Acarina 8 (2): 133–135

THE BASIC CONCEPTS OF ANTAGONISTIC AND SYNERGISTIC INTERACTIONS IN MULTI-COMPONENT HOST-PARASITE SYSTEMS

ОСНОВНЫЕ ЗАКОНОМЕРНОСТИ ВЗАИМОДЕЙСТВИЙ ХОЗЯЕВ И ПАРАЗИТОВ В СЛОЖНЫХ ПАРАЗИТАРНЫХ СИСТЕМАХ ПЕРЕНОСЧИК—ПАРАЗИТЫ И ВОЗБУДИТЕЛИ БОЛЕЗНЕЙ

A.N. Alekseev
А.Н. Алексеев

Zoological Institute, Russian Academy of Sciences, St. Petersburg, 199034 Russia
Зоологический институт Российской академии наук, Санкт-Петербург, 199034 Россия

Key words: concept, host-parasite system, antagonism, synergism, vector, pathogens, interrelationships.
Ключевые слова: концепция, паразитарная система, антагонизм, синергизм, переносчик, патогены, взаимодействие.

ABSTRACT

An attempt was made to discover the basic concepts of interrelationships between blood-sucking arthropods and transmitted by them pathogens. An analysis was made on the basis of rather long-term (1996–2000) studies of vector—pathogen interactions the cases of antagonism of different pathogens, inhabitants on some long-living host, ixodid tick, were examined. In some details were considered cases of antagonism on the organ level (*Rickettsia peacocki* – *Rickettsia rickettsii*), tissue level (*Salmonella typhimurium* — TBE virus), cell level (borreliae — TBE virus), and subcellular level (TBE and Povassan viruses). An attempt was made to discover the markers of synergistic interaction using as a tool the locomotor and «hunting» activity parameters of the multyinfected (*Borrelia* and *Ehrlichia*) host (*Ixodes persulcatus*).

РЕЗЮМЕ

На основании многолетних наблюдений (1996–2000) за взаимоотношениями кровососущих членистоногих с переносчиками или возбудителями сделана попытка рассмотрения основ, определяющих взаимодействие компонентов в сложных системах переносчик — возбудители, населяющие его. Рассмотрены случаи антагонизма возбудителей на примере мультиинфицированных долгоживущих переносчиков — иксодовых клещей на органном (*Rickettsia peacocki* — *Rickettsia rickettsii*), тканевом (*Salmonella typhimurium* — вирус КЭ), клеточном (боррелии — вирус КЭ) и субклеточном (вирус КЭ — вирус Повассан) уровнях организма хозяина. Сделана попытка выявления синергистических отношений разных возбудителей болезней путем измерения параметров поведения зараженных двумя возбудителями (боррелии и эрлихии) клещей-хозяев (*Ixodes persulcatus*).

An analysis of rather long-term (1996–2000) studies on the interrelationships between parasites and their invertebrate hosts, blood-sucking ixodid ticks first of all, allows for a number of general statements to be advanced that reveal the essence of the interactions in multi-component host-parasite systems. These statements are as follows.

As a form of their existence, multiple infections of the vector by parasites is a rule rather than an exception [Alekseev, 2000]. Microbes pathogenic to man is only a part far from the main one of the vector organism's microbiota.

Transmissible diseases of the geologically young species *Homo sapiens* known to have but very recently become ubiquitous is a rule. Man is a dead-end link in the network of most of the natural focal microbioses transmitted by blood-suckers. As regards the infections borne by ticks as the most ancient organisms in the network, man is always a dead-end. In contrast, some vertebrates as well being ancient members of host-parasite systems by serving natural reservoirs for microorganisms are only exceptionally susceptible to tick-borne diseases. It is because of this that the recently revealed distant transmission of pathogens by ixodid ticks jointly feeding on an aviremic vertebrate host [Jones et al., 1987; Alekseev, Chunikhin, 1991; Gern, Rais, 1996] is a rule. It is because of this that students searching for hosts showing high, superthreshold, levels of virusemy, e.g. TBE tick-borne encephalitis, have failed.

The species of microorganisms requiring for their existence/survival both in space and time the long-living species of the tick genus *Ixodes* whose life-history lasts 3–6 years use transphase (from one stage of tick ontogeny to the next, from one year to the next), sex (from the male to the female) and/or transovarial (from the female to the ova) ways of trasmission. Due to these mechanisms, ticks serve not so much as vectors but rather reservoirs for microorganisms, including pathogens [Alekseev, 1993].

In the globe's temperate belt, *Ixodes* species being relatively poorly vagile per se but highly tolerant to environmental conditions (temperature and, when attached to a host, even air humidity) appear highly potent to dispersal. This is secured by means of a strong apparatus of attachment, an extended period of feeding and a wide range of vertebrate hosts whose blood can be consumed, e.g. larger mammals by adult ticks, birds by tick preimaginal stages (larvae and nymphs). Parasites of ticks, including such pathogens as tick-borne encephalitis virus [Chunikhin, 1966] and borreliae [Olsen et al., 1995], thus take their advantage by also using this very potential.

The multiple pathways of germ transmission is a condition basic to a stable maintenance of tick-agent systems both in time and space [Alekseev, 1993].

Interactions between the pathogens inside the tick microbiota underlie the different reactions of uninfected vs. infected ticks to such abiotic environmental factors as temperature and humidity gradients as well as gravitation. Such a variety of reactions determines plasticity of the many vectors composing a population [Alekseev, Dubinina, 2000; Alekseev et al., 2000].

Polymorphism (often displayed even morphologically in the conditions of anthropogenic pressure) of and genetic variation in tick populations provide a sufficiently high diversity of tick pheno- and genotypes with qualitatively and quantitatively varying characteristics of accompanying pathogens. This is basic to variation in both extensity and intensity of infection, in the long run determining the stability of their foci [Alekseev, Dubinina, 2001, in press].

The main thesis concerning multiple infections, when analyzed as regards the various organisms populating the host microbiocosm, allows for a better understanding to be accomplished of at least some of the antagonistic and synergic interactions existing between the various microbial components. The interactions are known to occur at organ, tissue, cellular, and subcellular levels.

As an example of organ-level antagonism, interactions between some rickettsian species can be quoted. Thus, as discovered relatively recently, the «East side agent» preventing circulation of *Rickettsia rickettsii*, the agent of Rochy Mountain spotted fever, is still another rickettsia species, *Rickettsia peacocki* [Niebylski et al., 1997]. This latter agent seldom occurs in the hemolymph of the tick *Dermacentor andersoni*, its true concentration site being the female ovarioles. *Rickettsia rickettsii* fails to be transmitted transovarially in such ticks because the niche is taken up by *R. peacocki*, whereas transphase transmission alone appears insufficient for a stable germ circulation.

Tissue antagonism is demonstrable by the fact that so far all attempts at an induced infection by tick-borne encephalitis virus of *Ixodes persulcatus* ticks whose cell epithelium is destroyed by the bacterium *Salmonella typhimurium* have failed. Such ticks are simply «immune» to tick-borne encephalitis virus received with blood [Kondrashova, 1974].

Antagonism between borreliae, if bacteriosis is primary, and tick-borne encephalitis virus [Alekseev et al., 1996; Alekseev, 2000] seems to occur through borrelian ligands blocking the host cell membranes.

TBE and Povassan virus interference takes place at an endocellular, maybe even genome, level [Khozinskaya, 1986].

As one cannot exclude absolute antagonism between certain components of the host microbiocosm, this phenomenon would lead to complete immunity of the vector to the study agent.

Revelation of synergic relationships is far more complex. These are largely perceived by students as a «peaceful coexistence» of the various agents inside the tick organism. Yet tick locomotor activity estimates [Alekseev et al., 2000] reveal at least some combinations of microorganisms that tend to increase both locomotor and «hunting» activities in the taiga tick *Ixodes persulcatus*. Such a kind of synergism is observed in *I. persulcatus* infected by both borreliae and erlichiae. Thus, taiga ticks containing the spirochete *Borrelia afzelii* and/or *B. garinii* as well as *Ehrlichia muris* are significantly more active than monoinfected individuals [Alekseev, Dubinina, 2001].

A conceptual approach to assessing the interactions between the various components of a host microbiota, in particular as applied to such an ancient arthropod group as blood-sucking ticks, seems the only reasonable and realistic way of analysis in revealing the systemic properties of multi-component host-parasite systems. As it is ectoparasites (e.g. ticks) that are involved as model in such studies, there are no experimentation morals concerning lab animals that can be violated.

ACKNOWLEDGEMENTS

The research described in this paper was made possible by Grant No 98-04-49899 from the Russian Basic Research Foundation.

REFERENCES

Alekseev A.N. 1993. [Tick-tick-borne pathogen system and its emergent qualities] St.Petersburg: ZISP RAN. 204 s. [In Russian]

Alekseev A.N. 2000. The pathogen-vector interface: A history of paradigms // Acarina. Vol.7 (for 1999). No.2. P.111–120.

Alekseev A.N., Burenkova L.A., Vasilyeva I.S., Dubinina H.V., Chunikhin S.P. 1996. [The functioning of mixed tick-borne infection foci in Russia] // Med. parazitol. i parazitarnye bolezni (Moscow). No.4. P.9–16. [In Russian]

Alekseev A.N., Chunikhin S.P. 1991. [Virus exchange in ticks feeding on vertebrate host in the absence of virusemia (Distant transmission)] // Med. parazitol. i parazitarnye bolezni (Moscow). No.2. P.50–54. [In Russian]

Alekseev A.N., Dubinina H.V. 2000. Abiotic parameters and diel and seasonal activity of Borrelia-infected and uninfected *Ixodes persulcatus* (Acarina, Ixodidae) // J. Med. Entomol. Vol.37. No.1. P.9–15.

Alekseev A.N., Dubinina H.V. 2001. Heterogeneity of *Ixodes persulcatus* Schulz (Acarina: Ixodidae) population determines the qualities of infected specimen as a host and vector of parasite // Acarina. Vol.9. No.1. (In press).

Alekseev A.N., Jensen P.M., Dubinina H.V., Smirnova L.A., Makrouchina N.A., Zharkov S.D. 2000. Peculiarities of behaviour of taiga (*Ixodes persulcatus*) and sheep (*Ixodes ricinus*) ticks (Acarina: Ixodidae) determined by different methods // Folia parasitol. Vol.47. No.2. P.147–153.

Chunikhin S.P. 1966. [Role of birds in the tick-borne encephalitis foci treated by acaricides]. Moscow: Avtoreferat Kand. Diss. 21 p. [In Russian]

Gern L., Rais O. 1996. Efficient transmission of *Borrelia burgdorferi* between cofeeding *Ixodes ricinus* ticks (Acari: Ixodidae) // J. Med. Entomol. Vol.33. P.189–192.

Jones L.D., Davies C.R., Steele G.M., Nuttall P.A. 1987. A novel mode of arbovirus transmission involving a nonviremic host // Science. 1987. Vol.237. No.4816. P.775–777.

Khozinskaya G.A. 1986. [Investigation of ecological and virological aspects of mixtinfections by TBE and Povassan viruses ixodid ticks, vertebrates, and cell cultures] // Moscow, Avtoreferat Dokt. diss. 22 p. [In Russian]

Kondrashova Z.S. 1974. [The fate of TBE virus in ticks infected by salmonellae] // Trudy DVNC Biol. Inst. AN USSR. Vol.21(124). P.42–46. [In Russian]

Niebylski M.L., Schrumpf M.E., Burgdorfer W., Fischer E.R., Gage K.L., Schwan T.G. 1997. *Rickettsia peacocki* sp.nov., a new species infecting wood ticks in western Montana // Int. J. Sys. Bacteriol. Vol.47. P.446–452.

Olsen B., Jaenson T.G.T., Bergstrom S. 1995. Prevalence of *Borrelia burgdorferi* sensu lato — infected ticks on migrating birds // App. Environ. Microbiol. Vol.61. P.3082–3087.