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Correspondence

WHO study suggests low incidence of Hib in india is due to natural immunity

Sir,

We congratulate the authors of this meticulous study[1]. The authors found the incidence of Hib meningitis only 0.007 per cent and they speculate that the population may have 'natural immunity' to invasive Hib disease.

This paper is published 10 years after the data were obtained. Three years ago an editorial published in the 'Expert Review Pharmacoeconomics Outcomes Research', cited this study as an instance of selective non-publication of research[2]. To understand the interest in this paper it is useful to remember the context in which the study was done. Hib disease in Asia is very low – six in 100,000 compared with 109 in 100,000 in the Western Pacific[3]. The thrust of Hib research in Asia is to convince health planners that Hib was a major problem that had gone unrecognized due to poor microbiologic facilities and the technical inability to culture the organism. An Invasive Bacterial Infections Surveillance Group (IBIS) study performed over 4 years, in six large referral hospitals in India, employed sophisticated culture techniques to isolate the organism[4]. This study also revealed a remarkably low incidence of Hib disease[4,5]. Not convinced, the World Health Organization (WHO) undertook this large population-based study in Tamil Nadu, assuming that hospital-based study like the IBIS study would miss cases of meningitis that die in the community, before they reach the hospital. The very low incidence in this community based study, is therefore of great interest to epidemiologists and health planners.

Unfortunately, because of this delay in publication, the data could not inform the debate prior to decision of the WHO to recommend Hib vaccine to all infants. We have previously suggested that 'natural immunity' (due to infections with bacteria with cross-reacting antigens) was the reason for the low incidence of invasive Hib disease in India, and the reason why this population does not need vaccination with Hib[6]. It is gratifying that this is now borne out in a study supported by the WHO. We hope the government and public health planners will take note of this latest evidence against the need for Hib vaccine in India.

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Authors' response

Sir,

We thank Drs Gupta and Puliyel[1] for drawing our attention to several troubling underlying aspects of their correspondence.

Our correspondents have understood the meticulousness of our study, but have apparently misunderstood parts of our data, and seem to misinterpret its meaning.

The letter provides an interesting example of several common tactics sometimes used to attempt to influence opinion through respected scientific journals, without the trouble of actually producing scientific data and of assuming the ethical responsibility of accurately quoting the data of others. We provide responses below to some of the misquotes and misinterpretations in their correspondence.

The title of their letter seems substantially misleading[1] . The study was only funded by the World Health Organization, but not carried out by WHO. Their opinions regarding "low-incidence" and "suggests natural immunity" do not reflect the data in the paper.

They referred to our article[2] as an "instance of selective non-publication of research", which is illogical, since their letter is a response to its publication. Their statement regarding "published 10 years after data were obtained" is an exaggeration. Our study analysis was completed in the year 2001, and we submitted our manuscript in 2007. Unfortunately, a pattern of exaggeration and unsubstantiated assertions of the motives of others is evident throughout their letter.

They have misquoted the IBIS studies, stating they "revealed a remarkable low incidence of Hib [with]…sophisticated culture techniques"[1]. The report of the IBIS project describes a hospital-based study which did not provide any data on incidence, and used only routine standard microbiology tests. The IBIS studies importantly showed that 30 per cent of all bacteriologically defined meningitis cases in hospitalized Indian children were due to Hib, 69 per cent of cases were in the first year of life, and 20 per cent of the infants did not survive.

Similarly in reference to our paper[2], the correspondents state its purpose was to study "cases of meningitis that die in the community before they reach the hospital". They are mistaken, since our paper provides Hib data *only* from cases of meningitis that reached the hospital.

They raised the issue of "natural immunity" without defining it several times. In our paper, we did list the early exposure to and development of antibodies against Hib among several potential reasons for the age distribution of the Hib meningitis incidence we described. Their unsubstantiated assertion regarding "natural immunity" as the reason for the "low-incidence" is from their own study quoted as reference 6, a publication in 2001 that speculated on data now more than 10 years old regarding selected antibody titres mostly developed by multi-national pharmaceutical companies in small numbers of children in India.

They discuss "The reason why this population does not need vaccination with Hib". A review of their reference 6 (by one of the correspondents) reveals a summary of data generated by others, with uncharacterized populations labelled as group A, group B, with no ages. Geometric mean antibody data are quoted from RIA and ELISA laboratory assays, without noting that both antibody levels and the "protective level" are known to vary between these 2 different antibody assays. Some statistical means were provided, without regard for the distribution of antibody titres, and there was little analysis to support the assertion regarding no need for Hib vaccine in India. They also do not note the questions that have been raised regarding the concept of "protective levels" which were derived from post-immunization data from older vaccine trials in Finland, with no evidence that they apply to pre-immunization antibody titres in other settings[3,4].

We are concerned regarding the wholly inaccurate assertion that "the delay in publication… does not inform the public debate". Our data have been reported in public conferences in 2002 (as referenced by the correspondents in their Ref number 5) and in 2004[5], directly reported to WHO in project reports, as well as summarized in several reports available in the public domain[5,6] .

It is of greater concern that the authors did not formally disclose their major bias and ideological

position -- they apparently hold the belief that some relatively new, effective and safe vaccines should not be used in Indian children, an unusual stance for paediatricians. This failure to disclose a bias, combined with the use of the rhetorical techniques of selective quotes and misquotes of evidence published by others, in addition to unsubstantiated accusations suggest this letter is an example of opinion with little fact-based discourse. The correspondents may be successful in appropriating the mantle of seemingly unbiased and open-minded scientific inquiry. The lack of disclosure may mislead the less informed reader, and may lead some informed readers to speculate about the correspondents' motivations.

However, we are confident that the public health authorities of India will review the epidemiologic pattern of Hib disease, as well as the evidence regarding pre- and post-vaccine antibody titres in Indian children, to decide if Hib vaccines are needed. We are also confident these data will be used to develop an appropriate Hib vaccine strategy, tailored for the unique Indian data, and taking advantage of India's unique capacity to produce vaccines in large volume. We recommend that more data regarding Hib disease and the effect of Hib vaccine on disease in India be developed[7].

We encourage the full expression of opinions on national health policy in the proper forum. We suggest that additional Indian data are likely to be more useful to improve the survival and health of children in India, compared to the expression of partially cloaked ideological opinions unsupported by data, which may be submitted to the correspondence sections of science journals.

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