From: Rich Whitley, M.D. [mailto:RWhitley@peds.uab.edu] Sent: Friday, March 03, 2006 11:14 AMTo: Alan WerzbergerSubject: RE: yesterday's visit

Hi Alan,

It was my pleasure to meet with you and your colleagues.

My responses are below.

Best,

rich

From: Alan Werzberger [mailto:alan.werzberger@med.nyu.edu]Sent: Thu 3/2/2006 6:49 PMTo: Rich Whitley, M.D.Subject: yesterday's visit

Dear Dr. Whitley,

On behalf of Rabbi Niederman, Dr. Ditchek and Mr. Simins, thank you so much for meeting with us yesterday. Your generosity of time and spirit was greatly appreciated, and your willingness to lend your expertise to a cause as arcane as ours is truly heartening.

On our return flight, we discussed among ourselves what we learned from our visit, and thought it would be helpful if we attempted to paraphrase some important points made.

1. The rate of axonal progression of hsv1 is .1 mm/hr, precluding the idea that lesions caused by hsv1 introduced by mbp would be seen in the gluteal region of an affected child within the clinical time frame of primary disease.

Yes, this is correct but please remember that these data are derived from a mouse model.

2. There is no such thing as “underreported” neonatal herpes.

Correct.

3. The rate of viral shedding (in asymptomatic as well as symptomatic individuals) of hsv1 is much less than hsv2 (approximately 0.5% vs 5.0%) by culture. Corresponding rates by PCR (increased fourfold) would then be 2% and 20% respectively.

Here it is much less clear as these studies are only being done now. The current data exist for HSV-2. In those cirucmstances, about 5% of days seropostiive patients shed virus. If PCR is then applied, this figure increases to 20%. What is known about HSV-1 is that individuals only shed virus 1% of days -- as opposed to 5%. In the worst case, individuals would be PCR positive on 5% of days.

4. Hsv1 is much more sensitive to famciclovir and other antivirals than hsv2.

I would just say more sensitive as opposed to much more sensitive.

5. Based on the above, your clinical impression is that even if a mohel is felt to have "transmitted" hsv1 through mbp, an acceptable, adequate form of risk reduction would be administration of daily famciclovir or other similar antiviral.

We can only presume so because we have no data.

6. Positive PCR alone (i.e., negative culture) is sufficient for DNA fingerprinting.

We can use restriction enzymes onf PCR products for showing identity or non-identiy. Ideally, one needs whole virus.

7. DNA fingerprinting is not "interpretive," but rather yields clear match/not-match results.

It is not at all vague.

8. It is your overall impression that the Health Department's actions targeting mbp are not appropriate.

I can not say this. I do not have the actual charts to assure myself that the assumptions are correct. Without the real data, I can not draw any conculsions.

9. It would be helpful to undertake a study to confirm our impression that

the incidence of neonatal hsv1 disease is no different in the mbp vs non-mbp population. Your impression (contrary to Dr. Prober's), is that a 2-3 year case control study would adequately generate meaningful data. These prospective data, obtained under a study design carefully crafted to eliminate observer bias, would provide a much more powerful platform upon which to discuss this issue.

Charles and I are looking at the study totally differently. He approached it from the perspective on the actual number of cases of neonatal herpes. I am looking at it by saying if no cases occur we can provide a degree of confidence that the incidence is so, so low.

Please let me know if I "got it right ."

Again, on behalf of our group, please accept this heartfelt expression of gratitude. Your sacrifice of precious time and thoughtfulness for us has truly touched our hearts; we will be forever grateful.

We are very excited at the prospect of working with you in the near future.

Sincerely yours,

Alan Werzberger MD