June 2015, an 8-year-old child was rushed to hospital in Tours. He had contracted tetanus after falling on a piece of pottery. He stayed 3 weeks in intensive care for a disease that should never have touched him. The paediatrician, with the consent of the parents, had written him a false vaccination certificate. The doctor has since been removed from the *General Medical Council* and banned from practice.

In this article, we will first analyse the history of opposition to vaccination, before considering the causes of current resistance, then discussing in a last part the balance between obligations and recommendations.

1. Vaccine resistance: the product of a long history

1.1. Mockery of the first vaccines



Figure 1. "The Cow-Pock". Drawing mocking smallpox vaccination, published in 1802 in England. Source: James Gillray [Public domain], via Wikimedia Commons.

Resistance to vaccination appeared from the first vaccines. For example, **Edward Jenner**'s (1749-1823) **smallpox** vaccine, discovered in 1796, was mocked from the beginning. In 1802, pamphlets and satyric figures were circulating in England showing smallpox vaccinees turning into cows and pigs (Figure 1).

It should be remembered that smallpox is an eruptive viral infectious disease that already affected Egyptians (mummies display scares of infection). This millennial scourge struck all social classes alike (Louis XV succumbed to it in the small Trianon) and caused terrible epidemics. Smallpox killed half the patients it infected, left monstrous scars on those who survived it. Until the middle of the 20th century, it caused two million deaths annually and infected 50 million people [1].

But mockery turned into outright opposition, even bloody revolt, when vaccines were used as public health tools. They appeared as soon as the first laws imposing a vaccination obligation were drafted. They reflect social tensions, the complex relationships between obligation, state authority and individual freedom.

1.2. Very deep roots going back to Jennerian England

England, Edward Jenner's homeland, was the first country in the world to introduce compulsory vaccination in 1853. The laws imposed significant fines or jail time for parents who did not vaccinate their children. At that time, the country was poor, the health system non-existent, and epidemiological surveillance was almost non-existent. Vaccination coverage rates were not sufficient to control epidemics. The non-vaccinated were the poorest and vaccination followed a social divide in English society

between rich and poor.

In 1867, in view of the relative ineffectiveness of the law, the obligation was reinforced for all children over 14 years of age. Vaccinators visited the homes to verify that children on the birth records were properly vaccinated. The law was further consolidated in 1871. Vaccinators had to send the vaccination certificates that were checked against the birth certificate register. The effect of the law was relatively effective, although costly for the state that maintained the system. But the population was less and less tolerant of state interference in personal affairs. These laws were experienced as an attack on individual freedom.

In 1876, in Keighley, Yorkshire, vaccinators were arrested and briefly imprisoned in York by rioters. Anti-vaccine leagues were formed. In 1886, in Leicester, more than 6,000 people were prosecuted for lack of vaccines. Demonstrations by more than 20,000 people led to the discontinuation of the proceedings. The Leicester area became the spearhead of vaccine control in England [2]. Under the influence of the riots, English legislation was softened in 1895. Vaccine exemption was allowed in the form of a conscience clause. The law allowed citizens to refuse vaccination.



Figure 2. The smallpox vaccine is proof that it is possible to eradicate a disease on the planet. Before 1967, vaccination was carried out either by scarification or multipuncture technique. Two new methods were developed during the intensive program that eventually led to the eradication of smallpox: the injection gun and the bifurcated needle. Jenner's intuition had been correct: its method, vaccination, eliminated in a decade a disease that had previously killed, infected and disfigured thousands of people. Source : © James Gathany Content Providers(s): CDC [Public domain], via Wikimedia Commons.

Initially this clause was very restricted, because it required the signature of two judges. In areas where magistrates defended vaccination, the application of this clause was impossible. In 1907, under popular pressure, the application of the conscience clause became more flexible and reduced to a simple signed declaration. England became one of the first countries to abolish the requirement for smallpox vaccine in 1948 after almost a hundred years of war between pro- and anti-vaccines, ahead of many countries. As a reminder, in France, the smallpox vaccine requirement established in 1904 lasted until 1980 (the date of eradication of smallpox).

1.3. Vaccine resistance worldwide



Figure 3. The Rio anti-vaccine riots in 1904. Source: By A Revista da Semana, publicada em 27/11/1904 [Public domain], via Wikimedia Commons.

England was not an isolated case of violent reaction to vaccination obligations. Thus, in 1904, a revolt against smallpox vaccination took place in Brazil . This riot was called the *revolta da vaccina* (Figure 3). At that time, yellow fever and smallpox were wreaking havoc in Rio's poor neighbourhoods. On October 31, 1904, the Brazilian Congress passed a law that required people to be vaccinated against smallpox. It mainly allowed controllers to enter households by force. This attack on individual freedom led to a violent outbreak. The opposition formed a *Ligua contra a vaccina obligatoria*. For 6 days, Rio was paralyzed by barricades and looting scenes. When order was restored, 30 people were killed and 110 wounded. In the United States, anti-vaccine leagues have also flourished. Like English legislation, conscience clauses have been adopted in most states.

1.4. France: a singular case

France represents a special case in terms of opposition to vaccination. Thus, vaccines did not crystallize any major opposition during the 19th and early 20th centuries. Several factors may have played a role. First of all, it is not unrelated to the fact that France lived under the tutelary shadow of **Louis Pasteur** (1822-1895), the "father of modern vaccines". Pasteur victory over death and disease received all the honours a republic can offer. He was entitled to a national funeral. In Paris, Pasteur has his institute, his boulevard, his metro station. Even today, there is not a village in France that does not have its place, its street, its avenue Louis Pasteur. In the french republican imaginary, the vaccine is the embodiment of progress. It may seem like a smile, but it is a reality that Pasteur's work has been traced in a furrow that deeply marked France with its flagship Institute in Paris, its worldwide network of institutes that spread science and participated in the great vaccination epic.



Figure 4. Wearing Louis Pasteur by Félix Nadar. Pasteur discovered the first rabies virus vaccine (attenuated vaccine prepared from rabies spinal cord). [Source: Nadar [Public domain], via Wikimedia Commons].

Pasteur's system has been prolific. His "lieutenants" as Maxime Schwartz calls them, have directly developed diphtheria, tetanus and typhoid vaccines in Paris, the yellow fever vaccine in Dakar and tuberculosis in Lille [3]. Moreover, the vaccination obligation only arrived relatively late in France: in 1904 for smallpox vaccination (in England it was 1853), in 1938 for **diphtheria**, in 1940 for **tetanus**, in 1950 for **BCG** (Calmette and Guérin's "biliary" tuberculosis vaccine) and in 1964 for **poliomyelitis**. The obligation was lifted for smallpox vaccination in 1984 and for BCG in 2007. It is therefore easy to understand why opposition to vaccination only began to be active in France in the second half of the 20th century.

1.5. Where do we stand today?

Distrust of vaccines is a general phenomenon that is constantly increasing in developed countries for many reasons [4]:

In developed countries, infectious diseases have declined so much in less than a generation (thanks to the success of vaccines) that the feeling of infectious danger has almost disappeared;

Vaccines, (like all drugs) are likely to cause side effects, as modern epidemiology reveals, so they generate fears;

Finally, vaccines are single drugs that are administered to healthy people. The occurrence of adverse effects is difficult to tolerate in such a context;

More recently, there has been a suspicion of conflicts of interest or complicity between policy makers and vaccine manufacturers.

This is why anti-vaccine discourse is gaining ground, especially in France. In an international study published in 2016 on the study of confidence in the population, France took the lead in countries in which confidence in vaccines is falling dangerously [5]. In this study, 41% of respondents did not trust vaccines, placing France just ahead of Bosnia and Herzegovina (36%), while the international average of distrust was around 13%.

Governments were deeply concerned about these disappointing results. In recent years, several parliamentary reports have been issued on the vaccination policy to be adopted, in particular to achieve the vaccination coverage targets for the control of common infectious diseases. A major national consultation was launched, which produced its report at the end of 2016 [6]. In the recommendations of the consultation report, the extension of the obligation to all vaccines in the infant calendar is included. It is the famous "11 vaccines" that are now mandatory since January 2018.

2. Vaccine resistance and controversies

2.1. Old accidents with dramatic consequences



Figure 5. Image from April 1955 showing the effectiveness of the poliovirus vaccine discovered by Jonas Salk in 1954. After being tested on more than one million children, the vaccine was declared effective on April 12, 1955 by the University of Michigan. He chooses not to patent it in order to leave it affordable to the millions of people who need it. Poliomyelitis was eradicated from Europe in 2002 as a result of vaccination. Today, polio remains only in Pakistan and Afghanistan, and fewer than 100 cases were reported in 2015. [Source: By March of Dimes (March of Dimes) [Public domain], via Wikimedia Commons.]

The anti-vaccine discourse is based on real but ancient historical facts that date back to an era when there was no industrial production standard. We will recall the Lübeck accident in Germany in the 1930s with the **BCG vaccine** contaminated with a virulent strain of tuberculosis, which resulted in the death of 72 children out of 251 infections. The production of the first **polio** vaccines was also affected by the Cutter Laboratories incident in 1955. This laboratory produced the first batches of the inactivated vaccine invented by Jonas Salk. Less than two weeks later, Cutter Laboratory in California released batches of vaccines with poorly controlled inactivation processes. Unfortunately, 56 children reported paralytic polio and 5 died from it. This virus also infected families, with 116 cases of paralytic polio and 5 deaths among the children vaccinated. The damage was therefore considerable. Industrialists became aware of the crucial importance of quality controls.

Beyond these circumscribed and well-known examples, the recent history of controversies over modern vaccines reports either analyses with no proven scientific basis or cases of real malfeasance.

2.2. The hepatitis B vaccine: a French example

Hepatitis B is a real public health problem. In France today, nearly 280,000 patients suffer from chronic hepatitis B and the hepatitis B virus (HBV) is responsible for the death of 1,500 patients per year. Globally, an estimated two billion people have been infected with the virus (almost one-third of the world's population), and according to WHO in 2016, 257 million people were infected with chronic hepatitis B, resulting in 887,000 deaths. The disease is transmitted sexually, through exposure to contaminated blood, and during pregnancy from mother to child (transmission of between 40 and 90% of untreated cases). The hepatitis virus infects the liver and causes acute **hepatitis** (clinically in the form of jaundice), and in rare cases fulminant hepatitis: it is a death of the liver cells (necrosis) whose only treatment is liver transplantation. Finally, it is complicated by chronic hepatitis in 5% of cases. The virus then persists in the blood. Chronic hepatitis B slowly progresses for months or even years to cirrhosis and liver cancer.

To give an idea of the danger of this virus, HBV is 50 to 100 times more contagious than **human immunodeficiency virus** (HIV). It can be transmitted in everyday life by equipment contaminated by traces of blood (nail clippers, razors, earrings, etc...) or by poorly disinfected equipment used by professionals (acupuncture, tattoo parlours, piercing...). In France in 1990, it was

estimated that there were more than 20,000 new infections annually.

France decided to launch an HBV vaccination campaign targeting infants, adolescents and adults at risk. A few cases of neurological disorders with **multiple sclerosis** type have been described in the aftermath of hepatitis B vaccination in young adults. Associations were formed to consolidate patients' complaints and take them to court. In 1998, the French Agency for the Health Security of Health Products (AFSSAPS, which has since become the **ANSM**, for Agence nationale du médicament et des produits de santé) launched several scientific studies. This suspicion had only been reported in France and nowhere else in the world. In the autumn of 1998, under pressure from the media and associations, the Minister of Health decided to suspend the vaccination of adolescents in the sixth grade.

Since this suspension, all studies have consistently shown that there is no biological correlation between hepatitis B vaccination and multiple sclerosis. There was just a **simultaneity**, since the vaccines had been administered to young adults during the natural onset of multiple sclerosis. There was no causal link. The safety profile of hepatitis B vaccines is excellent given the safety and pharmacovigilance data and the decline over more than thirty years [7], [8]. Several billion doses of hepatitis B vaccine have been safely used.

The suspension of vaccination of adolescents in 1998 in France had negative public health effects, since these cohorts of young people are now in the age groups at risk of sexual exposure without any protection. It has been calculated that the continued vaccination of these adolescents would have prevented 1,000 acute hepatitis, 100 chronic hepatitis, and 5 fulminant hepatitis cases each year.

In the case of the hepatitis B vaccine, the health alert resulted in a health mess as a result of the overly broad use of the precautionary principle (see focus The precautionay principle).

2.3. Aluminium additives in France

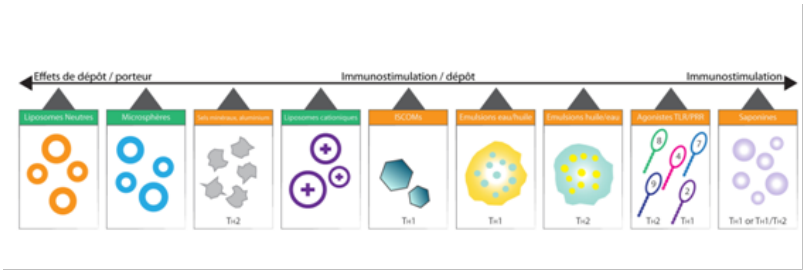


Figure 6. Adjuvants are mineral or organic components essential for most vaccines (see Table 1). Their role is to stimulate the mechanisms of innate immunity (still called non-specific) in order to activate specific immune cells of immunity (lymphocytes). The figure shows their mode of action: action on the prolonged deposition of vaccine compounds at the injection site, stimulating action towards auxiliary T lymphocytes (Th or T helper under Th1 populations - cellular immunity - or Th2 humoral immunity). Aluminium salts (microcrystals) have a mixed effect (deposition and immunostimulant). [Source: © Emmanuel Drouet, excerpt from the book "Introduction aux biotechnologies en santé 2015 Lavoisier, Paris].

Adjuvants are substances administered jointly with an antigen. The adjuvant stimulates or strengthens the specific immune response against the antigen without inducing a response against itself.

In France, the safety of aluminium used in vaccines as an adjuvant has been the subject of considerable controversy since 1998. Professor Romain Gherardi (at Créteil) threw a stone into the pond by publishing an article in the famous magazine *The Lancet*. This article described a new muscle pathology in 18 patients: Macrophagic *myofasciitis* [9]. It showed that the microscars observed were associated with the presence of aluminum, a possible residue of the vaccine introduced by intramuscular injection. In 2003, the Romain Gherardi's team linked macrophagic myofasciitis to a broader syndrome: chronic fatigue syndrome [10], [11]. The vaccine in question is again the one against hepatitis B widely used in adults in the 1990s.

These works were surprising in several ways:

Aluminium has been used as an adjuvant in vaccines since 1925 with safety data collected from populations around the world. The decline in the safety of this component is therefore enormous, since several tens of billions of doses of vaccines have been administered since the beginning.

Moreover, this syndrome was only found in France, and more precisely in patients of the Créteil team from which the cohort originated.

Finally, it is children who are significantly exposed to vaccines with an aluminic adjuvant, and the cohort even extended to other patients was made up only of adults.

Nevertheless, this problem has long been taken very seriously by health authorities. The World Health Organization (WHO) addressed the problem in 1999 by setting up an advisory committee for vaccine safety, the first issue of which was the problem of aluminium-based adjuvants. In France, the *Institut national de veille sanitaire* (InVS) launched a pharmacovigilance study in 2002. Since then, many reports have been produced on the subject: in 2012, the *Academy of Medicine*, in 2013 the *High Council on Public Health* (HCSP), in 2014 the Parliamentary *Office for the Evaluation of Scientific and Technical Choices*, in 2016 the *Academy of Pharmacy*. The Academy of Pharmacy report stated that "given the heterogeneity and non-specificity of the clinical manifestations associated with histological lesion, it is not possible to define a macrophagic myofasciitis syndrome" [12]. The disorders observed concern only a few exceptional, even unique cases [13], which could correspond to very particular genetic predispositions. In any case, the potential risk is disproportionate to the benefits provided by this vaccine, as recalled by the ANSM.

2.4. Thiomersal and autism

Thiomersal is an organo-mercurial chemical compound with biocidal activity (*i.e.* it kills contaminating microbes). Thiomersal also helps to improve drug stability. These properties are useful for vaccination campaigns where multi-dose packaging is used (when one vial is used to vaccinate several people). Multiple doses are not administered simultaneously to several patients and the doses can therefore remain open without any risk of contamination.

In 1999, in the United States, the hypothesis that thiomersal exposure could be associated with neurodevelopmental deficits in children began to circulate [14]. These concerns were based on the calculation of the cumulative mercury intake in infant vaccination schedules, which may exceed the maximum rate recommended by the American authorities. From a toxicological point of view, the vaccines contained minimal doses of thiomersal, between 0.003% and 0.01%, with a maximum of 25 to 50 µg/dose. At these doses and in the situations of use any toxic risk was excluded *a priori.*

However, the *Food and Drug Administration* (FDA) has requested the withdrawal of thiomersal from all pediatric vaccines, which was effective in the United States and Europe in 2001. Detailed scientific work published in 2007 in the *New England Journal of Medicine* showed that there is no link between thiomersal and autistic disorders [15].

Again, many agencies have addressed the problem. The WHO in 2006, the European Medicines Agency (EMA) in 2007 and AFSSAPS in 2009, agree that the existence of neurological risk is not established (even if it cannot be scientifically excluded). Given these properties as an essential preservative in multi-dose vaccine presentations, the benefits of using thiomersal outweigh the theoretical toxicological risk.

2.5. Polio vaccine and the AIDS epidemic

In 1999, a book brought another controversy. The oral polio vaccine used in a 1959 vaccination campaign in Africa was reported to have caused the HIV pandemic [16]. The vaccine would have been produced on chimpanzee kidney cells that would have been contaminated with the simian immunodeficiency virus (SIVcpz) that would have been transmitted to humans and would have caused the group M immunodeficiency virus (HIV) and the global acquired immunodeficiency syndrome (AIDS) pandemic. The vaccine is normally produced on green monkey kidney cells (Vero cells) that do not carry chimpanzee SIV.

This hypothesis has been largely refuted by molecular comparison studies of the viruses [17], [18]. Therefore, it is not the oral polio vaccine that causes HIV. These results are supported by more recent data on the emergence of HIV. It appeared well before 1959 on the banks of the Congo River, since it was already circulating in Kinshasa in the 1930s [19].

2.6. The speech on over-vaccination

When the previous claims are scientifically proven one after the other, not without a public health cost, other more pernicious arguments emerge.

After the meaningless naturalistic discourse "better to be sick than vaccinated", comes the argument that the vaccine makes you sick by tiring the immune system.

The multiplication of vaccines could lead to an over-activation of the immune system.

This idea is a scientifically false truth.

On the one hand, because the vaccines have become more refined. It is estimated that twenty years ago there were about 3,000 antigens in all vaccines in the vaccination schedule. Nowadays, the number of these antigens has dropped to 150 [20]. But it must

be understood that 3,000 or 150 antigens are a drop in the ocean of the 10,000 billion bacteria and viruses that surround us and against which our immune system has been constantly responding since birth. This represents a drop in the almost infinite possibilities of our immunological repertoire acquired during evolution. We are therefore far from saturating our immune system with our vaccination schedule [21].

On the other hand, modern immunology teaches us that the stimulation of the immune system by the environment is necessary for the harmonious development of immunity [22] (see Human microbiotas: Allies for our health).

3. What public health policy?

3.1. The beneficial effects of vaccines

Epidemiologically, vaccines are a real success story. The incidence of vaccine-preventable diseases fell by 100% in the United States in the 20th century [23].

In France, similar results are observed. The last cases of indigenous polio and diphtheria were in 1989. The **tetanus agent persists indefinitely in the soil thanks to its very resistant spores, it cannot be eradicated,** but it is controlled to less than ten cases per year. Since the introduction of *Haemophilus influenzae* type b vaccinations in 1992, the incidence of **meningitis** has dropped by 96% among children under 5 years of age [24].

The benefits of vaccines can be quite surprising, in some cases exceeding the simple direct effect on the drop in the number of cases. Thus, the measles vaccine increases the lifespan beyond the simple protective effect it provides against measles-related mortality [25]. This "additional" benefit is related to the fact that measles infection is highly **immunosuppressive** and causes us to lose immunity to many other diseases. By protecting us against measles, the vaccine increases immunity to other diseases.

Pneumococcus is a bacterium that causes ear infections, meningitis and serious lung infections mainly at both ends of life: in children and the elderly. The pneumococcal vaccine introduced into the childhood immunization schedule dramatically reduces not only childhood ear infections and meningitis, but also pneumonia in the elderly (which are not vaccinated), reminding us (or finishing to show us) that children are the vectors of pneumococcal infections in the elderly. By interrupting pneumococcal transmission by vaccinating children, the vaccine directly protects children and indirectly protects the elderly around them. Vaccines against early childhood infections have indirect beneficial effects on antibiotic resistance by saving unnecessary prescriptions and reducing health costs.

In a word, vaccines reduce infections. But infectious diseases, under control, have not disappeared. They patiently wait for the opportunity of a drop in the vaccine shield to reappear mechanically.

3.2. The mechanical effects of the decline in immunization coverage

In 1900, life expectancy in France varied around 45 years. By 2016 it had risen to an all-time high of 79.4 years for men and 85.4 years for women. Vaccines are not the only cause of this dramatic increase in life expectancy, but they have been a major contributor.

The decline in vaccination mechanically induces like a pendulum game the return of pertussis, terrible diphtheria (it had reemerged in Russia with the fall of the Soviet empire), meningitis in young children, a resettlement of measles, mumps, rubella, and why not polio if it were reintroduced in Europe. Finally, it leads to an increase in antibiotic resistance following their massive use to treat bacterial complications of viral infections.

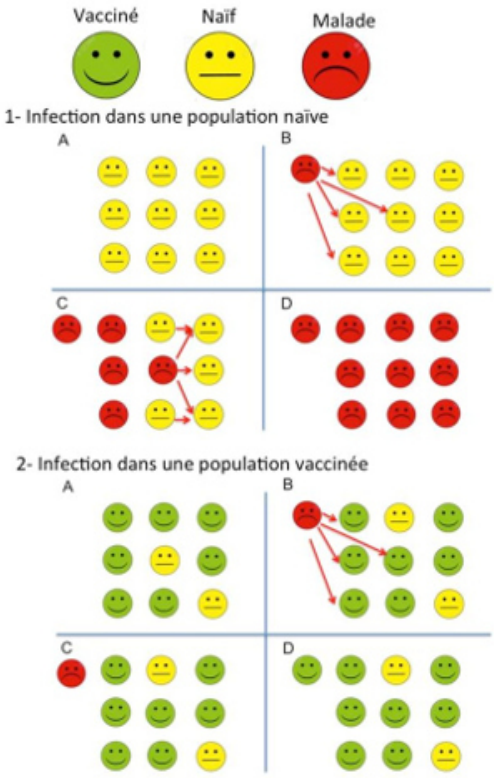


Figure 7. The phenomenon of group immunity. When in a group of people, the number of protected persons exceeds a certain percentage, the epidemic power of the infectious agent is blocked. [Source: © Jean-Nicolas Tournier, from the book "Les vaccins pour les nuls", in french].

The most obvious recent example was given to us in France by the measles epidemic between 2008 and 2012 [26], [27]. Measles is the most infectious disease known. Measles vaccination was included in the recommendations of the French vaccination calendar in 1983 (combined MMR vaccine), with a second injection recommended from 1996 one year after the first injection. In 2002, WHO decided to eliminate measles from the European geographical area by 2010. This objective involved maintaining the measles incidence rate (the number of cases per population) at less than 1 case per million inhabitants. The objective here was to play on group immunity, which is an epidemiological mechanism by which the spread of a contagious disease in a population is inhibited when a sufficient percentage of individuals are immunized (Figure 5). The emergence of an import case is then in a dead end epidemic bag, and the epidemic goes out on its own.

France launched a measles plan in 2005. Measles has become a notifiable disease. Cases were monitored by an epidemiological investigation at each report. In 2006, France had fewer than 50 cases per year, which is less than the target set by the WHO. Unfortunately, due to the decline in immunization coverage, a measles epidemic began in early 2008 and more than 23,000 cases were reported between 2008 and 2012. The epidemic has resulted in the hospitalization of almost 5,000 patients (1,023 severe viral or bacterial pneumopathies, 27 neurological complications such as encephalitis or myelitis), and 10 deaths, the majority of which were under 30 years of age. This upsurge had been predicted by modelling work due to insufficient measles vaccination coverage in France. While immunization coverage for the MMR infant vaccine has increased in recent years, it is still insufficient. It was 90% at one year for one dose, but dropped to 54% for two doses, while the elimination plan targets were 95% and 80%, respectively, for one and two doses.

This example illustrates that the guard can only be safely lowered if the disease has been completely eradicated worldwide. This is a long and complex operation that has been successfully carried out for smallpox. It is ongoing for polio and is being considered for measles. But it requires global coordination and very significant efforts. The eradication of a virus depends, as in a chain, on the resistance of its weakest link.

3.3. Obligation or recommendation?

Within the European Union, France shares with Italy the particularity of being one of the last countries to impose a vaccination obligation. This is the result of historical choices in the middle of the 20th century, at a time when infectious diseases were still causing considerable damage to the populations of these two countries.

For the legislator, it was a question of effectively combating serious diseases in a context of infectious risk. But since 1964, however, no new vaccines have been included in the vaccination schedule under the seal of obligation. These changes also correspond to societal changes in which the patient is more involved in the choices that concern him/her. The obligation appears to be in contradiction with the law of 4 March 2002 on the right of the patient and in particular the right to refuse treatment. The

result is a great paradox in terms of the readability of the vaccination policy into which many opponents have rushed.

Mandatory vaccines seem less important in terms of interest since they protect against diseases that have disappeared in France (diphtheria, poliomyelitis), while vaccines simply recommended such as hepatitis B and human papillomavirus protect against diseases that kill 1,500 and 1,000 people respectively each year.

Paradoxically, the disparity between mandatory and recommended vaccines creates in the imagination the idea that recommended vaccines are less important. This is very directly reflected in terms of vaccination coverage. In children, the official calendar recommends 11 vaccines, only 3 of which are mandatory (see Table).

Agent	Pathology (severity)	Epidemiology	Natural reservoir	Vaccine type (adjuvant)
Bacteria				
Corynebacterium diphtheriae	Diphteria (++++) Fatal	Aerial and cutaneous contamination	Essentially human. Some biotypes of C. diphteriae have been isolated on animals like cows, cats and horses.	Anatoxin (yes)
Clostridium tetanii	Tetanus (++++) Fatal	Wound contamination	Soil, feces, sewage, endogeneous microbiota of human and horses	Anatoxin (yes)
Bordetella pertussis	Pertussis (++)	Aerial inter-human contamination	Strictly human	Sub-unit vaccine - protein (yes)
Streptococcus pneumoniae (pneumococcus)	Pneumonia, sinusitis, meningitis (+++)	Aerial inter-human contamination	Strictly human	Capsular polysaccharides (yes)
Haemophilus influenzae	Otitis, meningitis (++)	Aerial inter-human contamination	Strictly human	Capsular polysaccharides type b (yes)
Neisseria meningitidis (meningococcus)	Meningitis (++++)	Aerial inter-human contamination	Strictly human	Capsular polysaccharides type C (yes)
Virus				
Poliovirus	Poliomyelitis (++++)	Digestive contamination	Soil, feces, sewage, marine sediments, food contaminated by water	Inactivated virus (yes)
Mesales virus	Measles (++++), Encephalitis Deadly	Aerial inter-human contamination	Strictly human	Attenuated virus (no)
Mumps virus	Mumps (++) fertility issue	Aerial inter-human contamination	Strictly human	Attenuated virus (no)
Rubela virus	Rubela abortion, fœtal malformations (++++)	Aerial inter-human contamination	Strictly human	Attenuated virus (no)
Hepatitis B virus	Hepatitis B (+++) Liver cancer	Sexual, blood, saliva interhuman contamination	Strictly human	Sub-unit vaccine - protein (yes)

Table. The 11 vaccines recommended for children. The severity of the diseases targeted by the vaccines is indicated. Although less dangerous than measles, pertussis (caused by Bordetella pertussis bacteria) can be severe for humans at any age. It is particularly dramatic, if not fatal, for infants under 6 months of age and people at risk such as pregnant women and the elderly. Pneumococcus, Meningococcus, Haemophilus influenzae (type b) are responsible for meningitis in children and adolescents, fatal without antibiotic treatment. Before the arrival of vaccinations, mumps (reaching the glandular system) and rubella (infantile eruptive pathology) were very highly epidemic diseases with major complications (respectively orchitis with sterility in males and foetal pathologies in pregnant women). Finally, vaccination against hepatitis B has significantly reduced the incidence of liver cancer.

WHO immunization coverage figures comparing European countries are not good for vaccines recommended in France. For example, in 2012, while hepatitis B vaccination coverage for children aged 2 years old was 74% in France, it was more than 86% in Germany and 96% in Belgium and Spain, three countries in which there is no vaccination obligation.

In 2012, the Court of Accounts reported on the cost and effectiveness of vaccination policy in France. This report was followed in 2013 by that of Mr Georges Labazée for the *Senate Social Affairs Committee*. In 2014, the *High Council on Public Health* (HCSP) issued an opinion on vaccination policy that called for a debate by the health authorities to decide on vaccination obligations. In 2015, the Minister of Health referred the issue to Senator Sandrine Hurel. Its 2016 report also called for an end to the *status quo* in this area and for a major consultation on vaccination to determine what collective risks France was prepared to take to remove individual coercion.

This major consultation took place during 2016 under the direction of Professor Alain Fischer. The report submitted to the Minister on 30 November 2016 concluded that the vaccination obligation should be temporarily extended to all the vaccines recommended in the schedule (by adding an exemption clause allowing individual refusal of the vaccine), while retaining in the long term the possibility of completely lifting the obligation once confidence in the vaccines is restored [6].

It is in this vein that the government announced in the summer of 2017 that it had decided in favour of mandatory vaccination for the 11 early childhood vaccines. These are not exactly 11 vaccines, but four vaccine preparations (several vaccines are multivalent) that protect against 11 serious diseases.

References and notes

Cover image. Computer generated image representing the tetanus bacillus in the form of persistent spores [Royalty-free]

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L'Encyclopédie de l'environnement est publiée par l'Université Grenoble Alpes - www.univ-grenoble-alpes.fr

Pour citer cet article: **Auteur :** TOURNIER Jean-Nicolas (2019), Vaccines, a proven protection against pathogens in our environment, Encyclopédie de l'Environnement, [en ligne ISSN 2555-0950] url : http://www.encyclopedie-environnement.org/?p=6796

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