There Is No Evidence That the Free-Living Ameba
Hartmannella Is a Human Parasite

Sir—We want to comment on the inclusion of Hartmannella species in the list of human parasites provided by Garcia [1]. There is ample evidence that Naegleria fowleri, Balamuthia mandrillaris, and several species of Acanthamoeba are involved in human brain disease; 179, 63, and 103 case reports, respectively, have been published, while an estimated 700 cases of keratitis due to Acanthamoeba species have been reported [2].

The evidence for Hartmannella involvement in human disease, however, is questionable because the pathogenic capacity of any Hartmannella isolate has never been demonstrated [3]. In addition, there is no indication that Hartmannella is a parasite. As the list of human parasites does not include references [1], we can only speculate on the reason Hartmannella is included in the list. Either the information provided is not up-to-date or conclusions to which some investigators jumped too easily have been accepted recently. We would be interested in knowing whether there could be a third explanation for the inclusion of Hartmannella in the list.

Because of past confusion over the taxonomy of ameboid organisms, Acanthamoeba was sometimes called Hartmannella [4]. However, this problem in taxonomy was solved long ago [5]. Furthermore, there have recently been a few reports on involvement of Hartmannella sensu stricto in brain [6] and eye [7, 8] infections, but in none of these reports was there proof that the isolated Hartmannella strains caused the disease [3]. In addition, in one of the reports on an eye infection, a Vahlkampfia species was also isolated [8], but again involvement of the isolated Vahlkampfia strain was not proven.

Therefore, we think there is no reason for including either Hartmannella or Vahlkampfia as human pathogens or parasites. Both Hartmannella and Vahlkampfia are free-living amebae that do not need to parasitize a host to complete their life cycles, in contrast to, for example, Entamoeba dispar. On the other hand, N. fowleri and certain Acanthamoeba species are opportunistic pathogens that are otherwise free-living in nature. Whether B. mandrillaris is also free-living or only parasitic is not yet known.

The isolation of Hartmannella and Vahlkampfia strains from human tissue can be explained by contamination with cysts in the processing of specimens or by the coincidental presence of these amebas on the surface of the tissue. Cysts are highly resistant forms that are ubiquitous in liquids, dust, and air. The involvement of Hartmannella in human disease can be demonstrated only if the isolated strains cause disease when inoculated into susceptible animals, as Koch’s postulates require.

In addition, there is a report of an ameba isolated from a patient with keratitis; although the ameba did not resemble Acanthamoeba morphologically, it reacted with antiserum produced in response to Acanthamoeba [9] but not with antisera produced in response to Naegleria, Hartmannella, and Vahlkampfia. Thus, morphological identification also might not be reliable. Before B. mandrillaris was described as a new genus and species, infections due to this organism had been classified as acanthamoeba infections [10], demonstrating that extreme caution is necessary when morphological identifications are used to make a diagnosis.

We do not exclude the possibility that genera of free-living amebae other than Acanthamoeba, Naegleria, and Balamuthia can cause disease, but we strongly believe that the parasitic role of an organism new to clinical science should be demonstrated [3] before it can be accepted for inclusion in a list of parasites.

Johan F. De Jonckheere and Susan Brown
Protozoology Laboratory, Scientific Institute of Public Health—Louis Pasteur, Brussels, Belgium; and Culture Collection of Algae and Protozoa, Institute of Freshwater Ecology, Ambleside, Cumbria, United Kingdom

References

Reprints or correspondence: Dr. Johan F. De Jonckheere, Protozoology Laboratory, Scientific Institute of Public Health—Louis Pasteur, J. Wytsmanstraat 14, B-1050 Brussels, Belgium.

Clinical Infectious Diseases 1998;26:773
© 1998 by The University of Chicago. All rights reserved. 1058-4838/98/2603-0047$03.00

Additional Cases of Herpes Simplex Virus Hepatitis

Sir—In their review of the literature regarding hepatitis due to herpes simplex virus (HSV hepatitis), Kaufman et al. [1] identified 51 previously reported cases in 46 publications in addition to their new single case. However, they omitted a case series of HSV hepatitis in bone marrow transplant recipients that appeared in Clinical Infectious Diseases in 1992 [2]. In the latter study (which added eight new cases of HSV hepatitis to the literature), 57 previously published cases of HSV hepatitis were identified in 50
describing cases of HSV hepatitis [1] that were missed by the nomic status. Furthermore, obtaining a careful history to establish BCV vaccine. That error led to an increase in the frequency of SIR ÐWe appreciate Arya’s interest in our review of disseminated 1058±4838/98/2603±0049$03.00 Vaccination 1998 by The University of Chicago. All rights reserved. Calmette-GueÂrin disease after vaccination: case report and review. Clin Infect Dis 90% of the BCG vaccine used q 1997;24:334±8. logic derangement or coinfection with HIV. Disseminated Bacille Calmette-GueÂrin Disease After 110048, India. Three parent strains of BCG (Glaxo-1077, Tokyo-172, and Pasteur-1173P2) account for >90% of the BCG vaccine used worldwide [2]. These strains differ not only in their physicochemical properties but also in the dose in mL volumes required. The Pasteur strain vaccine is offered in 0.1-mL-volume doses, while Tokyo strain vaccine is injected in 0.05-mL doses. During a change in the Pasteur to the Tokyo strain vaccine, it was recorded that some infants had inadvertently been given double quantities of BCG vaccine. That error led to an increase in the frequency of BCG-associated adenitis in neonates and young infants [3]. While collecting details about prospective cases of disseminated BCG disease [1], it is essential to collect additional details about the strain of BCG used; the life style of the recipient’s family; place of domicile; and demographic factors, including socioeconomic status. Furthermore, obtaining a careful history to establish the presence of factors leading to an aberrant immune response, such as substance abuse, vitamin A and/or protein malnutrition, and active and passive smoking in the household, would also be desirable. Any change in BCG strain used for vaccination and any inappropriate vaccination technique are also of consequence. The BCG strains responsible for disseminated BCG disease could be characterized by using gene probes derived from the insertion sequence IS986. Most BCG strains have a single copy of IS986 at the same chromosomal site, although the Brazilian, Japanese, and Russian strains have an additional copy at a different common location [4]. Moreover, retrospective and prospective BCG isolates implicated in disseminated BCG disease could also be examined for their large restriction fragment polymorphisms [5]. In all probability, there would be no difficulty in characterizing BCG cultures killed with ethanol before transportation at room temperature to a referral laboratory [1]. Last but not least, it would be intriguing to learn about dissemination, if any, of BCG vaccine offered as an adjuvant agent for the suppression of small, residual foci of tumor cells after surgery, radiation therapy, and/or chemotherapy. BCG is instilled in the urinary bladder to treat carcinoma in situ or to prevent relapse after resection of a superficial bladder neoplasm. In many such cases, recipients of BCG vaccine are likely to have some immunologic derangement or coinfection with HIV.

James R. Johnson
Medical Service, Veterans Affairs Medical Center, Minneapolis, Minnesota

References
1. Kaufman B, Gandhi SA, Louie E, Rizzi R, Illei P. Herpes simplex virus cases, recipients of BCG vaccine are likely to have some immuno-
2. Johnson JR, Egaas S, Gleaves CA, Hackman R, Bowden RA. Hepatitis due
4. Fomkung NG, Dale JW, Osborn TW, Grange JM. Use of gene probes based
5. Zhang Y, Wallace RJ Jr, Mazurek GH. Genetic differences between BCG

Disseminated Bacille Calmette-Guerin Disease After Vaccination

Sir—The comprehensive case report by Talbot et al. [1] on disseminated BCG disease in an 8-month-old Brazilian girl after vaccination with the Moreau BCG vaccine (Fundao Ataufo de Paiva, Rio de Janeiro) was supplemented by a literature search incorporating 27 additional cases [1]. However, it would be helpful to find out about the strains of BCG that were associated with the disseminated disease in the 28 cases. Three parent strains of BCG (Glaxo-1077, Tokyo-172, and Pasteur-1173P2) account for >90% of the BCG vaccine used worldwide [2]. These strains differ not only in their physicochemical properties but also in the dose in mL volumes required. The Pasteur strain vaccine is offered in 0.1-mL-volume doses, while Tokyo strain vaccine is injected in 0.05-mL doses. During a change from the Pasteur to the Tokyo strain vaccine, it was recorded that some infants had inadvertently been given double quantities of BCG vaccine. That error led to an increase in the frequency of BCG-associated adenitis in neonates and young infants [3].

While collecting details about prospective cases of disseminated BCG disease [1], it is essential to collect additional details about the strain of BCG used; the life style of the recipient’s family; place of domicile; and demographic factors, including socioeconomic status. Furthermore, obtaining a careful history to establish the presence of factors leading to an aberrant immune response, such as substance abuse, vitamin A and/or protein malnutrition, and active and passive smoking in the household, would also be desirable. Any change in BCG strain used for vaccination and any inappropriate vaccination technique are also of consequence.

The BCG strains responsible for disseminated BCG disease could be characterized by using gene probes derived from the insertion sequence IS986. Most BCG strains have a single copy of IS986 at the same chromosomal site, although the Brazilian, Japanese, and Russian strains have an additional copy at a different common location [4]. Moreover, retrospective and prospective BCG isolates implicated in disseminated BCG disease could also be examined for their large restriction fragment polymorphisms [5]. In all probability, there would be no difficulty in characterizing BCG cultures killed with ethanol before transportation at room temperature to a referral laboratory [1]. Last but not least, it would be intriguing to learn about dissemination, if any, of BCG vaccine offered as an adjuvant agent for the suppression of small, residual foci of tumor cells after surgery, radiation therapy, and/or chemotherapy. BCG is instilled in the urinary bladder to treat carcinoma in situ or to prevent relapse after resection of a superficial bladder neoplasm. In many such cases, recipients of BCG vaccine are likely to have some immunologic derangement or coinfection with HIV.

Subhash C. Arya
Centre for Logistical Research and Innovation, New Delhi, India

References

Reprints or correspondence: Dr. Subhash C. Arya, Centre for Logistical Research and Innovation, M-122 (of Part 2), Greater Kailash-II, New Delhi-110048, India.

Clinical Infectious Diseases 1998;26:774

Clinical Infectious Diseases 1998;26:774
© 1998 by The University of Chicago. All rights reserved.
1058-4838/98/2603-0049$03.00

Reply

Sir—We appreciate Arya’s interest in our review of disseminated BCG disease [1]. We have no systematic data regarding the effects of socioeconomic factors, substance abuse, malnutrition, or smoking on the occurrence of this disease. However, our review strongly