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Herpes Zoster

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H.W. Doerr Frankfurt a.M.

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Herpes Zoster

Recent Aspects of Diagnosis and Control

Volume Editors

Gerd Gross Rostock

Hans-Wilhelm Doerr Frankfurt a.M.

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Contents

VII Preface

Virology and Laboratory Investigations

1 Molecular Biology of Varicella–Zoster Virus

Rahaus, M.; Desloges, N.; Wolff, M.H. (Witten)

9 Latency and Reactivation of VZV

Lungu, O.; Gershon, A.A. (New York, N.Y.)

13 Laboratory Confirmation of Herpes Zoster

Ludwig, B.; Buxbaum, S.; Doerr, H.W. (Frankfurt am Main)

Spectrum of Clinical Manifestations and Outcome

20 Clinical Picture and Complications of Herpes Zoster: The View of the Dermatologist

Gross, G. (Rostock)

37 Ophthalmic Manifestations of Herpes Zoster Infection

Guembel, H. (Ulm)

47 (Herpes) Zoster Oticus

Pau, H.W. (Rostock)

58 Neuroanatomy of Pain and Neuropathology of Herpes Zoster and Postherpetic Neuralgia

Wree, A.; Schmitt, O. (Rostock); Usunoff, K.G. (Rostock/Sofia)

69 Postherpetic Neuralgia and Other Neurologic Complications

Baron, R. (Kiel)

81 Varicella–Zoster Virus Infections during Pregnancy

Sauerbrei, A.; Wutzler, P. (Jena)

93 Herpes Zoster in the Immunocompromised Host

Schöfer, H. (Frankfurt)

107 Chickenpox and Zoster in Marrow Transplant Recipients

Genvresse, I.; Maschmeyer, G. (Potsdam)

Therapy

117 General Aspects of Therapy

Gross, G. (Rostock)

123 Antiviral Therapy of Shingles in Dermatology

Lilie, H.M.; Wassilew, S.W. (Krefeld)

131 Highly Potent and Selective Inhibition of Varicella–Zoster Virus Replication by Bicyclic Furo[2,3-d] pyrimidine Nucleoside Analogues (BCNAs)

De Clercq, E. (Leuven)

143 Therapy of Zoster Pain, Postherpetic Neuralgia and Other Neurological Complications

Baron, R. (Kiel)

Epidemiology and Control of Herpes Zoster

154 Epidemiology of Herpes Zoster: What has Changed?

Allwinn, R.; Buxbaum, S.; Doerr, H.W. (Frankfurt am Main)

164 Live Attenuated Varicella Vaccine

Gershon, A.A. (New York, N.Y.)

170 Appendix

189 Subject Index

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Preface

Herpes zoster is a serious neurocutaneous disease which has been underestimated in terms of its burden, particularly in the elderly population. The overall incidence of herpes zoster in Europe is about 3 per 1,000 people and more than 10 per 1,000 people per year aged more than 80 years. Due to the growing life expectancy of the Central European population, the incidence of herpes zoster and its burden is very likely to increase further in the near future.

The onset of herpes zoster is almost always associated with waning varicella-zoster virus (VZV) specific cellular immunity. Herpes zoster is characterised by a more or less painful vesicular rash usually restricted to a defined area of the skin (dermatoma), which is innervated by the branches of a single sensory or a cranial nerve. The most common debilitating complication of herpes zoster is postherpetic neuralgia, which is especially seen in patients beyond 50 years of age.

The large majority of zoster cases are seen in elderly people. Nevertheless, a significant and increasing number is also diagnosed in young adults, in children and even in infants. As a rule of thumb, the risk to fall ill with zoster can be estimated as one-fourth of the age life span in years. In very early records, an association was recognized between herpes zoster and varicella, which is an ubiquitous and easily transmissible disease. After varicella has been clinically distinguished from smallpox, Steiner [1] postulated an identical infectious agent causing both herpes zoster and varicella. Kundratitz [2] described an identical histology of vesicles in varicella and zoster. Smears of affected cells show intranuclear inclusions in contrast to smears of smallpox vesicles presenting cytoplasmatic inclusions. Ruska, who had invented electron microscopy, first described the ultrastructurally indistinguishable morphology of herpes zoster virus and varicella virus [3]. In the same year (1943), herpes zoster was supposed by Garland [4] to be due to the

reactivated varicella virus infection. It took 10 more years, until Weller and Stoddard [5] succeeded in developing suitable cell cultures for the isolation of the herpes zoster agent. They and others detected indistinguishable cytopathological effects caused by this and by varicella virus. This finally leads to the description of VZV as identical virus causing both varicella and herpes zoster. For a long time herpes simplex and herpes zoster were considered to be different manifestations of basically the same recurrent infection. The term herpes describes microefflorescences on the cornea both of herpes simplex and herpes zoster patients (herpes reflects the Greek word *herpein* = to creep). The development of methods to propagate VZV in cell cultures helped to establish diagnostic serology and to determine the VZV-specific humoral immune status. These investigations revealed that preexisting VZV-serum antibodies protect against varicella, but not against herpes zoster. On the contrary, people without antibodies do not develop herpes zoster. With other words: Herpes zoster virus could only be isolated from people with a history of varicella confirmed by the detection of serum antibodies. Serologic assays also revealed the difference between VZV and HSV. Using molecular biological techniques (DNA—DNA hybridization) VZV was grouped into the same subfamily of alpha-herpesvirinae as HSV. Restriction endonuclease analysis of genomic DNA extracted from VZV strains isolated from patients, who first had varicella and later on herpes zoster, definitely proved the identity of the virus and its reactivation in the same patient [6].

Occurrence and course of herpes zoster and herpes simplex are strikingly different: While in predisposed individuals herpes simplex is frequently recurrent throughout life, herpes zoster is usually a unique disease of the elderly and of immunocompromised individuals of any age. Much more than herpes simplex, the eruption of herpes zoster is rather strictly correlated to a waning antiviral cell-mediated immunity. Thus, the diagnosis of zoster in a patient younger than 50 years demands to check for an immunocompromising disease such as leukaemia, Morbus Hodgkin, HIV-infection, AIDS etc. Herpes zoster in infants is a rather rare finding. Commonly it results from a prenatally or perinatally acquired VZV infection, when the cell-mediated immune system of the newborn is still immature.

Despite the advent of antiviral therapy, herpes zoster remains a challenge for both physicians and scientists. In particular in older people, the rate of severe herpes zoster complications is increasing, e.g. meningitis, less frequently encephalitis and optic nerve damage. Zoster may be associated with chronic pain, so called postherpetic neuralgia, which is especially harmful in the head region innervated by the trigeminus nerve. The ganglion Gasserii is a predilection site of VZV latency and similarly also of HSV latency. Nucleic acids of both herpes viruses have been detected simultaneously at this site. However, in contrast to HSV, VZV may be present also at all spinal ganglia after primary VZV-infection (chickenpox).

To fight the complications, it is mandatory to establish rapid clinical and, if necessary, laboratory diagnosis and to begin antiviral therapy in time. Correct diagnosis and indication of therapy challenge dermatologists, neurologists, ophthalmologists and otologists. This led to controversial discussions in the past. Thus, medical and scientific societies in many countries have established specific guidelines [7, 8].

Actually scientific interest focuses on VZV persistence. Similar to other herpesviruses two different forms of persistence seem to exist: (a) Proviral latency, which means genomic persistence without virus production and (b) low level VZV production. In this context immune escape has to be elucidated. It is obvious, that investigations, which study how VZV genome transcription is switched on and off, have great pharmaceutical relevance. This is particularly true with regard to the development of vaccines and new antiviral therapies.

Based on the preparation of clinical and laboratory medical guidelines for the management of zoster patients, the editors of this book intended to bring together leading specialists of clinical and scientific disciplines in order to compile the various insights and experiences concerning herpes zoster and VZV. It seems to be very useful at this time to present the state of the art and to describe the direction of further research activities, which will be focused on very early prevention of chronic zoster pain by a combined antiviral and analgetic therapy and on prevention of herpes zoster by use of a VZV-specific zoster vaccine.

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