An analysis of the critics expressed by EMA against 3 Danish scientific publications analyzing adverse drug reactions - reported by Danish girls/young women - appearing in relation to the HPV-vaccination

A public responsum – version 3.0

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Assessment report

Review under Article 20 of Regulation (EC) No 726/2004

Human papillomavirus (HPV) vaccines

Prepared by

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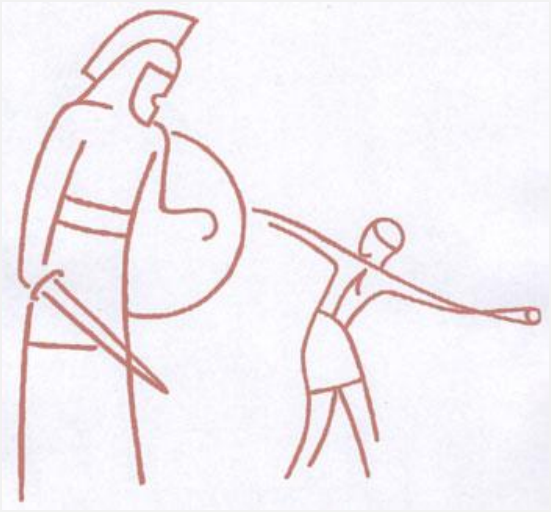
December 10th 2015



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Introduction

The interest in the issue originates from my participation in an advisory board recommending whether Denmark should choose the bi (Cervarix®) or the quadrivalente (Gardasil®) in the national vaccination program. This process opened the opportunity to acquire knowledge of the preclinical data as well as the experimental programs, which have been completed.

It appears – and is still not proven – that any of the vaccines can prevent the final transformation of the premalignant changes from evolving into a true cancer-disease.

At that time, there was safety data from a number of controlled studies, which showed that there were no serious side effects, such as POTS.

This is the basis and reasoning why I have closely followed the increasing amount of post-marketing information indicating that the HPV-vaccines may be associated with serious adverse reactions that has been widespread in the public media, the websites and press releases from the Danish Health and Medicines Authorities and the Danish Cancer Society.

Over the years, I have provided medical advice to a variety of media, organizations and associations, in this case, however, it is only to the Danish Cancer Society.

However, I have not updated my professional prerequisites to judge the knowledge-scientific strength in either the EMA-rapport nor the author's arguments and their scientific interpretations, hypotheses and views in the scientific field overall.

The analyses is therefore primarily focused on whether the criticism raised by EMA are based on factual substance, in comparison with the individual publications and the scientific strength in their arguments.

Many years of experience in design and implementation of scientific clinical trial protocols also constitutes the background for the analyses, whether the criticism is based on the science-theoretical paradigms that clinical research must respect. The competences are supplemented with review-tasks for a number of scientific journals, as well as scientific organizations.

I have no doubt that the vaccine works in the way, that it stops/inhibits the development of the premalignant changes and that this, together with the national screening programs may reduce morbidity and mortality in a vaccinated population. The additional effects of reducing the frequency of genital warts in women and men is also acknowledged.

However, patient safety must be prioritized very high, because this is a very large group of healthy people who are exposed to potentially serious side effects – with unknown prognosis – which may trump the benefits the vaccines.

This requires that there is a continuous focus on patient safety, and that this is reported, analyzed and interpreted. The data should originate from reports from the national HVP-centers based on national recommendations for clinical examinations and how to the register the complex symptoms.

These data may then be included in scientific clinical and experimental studies, both nationally and internationally.

My hope is that this analysis can stimulate a professional dialog among the experts in this research field. Feedback on this analysis is very welcome - hereby ensuring that factual errors can be corrected and additional aspects be added.

Copenhagen, December 10th, 2015,

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1 The Danish health service efforts in problem complex

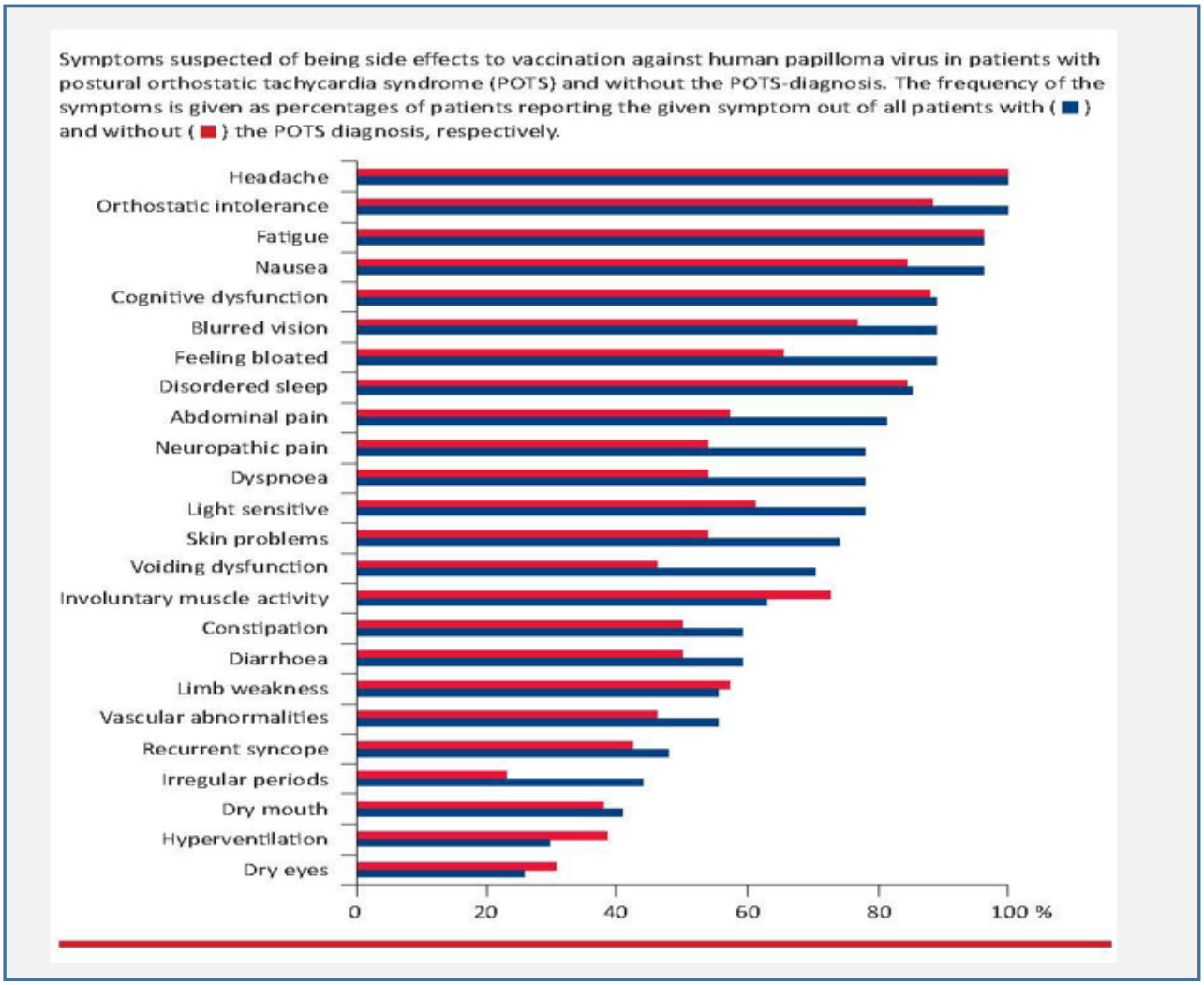
The syndrome- and symptom complex – as described in the three Danish publications - exists with an unknown frequency among women/girls no matter their HPV-vaccination status. An undocumented estimate is that the number of annual cases with POTS among girls and young women will constitute approximately 400 in the Danish background population [1].

The Healthcare system has unfortunately not yet established an effective and targeted action for the increasing number of patients who report that their symptoms occurred in relation to HPV-vaccination. A coordinated effort is expected to be activated early next year.

That it has been developed in the past is understandable, since it is a mix of five main syndromes, which can be mixed with symptoms from an additional 8 different categories [2].

The five main categories are: *' severe neurologic symptoms, circulatory symptoms, fatigue, pain and headache and the 8 additional categories: autonomic imbalance, abdominal discomfort, urinary tract symptoms, allergy, infections, menstrual disorder, thermal dysregulation and malaise. Details of definition of the categories and symptoms is provided in appendix 1 '* [2].

The figure below indicates the frequency of symptoms in 53 patients studied in the Syncope Center [3]. The blue and red bars indicate the frequency in those with and without the POTS diagnosis, respectively.



Many of these cases have not been recorded, since a diagnosis code system for the large number of syndromes and symptoms has not been established, either nationally or internationally. It has thus not been possible to identify the group of patients apart from those who have had a POTS like symptom picture – identified in various sectors of the health care system before the introduction of the HPV-vaccine.

The Syncope Center at Frederiksberg Municipal Hospital has been appointed a national center for patients with orthostatic imbalances and dysautonomy, since 2011. In 2013, they wondered about the fact that the number of referrals increased dramatically (see table below) and that the patients had other symptoms than is usual – i.e. they were younger and having more serious symptoms even though they were physically active. The immediate common denominator – mentioned by the patients was the HPV-vaccinations. Since June 2015, the Syncope Center was appointed an HPV-center.

2 The Danish Health and Medicines Agency´s request for an assessment of the safety profile of the HPV-vaccines

Since the introduction of the HPV-vaccination, there has continuously been a number of issues raised considering whether the vaccine could give rise to serious syndromes and symptom complexes.

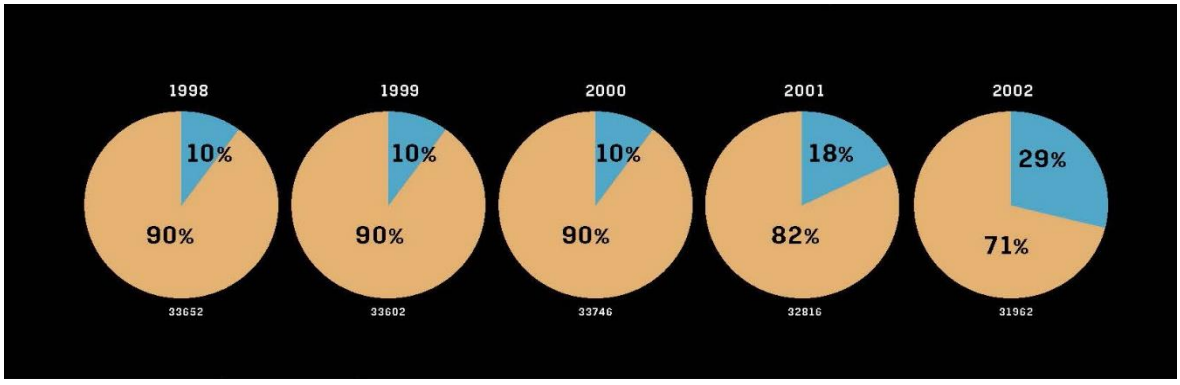
The Danish health authorities have been focused on these issues since 2013. This appears from the report (September 2015) [2] by the Danish Health and Medicines Agency to EMA as part of their request to assess the safety profile of the HPV vaccines.

The two tables below are included in the report by [2]. As apparent from the table below the number of adverse drug reactions increased dramatically in 2013, both in numbers and in seriousness. The Danish Health and Medicines Agency reported this observation to EMA and later initiated a clinical review of 363 reports with severe symptoms.

The results of this analysis did not indicate any correlation between the clinical content of the reports and HPV-vaccination, mainly due to uncertainty regarding the time when the symptoms started. It is recommended to initiate a project in which non-vaccinated is compared to those having received the HPV-vaccine.

Despite the lack of scientific evidence of any correlation between the observed symptoms and the HPV-vaccination, public concern has increased during recent years. The young girls/women and their parents have felt rejected and neglected by the health authorities and the system, medical experts, the drug companies etc. and, in principal, are regarded as having signs of functional diseases.

These frustrations have increasingly been shared on media- and social platforms and have been the main reason that the general participation in the HPV-vaccination program has decreased from 90 to 70 % - as appears from the table below covering year of birth from 1998-2002 [4].



It also appears also, in the table below, that the number of sold doses decreased significantly from 2013 to 2014 due to the closure of the ´catch up programs´ offered to women <28 years.

HPV vaccine	2009	2010	2011	2012	2013	2014	Q1 2015	Total
Number of reports	288	66	43	96	511	224	77*	1305
– of which serious	25	5	6	18	177	91	41	363
Number of doses sold	347,690	151,476	163,374	349,730	488,224	114,457	20,817	1,635,768

*The number of reports received in 2015 including both Q1-Q2 is 385

As shown in the table below, it is not only in Denmark that there is a high number of adverse drug reactions reported related to the HPV vaccines [2].

Country	Number of HPV Reports	Number of other vaccine reports	Log OR	Log OR 005	Log OR 095	% of total HPV reports	% of total other vaccine reports
Malaysia	5927	135	3.56	3.52	3.61	12.9%	0.2%
Italy	4622	1229	2.04	1.99	2.09	10.1%	1.8%
Japan	918	141	1.31	1.21	1.41	2.0%	0.2%
Denmark	549	210	0.74	0.62	0.86	1.2%	0.3%
Australia	2420	1930	0.72	0.65	0.78	5.3%	2.9%
New Zealand	449	1660	-0.83	-0.96	-0.71	1.0%	2.5%
France	620	2792	-1.17	-1.29	-1.06	1.4%	4.2%
Sweden	585	3236	-1.41	-1.52	-1.29	1.3%	4.8%
United Kingdom	1048	8096	-2.14	-2.24	-2.05	2.3%	12.1%
Canada	43	6034	-3.32	-3.49	-3.16	0.1%	9.0%

The report from the Danish Health and Medicines Agency [2] includes the following statements.

- In September 2013, the European authorities were informed about the growing number of adverse drug reactions (ADR)
- An increase in the number of cases of ´complex regional pain syndrome´ (CRPS) have been reported internationally - especially from Japan
- It is emphasized that the Danish publications, including 53 patients, demonstrated that 53% had POTS and 90% met the criteria for chronic fatigue syndrome

- Reference is made to a publication from 2015 concluding that it is difficult to diagnose the various syndromes after HPVvaccinations, as they have more overlapping clinical symptoms
- It is stated that the Danish authors highlight a theory that, besides POTS, the patients demonstrate a mix of symptoms that can be described as dysautonome, which may be due to an autoimmune response - triggered by the vaccination. The Danish Health and Medicines Agency supports this theory with additional references to publications, which deal with the subject, and indicate that there is a special focus on the aluminum-additive
- It is stated that a number of internal studies have not found any correlation between the HPV-vaccine and serious ADR – including a British study [5]. The study is discussed in the Danish publications and in the EMA report. The Danish Health and Medicines Agency here agree with the Danish authors that as it is a register based-study, the data are uncertain due to the fact that the syndromes are difficult to diagnose and have over-overlapping clinical manifestations. This will lead to a number of patients not being diagnosed
- In March 2015 a clinician appointed by the Danish Health and Medicines Agency reviewed a total of 363 reports of serious character, of which approximately half came from non-health-professionals
- The conclusion was that the symptoms could be divided into the categories listed in the table shown in paragraph 1. The review concluded that POTS was confirmed in 40 cases.
- The huge increase in reported adverse events in 2013, may be partially due to a strong public focus and concern for risks in relation to the vaccination
- The high average age given in the Danish publications is due to a number of vaccination follow-up programs, including women up to 28 years of age
- It is concluded that the reported symptoms, their severity and duration, is not in accordance with the information provided by the manufacturer of Gardasil® in their product information concerning side effects
- The number of POTS-cases in Denmark is high, and the symptom pattern is the same as those registered in a number of other countries
- In conclusion, it is recommended that there should still be a focus on the reported adverse events, and that research into the whole issue must continue.

As evidenced by the above, there is no criticism of the content of the Danish publications. There is especially an acceptance of the authors hypotheses concerning the autoimmune aspect, as well as that a number of patients both here and abroad remain underdiagnosed.

The report offers an explanation of the unexpected high average age of the patient group in one of the Danish publications [6].

It is also underlined that the symptom pattern in the Danish reports is comparable to what has also been registered in other countries.

It therefore seems surprising that the Danish Health and Medicines Agency joined EMA´s very heavy-handed and general criticism of the scientific quality of three Danish publications a few days after the release of the report.

EMA´s criticism [1] of three Danish HPV publications

3 Scientific bases

The suspicion that a possible link between the vaccine and a number of symptom complexes have been raised in a number of international publications [1,2] since 2010.

In 2013, the Syncope Center wondered about the fact that the number of referrals increased dramatically (see table page 4) and that the patients had other symptoms than was usual – i.e. they were younger, having more serious symptoms and were physically active. The immediate common denominator was the HPV vaccinations especially the third.

The Syncope Center concluded, based on these observations, that there was scientific ground to examine whether there might be a correlation between the symptom complexes and the vaccine.

The scientific investigation is based on the so-called H_0 hypothesis stating: that there is no correlation between symptom complexes and the vaccine.

The scientific studies are then primarily targeted with the aim to reject the hypothesis (i.e. to falsify the hypothesis) by demonstrating that there is a correlation (with a previously described statistical uncertainness that this conclusion is not true) – or confirm it, and thus reject that there is a correlation (with a statistical uncertainty to fail to find a real difference).

The Syncope Center hereby defined the criteria for patients to be included in the scientific studies, but was not taking such a relationship as existing in advance.

3a EMA´s assessment

EMA claims in their report that patients should fit into the Center´s assumption that there was a correlation between the symptoms and the vaccination.

3b comments

This allegation is populist, but unfortunately at the same time it indicates a lack of understanding of the theoretical basis on which the scientific human experimental projects shall be carried out.

4 Patient material

Patient material was – as is clearly stated in the publications - selected, and consists of patients referred from general practice, hospitals, relatives etc. A total of 75 – 90 patients were referred to the Syncope Center during the period 2011-2015 for the purposes of assessing their orthostatic intolerance and dysfunctions of the autonomic nervous system.

Patients were evaluated consecutively – i.e. successively as they were referred – and those who presented a relationship to HPV vaccination, were included in the projects for further investigation, which is completely in accordance with the project's scientific hypothesis.

4a EMA´s assessment

EMA notes that patient materials in the three studies are not representative of the population.

4b comments

It was not the aim of the projects to investigate the general frequency of the investigated syndromes and symptom complexes. It is stated several places in the publications that a number of similar conditions are described in the literature, which are probably triggered by other provocateurs than HPV vaccine.

The frequency of the entire syndrome complex in the background population is unknown, but EMA estimates POTS to occur yearly in 150/million [1].

4c EMA´s assessment

In the publication in which the symptomatology is described [3] (see page 3) EMA criticizes that the elimination of some patients excludes the possibility to detect when symptoms start, regardless of the time interval between the vaccination and the onset of symptoms.

4d comments

The conditions to participate in the scientific clinical protocols is defined by the inclusion and exclusion criteria. These serve to define the patient material, which is the most optimal in order to examine the scientific hypothesis.

The patient material included in the publication, in which the symptomatology is described [3], is limited by a number of exclusion criteria, which should reduce the possibility that a different event to the HPV-vaccine is a possible trigger for the symptom picture.

Patients were excluded if they were unable to accurately indicate when the symptoms occurred for the first time after the vaccination, as well as those for whom the symptoms appeared more than 2 months after vaccination. This reduces the experimental material from 75 to 53 patients.

EMA´s criticism is therefore unjustified.

4e EMA´s assessment

EMA states that the criteria is not specific on how the 35 patients are selected and included in the publication concerning the evaluation of the suspicion that orthostatic intolerance and postural tachycardia syndrome (POTS) is a side effect of HPV vaccination [7].

4f comments

This assertion is not correct, since, at the outset, the patient material at the outset in the publication is described as: *' We included 35 patients consecutively referred two our syncopeunit for head-up tilt test under the diagnosis of orthostatic intolerance as a suspected adverse event following vaccination with the quadrivalent HPV vaccine (Gardasil ®). Informed consent was obtained from all patients '.*

5 Methods/Clinical Observations/Results/Discussion

The clinical records registered by the Syncope Center in the report by the Danish Health and Medicines Agency report to the EMA (sept. 2015) [2] are mentioned as being of high quality because they have been produced by specialists.

The diagnosis of POTS is an objective and reproducible objective diagnosis, as examined according to international guidelines. The non-quantitative clinical observations (i.e. pain, fatigue etc.) have been assessed in accordance with international practices and models.

The participating patients have undergone an extensive investigational program including comprehensive studies of the nervous system, immune and reumatoroid blood tests etc.

5a EMA's assessment

One of the publications [7] investigates whether the chronic fatigue syndrome (CSF) and a brain syndrome (ME) can be a side effect to the HPV-vaccine.

EMA raises the question whether the results of the symptom panel that the patients must make a decision on, would be the same as if it had not been presented to them. They also believe that other symptoms will hereby be excluded.

EMA also calls for an objective assessment of a variety of patient experienced symptoms.

5b comments

The criticism of the method for collecting answers underestimate both the professional standard of the interviewer, as well as the patients' ability to independently deal with the issues raised, and to supplement with symptoms, which are not covered by the symptom list.

The Danish Health and Medicines Agency found in its review of 363 reports, the same symptom-pattern as described in the publications.

It is frivolous of EMA to call for objective measurement of symptoms such as fatigue, pain, etc., that will always be based on subjective assessments – compiled systematically by apply internationally validated questionnaires.

The authors discuss the limitations of the investigation and encourage, among other things, the development of international guidelines for how the syndrome and symptom complexes, which may be related to HPV-vaccines or other causative factors, are handled scientifically.

5c EMA´s assessment

EMA wonders why the average is 1.9 years passing from the onset of symptoms until the clinical examination is performed at the Syncope Center [6]. In addition, why is there only about 10 days from the time of vaccination until the onset of symptoms?

Their argument is that, orthostatic tolerance and other symptoms especially, often appear creep. It is therefore striking that patients can specify the onset so accurately up to 2 years after vaccination.

The methods thus gives rise to doubt of the reliability and objective quality of the answers.

5d comments

The average of 1.9 years is explained by the fact that the Syncope Center has been the only national clinic to which patients with orthostatic intolerance could be referred to, since 2010 There was no requirement of the vaccination status for the referrals. This aspect is included in the discussion section of the publication [6].

The onset of symptoms after 10 days should be seen in relation to whether it was after the first (about 25%), the second (about 50%) or after the third vaccination (25%).

The explanation that the patient´s remember correctly is that the symptoms were serious, implying that the daily life of 34 of 35 patients was heavily affected, as indicated by 21 patients who had to disrupt work and school due to sickness.

Furthermore, the majority of patients were physically very active before the onset of symptoms, meaning that these above-mentioned factors may attribute to a precise recall of the onset of the symptoms.

5e EMA´s assessment

EMA wonders why the average age is higher than expected [6] – i.e. 21 years against the expected close to 12 years – which speaks against a coupling to the HPV-vaccine.

5f comments

The authors note this age shift in the conclusion section of the publication, but do not explain it further. Around 40% were in the age group 12-19 years.

However in the report of the Danish Health and Medicines Agency, an explanation for the relatively high average age (see page 5) is offered with reference to the 'catch-up' programs for women up to 28 years.

5g EMA´s assessment

EMA argues why they disagree with the authors' hypothesis that the syndrome- and symptom complexes may be due to an autoimmune response [1].

Furthermore, it is stated in the report that the authors do not notice that the presence of POTS is generally related to individuals with a high level of physical activity level. The study shows that 2/3 of the patients had a high level of physical activity and therefore not should be linked to the HPV-vaccine as a special risk parameter.

5h comments

The authors supply their hypothesis with four references supporting the hypothesis that a reaction against the HPV-vaccine can be immune/autoimmune triggered [6].

In the discussion section, the authors mention another seven references, which support the hypothesis that high physical activity can affect the patients' immune response to the vaccination.

This is an indirect answer to the statement by EMA, that the presence of POTS is generally related to individuals with a high level of physical activity.

In their report, the Danish Health and Medicines Agency support the hypothesis offered by the Danish authors regarding the immune/autoimmune link (see page 5).

Therefore it is a scientific discussion, which should have been a dialogue between the opponent and the authors. However, arguments on each side should be included in further research.

5i EMA´s assessment

One of the three Danish studies [7] investigates whether the chronic fatigue syndrome (CSF) and a brain syndrome (ME) can be correlated to the HPV-vaccine.

EMA notes that the results should call for the reflection of whether the examined patients in the 3 publications constitute a representative sample of the ground population with the described syndrome and symptom complexes, triggered randomly in relation to an HPV-vaccination.

EMA state that their argument is supported by a British study, which could not demonstrate any connection between the prevalence of the chronic fatigue syndrome and HPV-vaccination [5].

5j comments

That fact that EMA now indicates that the examined patient material simply represents a sample of the background population who have syndrome and symptom complexes independent of their vaccination-status, which is contrary to the EMA´s primary objection to the patient material saying that it is not a representative sample of the population (Section 4a, page 7).

The authors refer to the British study [5] but raise doubts about how the exact fatigue diagnosis is made. This relationship is also an element in the discussion section, where it is stated that a number of differential diagnosis should have been resolved in their own investigation before the final diagnosis of the chronic fatigue syndrome is confirmed.

The Danish Health and Medicines Agency agree with the Danish authors on the fact that the whole symptom pattern is so diffuse that a number of patients are likely not to be diagnosed. This will dilute the data by which the register studies are based - including the British investigation.

It is also mentioned in the report from the Danish Health and Medicines Agency that the symptom pattern as identified in the Danish publications have also been reported from a number of other countries (page 6).

6 Overall assessment of the EAM criticism and the scientific quality of the three Danish publications

6.1 EMA´s report [1] and the criticism of the Danish HPV-publications

The report is very thorough and has drawn on many sources and experts. It is outside the aim of this analysis to evaluate the content outside the specific comments to the Danish publications.

It is quite reasonable that EMA reviews the three Danish publications critically, since the overall results have not been reported from other research groups. However, there are no similar studies, which the Danish projects can be directly compared with.

EMA raises a number of scientific points of view, which are relevant, and should be included in further research.

The EMA report's criticism of the Danish publications are, on almost all points, rejected in the above review and analysis.

However, with this extensive report, EMA is at the forefront of a new, updated version, since it hardly lasts long before other national health authorities put forward the request for a review of a possible association between HVP-vaccinations, and a synchronous emergence of the same syndrome- and symptom complex as described in the Danish publications.

EMA´s concluding remarks about the Danish publications include expressions and phrases such as:

Inherently biased ♦Pre-specified hypothesis♦Do not acknowledge or discuss Do not reflect upon the available medical literature ♦ The reliability and objectivity Dismiss an existing study ♦etc.

Such comments would provoke both editors and reviewers to request significant changes or otherwise completely reject the manuscript – provided that it was justified to describe the scientific quality with these terms.

It appears from the examiner's comments that the vast majority of EMA´s criticisms are dismissed with reasons such as:

Contrary to the EMA´s primary objection ♦ A scientific discussion, which should have been a dialogue ♦ Underestimates both the professional standard of the interviewer, as well as patients' ability to independently relate to the raised questions ♦ It is frivolous by EMA to call for objective measurement of symptoms such as fatigue, pain ♦ This assertion is not correct ♦ EMA´s criticism is therefore unjustified ♦ The allegation is populist ♦ Lack of understanding of the scientific-theoretical basis ♦ Supported by the Danish Medicines and Health Agency

6.2 The scientific quality of the Danish publications

It is the examiner's overall assessment that the three studies are of a scientific quality, which is clearly above the common recognized standard.

They follow the scientific disciplines that are required to implement reliable and conclusive scientific experimental projects.

The hypotheses are relevant and the choice of method satisfies that the hypothesis is tested based on optimal patient material. As noted by one of the sources consulted by the Danish Health and Medicines Agency [2] the Danish clinical information is of high quality.

The associated para-clinical examination programs are extensive but focused, and contribute with valuable information about what other trigger mechanisms might be involved. This is an attempt to identify specific risk groups, which must be taken into account, having specific safety precautions.

The authors stress, in all three publications, that there is no evidence of a link between the investigated syndrome and disease complexes and the HPV-vaccine. The discussion is focused whether the aluminum-adjuvant – which has not previously been used in this form – could be the cause of immune/autoimmune reactions to the vaccine.

The authors formulate new hypotheses, which will be included in the further research work – e.g. the study of tissue and blood samples, and call for the implementation of a case-control study.

They also call for international recommendations regarding methods, registrations and international cooperation of how to establish common, systematic, clinical and scientific approaches to the issue.

The authors´ hopes that such a focus on knowledge-based information from patients, and a continued analysis of this in scientific projects, will contribute to regaining public confidence in the vaccine.

7 Public criticism

The terms used by EMA and the investigator as outlined in section 6.1 (page 10) raises the question whether EMA or the Danish authors were the right/most right/wrong etc.

This was decided shortly after the release of the EMA report. A number of central authorities: the Danish Health and Medicines Agency, Danish Cancer Society, newspapers etc. joined EMA´s criticism [8, 9], who were later supplied with remarks from the senior author and others [10-12].

It´s impressive that some could conduct a thorough analysis so quickly, but they may just have joined the convenient – but tendentious – and dismissive treatment of the Danish results in EMA´s report in order to close the case and to calm down the population.

These controversies will unfortunately continue, but will hopefully be complemented with a discussion in the academic environments, when there has been time for analysis and reflection.

This discussion should include a long-lasting worry whether the HPV-vaccination could accelerate late premalignant cells into real cancer.

7.1 Impact of the criticism

My estimate is that the criticism by EMA, paradoxically, may raise the concerns among those who shall or have been vaccinated – especially their parents.

This is reinforced by the fact that there is generally no real confidence, especially to foreign authorities, and the attention will be sharpened in the newly created 'National Association of HPV Adverse Reaction´, as well as in the organization 'HPV Update'.

It is worrying that the affected girls/young women – especially those who have participated in the scientific investigations, may understand the criticism as a rejection of their illness, as well as an expression of not being taken seriously. These frustrations will be reflected on the social platforms, which is their primary communication forum – and which is often communicated to the press.

If, over time, it turns out that the suspicion of severe adverse reactions to the vaccines is confirmed in one degree or another, it may perhaps be the biggest scandal in the history of medicine.

7.2 Rehabilitation of the scientific reputation

I recommend that the scientific environment also evaluate this criticism of the Danish clinical research, and hopefully help the authors and the others closely concerned to be rehabilitated.

The Danish authors have in a public spectacle-process been scientifically compromised. The critics in the EMA-report will also affect their institution, the reputation of Danish research for being of high international standard, the participating patients, as well as the publishing journals, editors and reviewers.

This may also have an impact on, in particular, the youngest of the authors' careers, and can shape attitudes towards the approximately 780 patients who are awaiting assessment at the regional HPV-centers.

Moreover, it will be difficult for the critical research that is challenging conventions, authorities and pharmaceutical companies, etc. to get support for their research.

The authors have rushed to express two ´damage control´ opinions containing elements from the comments made here and ask the question what errand EAM follows [10-13].

8 The future role of the Syncope Center and the regional HPV-centers

Such a national rehabilitation is crucial for the Syncope Center in order to preserve and maintain the amassed expertise, competence of people and research environment. This scientific backing is to be followed by a statement from the hospital trust owners, as well as from the sources that can support a continuation of the research program. Funding for the continued research expires very soon.

It is recommended that Syncope Center will be the coordinating Centre for the regional HPV-centers, and all efforts are made to ensure that the work in the HPV-centers is based on national

guidelines for testing programs, central registration of data as well as a coordination of the research tasks – nationally and internationally.

The Danish Cancer Society has recently indicated that it wants to support qualified research projects within this research field, as well as to provide support for the registration of the collected data.

Unfortunately, it has, due to economic factors, been decided to replace Gardasil® with Cervarix® in the national program starting January 2016. This will complicate the collection of research data related to the Gardasil vaccine.

The decision has been made despite the fact that Japan closed their program containing Cervarix due to a high number of severe pain syndromes reported from a population of 500.000 vaccinated.

9 References

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