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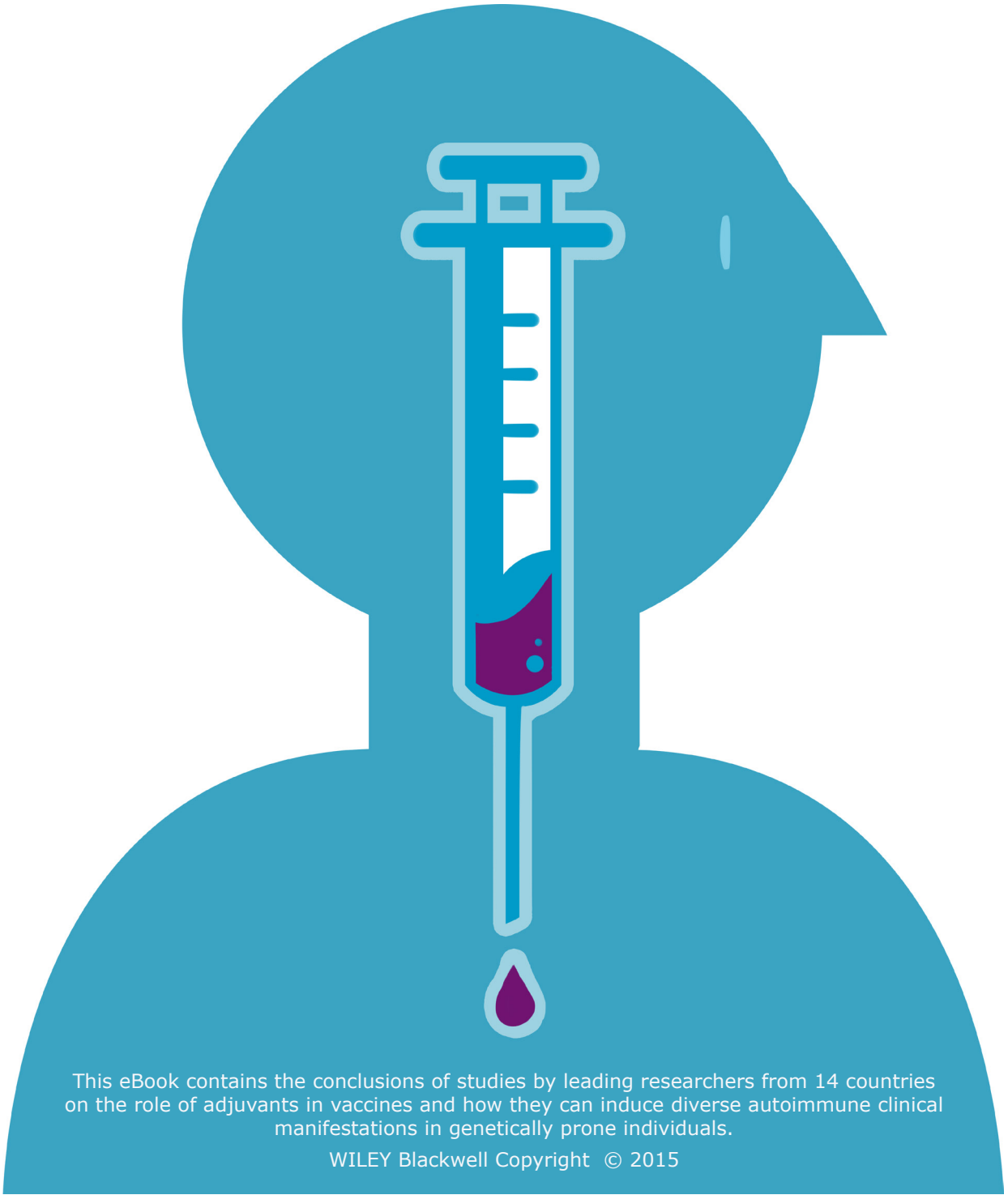
Summary of Studies Featured in

VACCINES & AUTOIMMUNITY

Edited by Yehuda Shoenfeld, Nancy Agmon-Levin and Lucija Tomljenovic



This eBook contains the conclusions of studies by leading researchers from 14 countries on the role of adjuvants in vaccines and how they can induce diverse autoimmune clinical manifestations in genetically prone individuals.

PART 3 Autoimmune Diseases Solicited by Vaccination

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Vaccines, Infections, and Alopecia Areata

CHAPTER 26

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Conclusions

Although AA is not life-threatening disease, patients may experience devastating effects on the quality of life and self-esteem. A possible association between vaccination and AA has been suggested by a few case reports concerning different vaccines; the largest case series reports such a link with HBV vaccine (Wise et al., 1997). Further research on the various environmental and genetic factors which may lead to the development of AA and, especially, on the link between AA and permutation is warranted.

Aluminum Particle Biopersistence, Systemic Transport, and Long-term Safety; Macrophagic Myofasciitis and Beyond

CHAPTER 27

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Introduction

Over the last century, billions of humans have been vaccinated, and marked regression or eradication of several severe infectious diseases has been observed. Today, the potential applications of vaccines extend far beyond prevention of infectious diseases, and vaccination is considered to be the most promising weapon against a variety of different conditions. In general, vaccine safety has been regarded as excellent at the level of the population (Moxon and Sigriest, 2011), but adverse effects have also been reported (Agmon-Levin et al., 2009). Given the considerable worldwide development of vaccination, safety signals in the field require the attention of the medical and scientific community, even of their intensity seems a priori to be low.

Concerns linked to the rise of aluminum adjuvants (known as alum) have emerged following the recognition of

their role at the origin of the so-called macrophagic myofasciitis (MMF) in 20001 (Gherardi et al., 1998, 2001). MMF reveals a fundamental misconception of their adjuvant effect and points out their unexpectedly long biopersistent (Gherardi et al., 2001). Recent demonstrations of their apparent capacity to migrate in lymphoid organs and to progressively accumulate in the brain (Khan et al., 2013) suggest that alum adjuvant safety should be assessed in the long term, that administration of escalation does of this compound to the population should be avoided, and that individual susceptibility factors to the development of alum adjuvant intolerance should be investigated.

Aluminum Particle Biopersistence, Systemic Transport, and Long-term Safety; Macrophagic Myofasciitis and Beyond

CHAPTER 28

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Conclusions

Vaccinations have proved to be great advantage to the general population in preventing the spread of infectious diseases. Vaccine safety has improved improved in recent years, and the incidence of vaccine-induced autoimmunity is rare, but they are not yet free of risk. It is becoming apparent that is not only the active components that could drive autoantibody production, but also the excipients, such as adjuvant (pristine, aluminum, squalene), or even the residual traces of yeast from the manufacturing process (Rinaldi et al., 2013). The course of ITP can be very serious, even leading to fatal intracranial hemorrhages, although usually the platelet count improves spontaneously or normalizes after therapy. Unfortunately, in some patients, especially in adulthood and adolescent, ITP can be chronic disease that must be continually monitored and treated.

Infections are much more likely to trigger ITP than are preventative vaccines. However, it should be borne in mind that preventative vaccines are usually administered to otherwise healthy subjects who are not yet fighting the infectious disease for which they are considered at risk. Thus, we must be careful not to cause harm to healthy individuals. Furthermore, it is critical to recognize that the induction of autoantibodies by any infectious or a vaccine-component trigger, and therefore the onset of autoimmune disease (including ITP) can occur in a period of days or years. While the short latency of post-streptococcal-induced rheumatic fever is a few weeks (Arbuckle et al., 2003). The temporal relation between vaccinations on immunity depends on the particular vaccine used and its associated phenomena. Finally, following from the displaced efficacy of eradication therapy in H. pylori associated ITP, therapy should always be consistent with the principle of removing the pathogenic

Vaccinations and Type 1 Diabetes

CHAPTER 29

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Conclusions

The results of many studies do not support an association between vaccination and T1D in either young adults or children. However, available data are incomplete and difficult to interpret, partly because several factors are thought to be involved in the development of T1D. Well-designed and long-term studies into the use of vaccines and an incidence of childhood diabetes are ongoing.

Narcolepsy and H1N1 Vaccine

CHAPTER 30

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Conclusions

All the evidence mentioned in this chapter suggests an important role for an immune-mediated process induced environmental factors, especially the ASO3-adjuvanted Pandemrix vaccine, in the development of narcolepsy in genetically susceptible populations. However, the precise mechanism by which the ASO 3-adjuvanted Pandemrix vaccine or the H1N1 infections itself might induce the onset of the disease is still not clear. There has been much speculation regarding this issue. Singh et al., (2013) have proposed a model, which explains how H1N1 infection or vaccine can induce the loss of orexin neurons, via an interaction between infections and genetic factors (Figure 30.2). Different mechanisms may be involved in this process, including bystander activation of autoreactive B and T cells in response to the vaccine's adjuvants. Moreover, the HLA association may suggest that antigen presentation of cross-reactive peptides can lead to the activation of the immune response against the orexin neurons. Another explanation is molecular mimicry between orexin neuron molecules and the vaccine, the H1N 1 virus, or other infectious agents (e.g. Streptococcus sp.) found to be associated with the development of the disease (Kornum et al., 2011; Singh et al., 2013; Mahlios et al., 2013). Regarding the role of the vaccine, two interesting options have been proposed. First, the AS03 adjuvant may catalyze the molecular mimicry between orexin and neurons and H1N1 molecules, due both to its nature and to its method of immune system activation (Mahlios et al., 2013) Second, the presentation of normal post-vaccinated events, such as fever, may favor the migration of pre-existing auto reactive cells or antibodies through the BBB, leading to loss of orexin neurons (Kornum et al., 2011).

Finally, all the data together support the relationship between the H1N1 vaccine in the development of narcolepsy under certain conditions. Therefore, these observations should raise awareness regarding the risks and benefits of H1N1 vaccination versus non-vaccination (Caplan, 2010). Perhaps in the future the genetic and environmental background of a given individual should be taken into account before making a decision to vaccinate

Non-nutritional Environmental Factors Associated with Celiac Disease: Infections and Vaccinations

CHAPTER 31

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Conclusions

CD is an autoimmune disease induced by well-known nutritional environmental factors (nondietary factors are less studied and less well established). Several pathogens are associated with CD, but in none of them have cost-effect associations but been established. Evidence is accumulating for possible role of rotavirus in CD pathogenesis. The rotavirus VP7 shares homology with a celiac peptide and with the autoantigen tTg. Anti-VP7 antibodies are predictive for CDN modulate genes involved in pathophysiology. In view of the role of rotavirus in type 1 diabetes induction, the increased incidence of type 1 diabetes in CD patients, and the relationship between rotavirus, gliadin, and CD, the enigma of the rotavirus vaccine as an inducer of CD is awaiting further exploration. In fact, in a very recent publication, Parez et al. (2014) indicate potential safety concerns around rotavirus vaccination in Europe.

Polymyalgia Rheumatica

CHAPTER 32

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Conclusions

Post-vaccinal PMR remains a very rare entity and further efforts are needed to better identify individuals at risk of developing this particular type of disorder.
An accurate clinical history, including vaccine history, is mandatory for all elderly patients fulfilling the diagnostic criteria for PMR, as the rate of many post-vaccine autoimmune and rheumatic disorders - including PMR- may be biased by underreporting. A careful risk-benefit assessment must be performed for patients already diagnosed with PMR who are in clinical remission at the time of clinical evaluation for further immunization.

Undoubtedly, further insight into the pathogenesis of post-vaccination phenomena and the identification of markers of genetic predisposition could be useful in preventing these conditions and in developing personalized and safer vaccines in the future.

Acute Disseminated Encephalomyelitis: Idiopathic, Post-infectious, and Post-Vaccination

CHAPTER 33

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Conclusions

ADEM is an acute demyelinating disease of the CNS that usually affects the very young. Although well defined clinically, its pathogenesis remains not fully understood. Its resemblance to other —chronic — demyelinating diseases, and especially MS, raises the possibility of common immunopathogenetic paths. Some might claim that ADEM is to MS what AIDP is to CIDP. In support of this are reports of the "transformation" of ADEM into MS and our increasing knowledge of recurrent or relapsing types of ADEM. Others insist that ADEM is a completely different nosological entity, in terms of pathogenesis, course, and prognosis, and that cases of the "transformation" of ADEM to MS were really just MS from the beginning. There are indeed several clinical and paraclinical parameters that clearly differentiate between the two diseases. ADEM is almost always a post-infectious disease, and molecular mimicry and antibody-mediated autoimmune mechanisms seem to play a crucial role in its pathogenesis. Of special interest is post-vaccination ADEM, which accounts for 5—10% of all ADEM cases. The widespread use of vaccinations in recent years (including new types of influenza vaccines and vaccines against HPV for the prevention of gynecological malignancies) has caused an increase in reported cases of ADEM, often with unique (NMO spectrum-like) manifestations. The central role of adjuvants in post-vaccination ADEM (and related conditions) has lately been highlighted. Treatments with steroids or antibody-targeting modalities usually have a favorable effect, and the prognosis is generally good. However, severe, hyperacute, and even lethal forms of ADEM do exist.

Fibromyalgia, Chronic Fatigue, Functional Disorders, and Vaccionation: Where do We Stand?

CHAPTER 34

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Conclusions

Within the complex etiological scheme evolving for FMS, a variety of environmental exposures have been recognized as or suspected of being potential triggers, presumably capable of instigating central sensitization of the genetically prone individual. Within this context, a variety of vaccinations have been documented as being associated with a range of symptoms at least partially overlapping with FMS, such as widespread musculoskeletal pain and fatigue. GWS poses a unique circumstance in which a multisymptom functional disorder developed among many thousands of healthy young individuals, following exposure to a constellation of environmental and stressful circumstances, including the administration of multiple simultaneous vaccinations within a short period. The current evolution of the ASIA syndrome, as well as intriguing indications regarding a role for previously unrecognized CNS inflammation (e.g. microglia activation) in the pathogenesis of central sensitization and chronic pain, indicates that we may currently be standing on the brink of a new era of understanding of the enigma of chronic pain.

Bullous Dermatoses, Infectious Agents, and Vaccines

CHAPTER 35

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Conclusions

The possible association between vaccines and bullous diseases such as BP and PV is still a matter of debate and is supported only by case reports. Importantly, this plausible association has been related to different vaccines most notably anti-influenza vaccine, dTP, polio, and hepatitis. Further research including long-term follow-up studies, on the various environmental factors that may lead to the development of autoimmune bullous dermatoses and especially in the association between immunization and the development of these diseases warranted

Infectious, Vaccinations, and Chronic Fatigue Syndrome

CHAPTER 36

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Conclusions

Except for several case reports, there are no studies that indicate vaccines might have a deleterious effect in patients with Chronic Fatigue Syndrome (CFS). However, it is possible that various vaccines or exposures to various pathogens might take part in the induction of CFS.

Myositis and Vaccines

CHAPTER 37

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Conclusions

Several authors (Orbach and Tanay, 2009; Stuebgen, 2014) have reviewed the association between vaccine administration the development of inflammatory myopathy, but there are few well-designed studies that have directly addressed this issue. Studies performed to date lack power in some cases and have been unable to find a conclusive association between vaccination and IIM. it is not possible to exclude a relationship between vaccination IIM, however, and vaccines probably do cause IIM in genetically predisposed individuals.