

How predictable were the outbreaks of foot and mouth disease in Europe in 2001 and is vaccination the answer?

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This article reflects solely the opinion of the author.

Summary

The author raises three important questions on the outbreaks of foot and mouth disease (FMD) in Europe in 2001: were these linked to stopping preventive vaccination, could these outbreaks have been forecast and were they avoidable, and is vaccination an efficient tool to control outbreaks?

The replies to these questions are based on recent history of FMD in Europe. The author demonstrates that the 2001 outbreaks were not linked to ceasing vaccination in Europe in 1991. He also attempts to understand the reasons which encouraged the United Kingdom not to use vaccination to halt the progression of the disease, despite the clear demonstration that vaccination is a useful tool in arresting the spread of an epidemic.

In conclusion, the author suggests that substantial changes to European policy for FMD control used for the past ten years are not necessary, but that recourse to emergency vaccination should be considered as an important control option in the future. This option should be optimised by ensuring that differential serological tests are performed in parallel with emergency vaccination, thereby enabling the identification and subsequent elimination of infected herds.

Keywords

Control – Europe – Foot and mouth disease – Slaughterer – United Kingdom – Vaccination.

Introduction

Many things have been said and written about foot and mouth disease (FMD) since the disease suddenly and, for many, unexpectedly occurred in the United Kingdom (UK) and three other countries of Europe in 2001. The topic hit the headlines and made the news in the media for several weeks. Europe as a whole and the entire world discovered this new disaster that had struck the UK and threatened the whole of Europe soon after the bovine spongiform encephalopathy (BSE) epidemic. Many people, both experts and others, expressed opinions, generally criticising the methods used for control, in particular the slaughtering of the animals, and advocated the return to vaccination as an alternative to massive slaughtering. The other economic and environmental aspects connected with this exceptional epidemic were also widely discussed (3, 4). Three separate investigations were conducted in the UK to draw conclusions from this crisis and an Inquiry Committee

(Temporary Committee on Foot and Mouth Disease) was formed by the European Parliament.

Rather than attempt to answer all the questions raised by this episode, the purpose of this article is to re-evaluate the outbreak within the perspective of the history of FMD in Europe and in the world over the last ten years.

The scope of this paper shall be limited to trying to answer the three following questions based on historical data and facts pertaining to control of recent episodes of FMD in Europe:

- 1) Was the introduction of FMD into Europe in 2001 made inevitable by the abolition of preventive vaccination in Europe?
- 2) Was the magnitude of the episode in the UK (and to a lesser degree that in the Netherlands) predictable and could such a large outbreak have been avoided?
- 3) Is vaccination effective in controlling and containing FMD outbreaks?

Was the introduction of foot and mouth disease in Europe in 2001 inevitable since preventive vaccination was discontinued in Europe?

Europe is situated in proximity to countries in which infection is present

Traditionally, FMD has been introduced into Europe from the east or the south.

The eastern borders of Europe have been extensively opened since the Iron Curtain collapsed at the beginning of the 1990s. However, the situation in Central European countries is largely identical to that in Western Europe. They too stopped conducting preventive vaccination of cattle concurrently with the European Union (EU), and imposed restrictions at their borders so as to abide by the EU regulations. If these regulations are respected, there is no real reason to fear infection across the eastern border of Europe when the EU is enlarged.

The situation in Russia and the countries of the Commonwealth of Independent States (CIS) is different inasmuch as there is *de facto* freedom of movement of people and goods (including animals) between those countries. The situation in the European part of Russia is good, but in Transcaucasia (Armenia, Georgia, Azerbaijan and southern Russia) the risk is high because of the shared borders with countries where the infection is present (Iran, Turkey, the Republics of Central Asia). The far-eastern part of the Russian Federation is also at risk because of its borders with infected countries (Mongolia) and with those, whose status is unknown but which are probably not FMD-free (People's Republic of China).

Foot and mouth disease is endemic in Turkey and in other countries of the Middle East. In recent decades, Europe has considered this region, and in particular Turkey, as being the major potential source of the virus for Europe. As a protective measure, Europe continues to help Turkey to control the disease by maintaining a buffer vaccination zone in Turkish Thrace. Furthermore, a co-operation programme between the Veterinary Services of France and Iran has been set up, which currently focuses on FMD control in the region, and a Foot and Mouth Disease Monitoring Scheme for the region is being established in Iran and in Central Asia with EU aid.

Some key elements concerning the discontinuation of vaccination in Europe and its effect on the 2001 episode

Three elements need to be considered, as follows:

- vaccination was discontinued in Europe in 1991
- until then, vaccination in continental Europe was performed annually and only cattle were vaccinated
- the UK has never vaccinated against FMD; the same applies to Ireland, Norway and Sweden.

Considering this background, the British episode was unrelated to the interruption of vaccination in continental Europe. If European countries had continued to vaccinate after 1991 – all other changes and developments being the same – the British episode would probably have followed a similar pattern. In regard to the introduction of the disease into France and the Netherlands, the disease would undoubtedly have not occurred in cattle, which would have been vaccinated, but the virus would probably have been introduced by sheep. Three scenarios could then have occurred, depending to a large degree on the time taken to detect the disease and on measures implemented, as follows:

Scenario 1: spread of the disease as in South America; a little unlikely if vaccination of cattle continued regularly, using good quality vaccine.

Scenario 2: spread of the virus to pigs and adaptation of the virus to this species; the consequences could have created an isolated incident in pigs, as was the case in Brittany in 1981; this scenario of the virus adapting to pigs is, however, unlikely if one considers that there were virtually no cases of the disease in pigs in the UK where, with over 2,000 outbreaks, the risk of spread to this species was high.

Scenario 3: the virus could have circulated unnoticed in sheep and could have infected young cattle which were not fully protected by maternal antibody or by the first vaccination. However, as FMD can incur significant mortality in young lambs, the presence of the virus would then be obvious. This occurred in North Africa between 1989 and 1993 but was not recorded in recent outbreaks in Europe or in other countries affected by the pan-Asian strain.

This final scenario is therefore the most likely, but the others cannot be excluded.

In short, considering the mode of transmission of the virus, essentially via sheep, it is reasonable to believe that the outbreaks of FMD in the UK and Europe in 2001 would have followed the same pattern if preventive vaccination of cattle had been maintained in Europe in 1991. However, it is likely that in France and the Netherlands, had ring vaccination of susceptible animals been applied immediately, preventive

slaughter of 50,000 animals in France and 270,000 in the Netherlands would have been avoided.

Introduction of foot and mouth disease in Europe since vaccination ceased in 1991

Introductions of FMD into Europe between 1991 and 2000 are described in another article in this book and elsewhere (5, 6, 7, 8).

The probable origin of the outbreaks shows that illegal movements of animals (Italy, Turkish Thrace), of animal products (Albania) and of people (Greece) are most often the cause of introduction of the virus.

The virus was also probably introduced into the UK by pig swill in 2001. The origin therefore does not differ from previous introductions into Europe. Only the magnitude of the consequences differs in this case.

Live animal movement has often been the cause of virus introduction into Europe and among the 'unknown' causes, illegal movements often appear to be involved. Two important factors that cause an increase in both legal and illegal movements of animals, and consequently the introduction of the virus, should be considered, as follows:

- religious feasts (the cause of the introduction of the disease in Turkish Thrace in 1995 and 1996)
- the adverse effect of EU support measures for livestock raising (premium calculation based on the number of animals) which encourages farmers to increase animal populations so as to obtain premiums (this was the case in Greece in 1995 and possibly also in the UK in 2001); in addition, movements of animals occur when population surveys are made for the calculation of these premiums. Furthermore, of significance was the increase of the sheep population in the UK encouraged by demand from Europe, and in particular France, for the Eid feast.

According to data provided by the countries involved, the virus was introduced 21 times in 10 years (1991-2000) into Europe, i.e., approximately twice a year, causing a total of 343 outbreaks, i.e., 34 outbreaks per year and a ratio of $322/21 = 15$ secondary foci for each introduction.

To determine whether that is a lot or little depends on the arguments one supports, but in any case these figures are similar to those for the medium scenario that had been predicted by the European experts when the decision to stop vaccinating was taken – 13 primary outbreaks (= introductions), 20 secondary foci for every primary outbreak, i.e. 260 secondary foci for the countries of the EU alone.

Measures were taken in Europe when preventive vaccination ceased in 1991, as follows:

- foot and mouth disease emergency plans were established in every country
- European and national antigen and vaccine banks were set up for the purposes of emergency vaccination
- awareness-raising campaigns were conducted among veterinarians, stock farmers and livestock professionals.

The methods used for foot and mouth disease control in Europe over the past ten years

Broadly speaking, two methods have been used in Europe, i.e., slaughtering alone or slaughtering combined with vaccination. Among the EU countries, Italy (1993) and Greece (1994, 1995, 1996, 2000) have always resorted to slaughtering alone. The decision not to make use of vaccination was based on an assessment conducted by national and EU authorities (opinion of the Standing Veterinary Committee) concerning the capability of the countries concerned to control the disease without resorting to emergency vaccination. The EU authorities have never exerted pressure to prevent any country that so requested to make use of vaccination, since European legislation allows this and vaccine banks were established for that very purpose.

It is remarkable that there has been no recorded instance of significant FMD occurrence affecting sheep in particular, that was controlled with success by using only sanitary measures (restriction of movements and slaughter). Detection of clinical cases is a risky method for diagnosis of FMD in sheep inasmuch as the disease is present in most infected animals in a sub-clinical form. As such, when clinical signs appear in a flock, most of the animals are already infected and have transmitted the virus. Consequently, one cannot wait for the clinical diagnosis in sheep to initiate the control strategy.

Conclusions

Regular introductions of FMD into Europe can undoubtedly be considered as inevitable but unrelated to cessation of vaccination. The key factor remains neighbouring countries where the infection persists. The latter are themselves at high risk of infection from their neighbours situated to the east (Turkey for example) or to the south (countries of North Africa in 1999).

During the last ten years prior to 2001, FMD was rapidly controlled at a reasonable cost every time it was introduced into Europe, without vaccination being used in the EU countries, and both with and without vaccination in non-EU countries.

The magnitude of the epidemic in the United Kingdom (and to a lesser degree the Netherlands) challenges forecasts. Was it predictable and could it have been avoided?

In September 2000, a study on the risk of introduction of FMD into the various regions of Europe based on expert opinions was conducted during a workshop organised in Bulgaria (2). Europe was divided into five regions: the Balkans, Eastern Europe, Southern Europe, Western Europe and 'the Islands'. Experts were asked in which regions they thought there was the highest risk of introduction of the virus over the coming five years. Out of the ten introductions hypothesised for that period, the experts estimated six would occur in the Balkans and 0.2 in the Islands. For all FMD experts, the UK was considered to be a low-risk country.

The isolation of the UK was considered to be a protective feature, particularly by comparison with the countries in the Balkans, such as Greece and Bulgaria, which share borders with countries where FMD is endemic.

The presence of the World Reference Laboratory (WRL) for FMD at Pirbright and of the best international experts on FMD was also something that led people to believe that the UK had a degree of 'immunity' from FMD. It should be noted that this concept is undoubtedly in contradiction with the risk posed by a laboratory or a vaccine production institute that manipulates the virus and receives virulent material. However, the WRL in Pirbright has never in recent years been the source of virus escape.

Furthermore, as early as 1892, the British were the first in Europe to develop an emergency response for FMD outbreaks. The 1967-1968 outbreak, also very destructive, provided valuable experience and it was thought that should the virus by any chance be introduced again, there would be rapid and efficient control within a matter of days.

However, a first flaw in the surveillance system for animal diseases in the UK should have served as a warning when in 1999 an epizootic of classical swine fever (hog cholera) occurred, the origin of which was never clearly elucidated and for which eradication took several months. It is noteworthy that just as with FMD, the classical swine fever virus is commonly introduced through swill and waste food that is fed to pigs. The reduction in size of the public service in the UK as a result of budgetary restrictions was no doubt largely responsible for the

flaws in the surveillance system that enabled the outbreaks of classical swine fever in 1999 and of FMD in 2001 to gain the initial foothold. A staff of 220 State veterinarians, even if highly competent, cannot ensure the surveillance of an entire area the size of Great Britain.

Conclusions

The outbreak of FMD in the UK was not predictable, but a number of elements, such as the understaffing of the Veterinary Services, the consequential inadequate monitoring of farms and imports and the feeding of swill, facilitated the introduction of FMD.

In this context, introduction could hardly be averted. What might have been avoided to some extent was disease spread. Based on the analysis of the situation during the first few weeks of the epidemic, the question can be raised as to the circumstances that dissuaded the British experts from selecting vaccination as a valuable option (see below regarding why vaccination was not used in the UK). Indeed, for what purpose have stocks of vaccine been created unless they are to be used in a situation like this when sanitary measures are not sufficient to control the disease?

Is vaccination effective for foot and mouth disease control?

Recent examples of the successful use of vaccination to control foot and mouth disease

Countries or areas that implement preventive vaccination

In Israel, all susceptible species (cattle and small ruminants) are vaccinated regularly every year. In the event of an outbreak, the veterinarian immediately revaccinates all the animals at the outbreak site and in the surrounding area.

In Turkey in July 2001, an outbreak due to virus type O occurred in a herd of goats in the Province of Tekirdag in Thrace. The authorities of Turkey immediately isolated the herd and the village and revaccinated susceptible animals. The disease was halted immediately.

In North Africa in 1999, a serious epidemic due to virus type O initially affected Algeria in the Algiers area before spreading west towards Morocco and east along the border with Tunisia. A total of 165 outbreaks were reported in Algeria, 10 in Morocco and 2 in Tunisia between February and April 1999. All three countries resorted to emergency vaccination of cattle from the initial weeks, beginning with ring vaccination and gradually extending it to the entire country. The spread of the disease was halted within six weeks in spite of the great difficulties encountered in enforcing animal movement

restrictions during the period of religious festivities (Eid). Morocco had just stopped annual vaccination of cattle which had been practised regularly until the end of 1998. Tunisia continued to vaccinate all species regularly every year, while Algeria vaccinated only the cattle in border areas prior to this epidemic.

Countries or areas that do not implement preventive vaccination

In Albania in May 1996, an outbreak due to virus type A occurred in the District of Korsha, in the south-east of the country, affecting ten villages within a radius of 15 km. Until then, vaccination had not been practised in Albania. A team of international experts from the EU and the European Commission for the Control of Foot-and-Mouth Disease (EUFMD) was immediately despatched to assist the authorities in Albania to define a control strategy. It was unanimously decided by the experts and authorities that, in view of the local socio-economic and geopolitical circumstances, systematic slaughter of the infected animals, together with ring vaccination in and around the infected area was the best control method. Monovalent vaccine was immediately supplied – within two weeks – by the EU and the Food and Agriculture Organization (FAO) and two vaccination campaigns were conducted at a four-week interval on all susceptible species in the area. The disease was halted as soon as the first round of vaccination was completed. The disease was eradicated within two months by associating vaccination with sanitary measures and no further FMD outbreak has since occurred in either the affected area or the surrounding villages where vaccination was performed. Serological tests conducted a year later showed that the virus had not spread beyond the initially infected area. It is worth mentioning that the non-structural protein (NSP) 3ABC enzyme-linked immunosorbent assay (ELISA) developed by the Istituto Zooprofilattico Sperimentale in Brescia, Italy, was used for the first time in the field on this occasion. This test demonstrated that although the clinically affected animals had been slaughtered, a few infected animals (contacts or subclinically infected) had escaped detection. The test enabled identification and elimination of these animals a year later.

The same strain of the virus had been introduced into the **Former Yugoslav Republic of Macedonia in 1996**, initially at Aracinovo and later in the Skopje area, affecting 18 villages. The authorities decided to resort to slaughter in combination with vaccination (vaccine supplied by the EU and FAO). In all, 4,500 animals were slaughtered. Vaccination was performed immediately on all the cattle in the area. These efforts were successful and the spread of the disease was halted in less than three weeks.

Why did the British not vaccinate in 2001?

Historical and doctrinal reasons

First and foremost, for historical and 'doctrinal' reasons, the UK has never vaccinated against FMD. The experience of the

1967-1968 epidemic which was successfully managed by the Veterinary Services perhaps played a part in the decision not to vaccinate in 2001, thereby ensuring coherence with the non-vaccination policy that the British have vehemently advocated for fifty years.

Scientific grounds

Vaccination does not prevent the occurrence of carriers which are difficult to detect. In the context of the British outbreak, this argument hardly holds water inasmuch as the few, hypothetical carriers of the virus – whose ability to transmit the disease has never been demonstrated in the field and which can now be serologically screened – constituted a negligible risk in relation to animals (mainly sheep) that actively spread the virus.

Economic reasons and use of predictive models

Given the nature of disease spread, various computer simulations were performed, all of which indicated that vaccination (either ring vaccination or immunisation in buffer zones) would not halt the disease and instead could, under certain circumstances, increase spread, in addition to costing more than continuing with a policy of slaughter. This is in contradiction with observations made elsewhere, whereby rapidly implemented emergency vaccination has always stopped the spread of the disease. The argument that vaccination would limit exports carries little weight inasmuch as the duration of the outbreak (from February to September) actually restricted exports for nearly a year. Furthermore, these exports had already been severely restricted in regard to cattle and beef by measures related to bovine spongiform encephalopathy.

Objections of farmers

Unions of farmers and livestock owners, especially the largest, the National Farmers' Union (NFU), rejected the vaccination alternative more because of the doctrinal reasons described above than because of scientific reasons. Long-term economic interests perhaps also played a role in the position taken by the UK farmers, especially considering that farmers who had taken the same stand against vaccination in 2001 would find it much easier to defend future bans on meat imports from FMD-free countries which vaccinate. However, professionals were not unanimous in opposing vaccination. A large section of public opinion had opted in favour of vaccination and at the beginning of August 2001, a new campaign in favour of vaccination was launched by politicians and the media in the UK.

Practical considerations and difficulties in organising the vaccination campaign

These difficulties – which were overcome in Algeria, Morocco, Tunisia, Albania and Macedonia – cannot be presented as obstacles to vaccination by the British who in addition would have had the logistic support of other EU and non-EU countries. Furthermore, the practical organisation of a

vaccination campaign would seem a fairly simple and easy matter compared to the complexity of slaughter and disposal of animal carcasses.

Availability and cost of vaccines

A total of 500,000 vaccine doses were prepared by the Pirbright international bank and the EU banks had 5 million doses of serotype O₁ Manisa available. This serotype is active against the causal strain. Furthermore, the three European manufacturers have a production capacity of more than 5 million doses per month. The required amounts of vaccine could therefore have been made available rapidly. In regard to the cost on the international market, it can be estimated at between €0.5 and €0.7 per dose depending on delivery date requirements.

Objections of traders/wholesalers and consumers

Objections to the sale and consumption of products derived from vaccinated animals appear to have been the determining factor in the decision of the UK Government not to resort to vaccination. This argument is astonishing to scientists who unanimously recognise the complete absence of any danger associated with such products. It is also surprising as other vaccines are used on livestock in the UK. Furthermore, Europe and the UK import beef from South America where cattle are vaccinated against FMD. It is therefore surprising that scientists in the UK did not state more forcefully the harmlessness of products derived from animals vaccinated against FMD when this issue was raised by the public and by politicians.

Belated decisions

The delay and procrastination relating to the decisions on vaccination are rather surprising, particularly in view of the fact that the disease continued to spread and that experts, as early as the month of March, were predicting that the disease would last at least six months. Clearly, the effectiveness of emergency vaccination against the spread of the disease is enhanced the earlier it is applied. It is therefore difficult to understand that in August, i.e., six months after the outbreak commenced, the experts continued to wonder about the suitability of strategic vaccination in certain areas (Cumbria and Devon). The harm had been done and common sense indicated – as did computerised prediction models – that at this stage, the tail-end of the epidemic, the suitability of vaccination was debatable.

Vaccination and differential tests that distinguish between infected and vaccinated animals

The vaccines currently produced in Europe are not fundamentally different from those used in the past for preventive vaccination.

The main differences are the more thorough purification that removes proteins other than those that comprise the viral capsid (which is responsible for stimulating immunity) and also earlier immunity due to higher antigenic load, generally

within a week. Major progress has also been achieved in the area of adjuvants, particularly oil-based, and there is now a choice between aluminium hydroxide- and oil-based vaccines. Additional progress has been made in inactivation techniques. This is now performed in two phases with binary ethylene imine rather than formalin, resulting in a higher level of safety in terms of innocuity. To date, no FMD recombinant or peptide-based vaccines are available on the market.

Biosecurity measures in vaccine production facilities in Europe are very stringent everywhere and the risk of a virus leak – which was real until the end of the 1980s – is now relatively slight.

Differential serological tests that distinguish infected animals from vaccinated animals have been available for a long time. Tests based on detection of antibodies against viral infection-associated antigen (VIA) were used in Brazil as early as 1985 and enabled identification of infected herds. The new 3ABC test presented by the team from Brescia at a meeting of the EUFMD Research Group in Israel in September 1996, demonstrated the high specificity and sensitivity of the test which they had just developed (1). The test was validated in field conditions in Albania, Macedonia (see above) and later in the Caucasus. The test has just been approved by the Standards Commission of the Office International des Epizooties (OIE: World organisation for animal health) as a test to ascertain the absence of circulating virus within a population (9, 10).

Conclusions

Every time vaccination with a reliable vaccine (adapted to the causal strain) has been applied rapidly, the spread of FMD has been halted, whether or not the animals had previously been vaccinated. The examples provided above relate to countries where the policy of stamping-out and compliance with restrictions on movements of animals and their isolation are difficult to enforce. It is reasonable to believe that vaccination schemes of this type, if applied in Western Europe, would yield similar results, i.e., would halt the spread of the disease. The considerations that question the effectiveness of vaccination are not confirmed by the experience acquired in the field in recent years.

There has been no instance of vaccinated carriers of the virus being the cause of the introduction or recurrence of FMD. Furthermore, there are no cases where the disease has originated from carriers, except for one suspicion concerning a case of the SAT (South African Territories) type in Zimbabwe, i.e., very different circumstances from those prevailing in Europe.

Effective vaccines that are capable of inducing good immunity and protection within approximately one week are available world-wide.

Whether a virus is in circulation in a vaccinated population can be established using differential tests that distinguish vaccinated from infected herds.

In view of the above, no truly scientific or technical obstacle exists to prevent vaccinated animals from a herd or zone with negative NSP test results (i.e. non-infected) from being treated in the same way as non-vaccinated animals. However, urgent attention is required to enable the experts to agree on the levels of sensitivity and specificity of NSP tests available. Once these have been established the details of testing protocols can be determined.

Overall conclusions

Despite its magnitude, the epidemic in the UK should not undermine the FMD control policy conducted in Europe over the last ten years which is based on the absence of preventive vaccination and on the implementation of emergency plans in the event of introduction of the disease. A return to preventive vaccination would be justified in Europe only under certain specific conditions (in particular a marked deterioration in the world situation and more importantly a threatening situation in a neighbouring country or the threat of an agroterrorist act, etc.) and only for certain susceptible populations at very high risk.

Continuing with the policy of preventive vaccination for cattle after 1991 in continental Europe would neither have affected the outcome of the UK epidemic (inasmuch as the UK did not carry out vaccination), nor would it have prevented the introduction of the disease into France and the Netherlands through sheep.

The slaughter of infected or at-risk herds should be the primary means for controlling diseases such as FMD and swine fevers as long as they are detected at an early stage. This method has proved its efficiency in halting the spread of FMD in most of the situations that have occurred in Europe over the last ten years.

Vaccination will continue to be considered as a second line of defence when the disease cannot be controlled by slaughter alone. Resorting to vaccination should therefore be considered in Europe in the future as a major means for controlling the disease when slaughter alone proves to be insufficient. The time taken to detect the primary outbreak (i.e. the time between the introduction of the virus and the detection of disease), if known, is the deciding element in the choice of control method. The key elements that indicate that a slaughter policy alone is insufficient to halt the disease are, firstly, the number of outbreaks and the rapidity with which the disease spreads. Whatever the circumstances, the decision to use vaccination should be taken very rapidly (between a few days to a week after the detection of disease).

Methods for differentiating between vaccinated and infected animals should, in the near future, remove the obstacles to a more routine use of vaccines as a means for controlling the disease without penalising trade between countries that use it and demonstrate, by serology, that they have eliminated the infection.

There is no real proof in the field of the danger of vaccinated carriers and the use of differential serological tests would reduce this hypothetical risk further. In comparison, when the slaughter method is used, there is also a risk of overlooking animals that are affected sub-clinically and which could also become carriers. This was observed retrospectively in the UK after the 1967-1968 outbreak and in Greece after the 1995 outbreak. Overall, vaccination does not increase the risk of the carrier state.

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