

July 11, 1984

TO: Charlotte G. Neumann

FROM: James Cherry, M.D.
Department Pediatrics
UCLA School of Medicine

RE: Trip Report: Nutrition CRSP Kenyan Project -- Embu, Kenya

Dates: June 7 through June 19

Purpose of Visit:

1. Evaluate Immunology work at Embu (cellular immunity).
2. Evaluate Immunology work in Dr. Bowry's lab (humoral immunity).
3. Evaluate morbidity data collection and physician performance.
4. Explore the possibility of introducing a functional test to assess the immune system.

Nairobi, June 9-12

Visit to University of Nairobi School of Medicine.

(1) Dr. Julius Meme, Chairman, Department of Pediatrics, Child Development (Specialty)

I discussed the project in general and more specifically, the planned pertussis immunization procedures as a functional test of the immune system.

Dr. Meme was briefed about the medical student, Ulrike Ochs, who will be working for the project this summer as a volunteer. I explained her role, that of working in the laboratory. She would help with immunology and freezing lymphocytes so that they could be brought back to UCLA for replicate testing of T-cells for quality control. The results would be compared to those in Embu on a given specimen.

I was asked to give a lecture to many residents and medical students and others at 2:00 p.m. on June 18. The title was "Immunization"

(2) Dr. Tulia Bowry -- Immunology

I met with Dr. Bowry to discuss the current status of the immunology work.

My first responsibility was the check on the progress she had made with the immunodiffusion studies. Specifically, she was to have run the quantitative globulins, C-reactive protein, Transferrin, Albumen, Pre-albumen, and C₃

determinations on all the serum samples that she had received from the field. She stated that she had received over a hundred serum specimens but as yet had done none. Her explanation as to why was vague and did not make much sense. The kits (immunodiffusion kits) that were supplied to her had not been used, and I got the impression that they were either used for some other purpose or that she had no intention of using them since the kits had passed the expiration date. However, she had been assured by Dr. Stiehm that they were still able to be used satisfactorily. However, Dr. Bowry said she would make up the plates and that she had all the necessary anti-sera, etc., to do this and that she would be starting on the specimens very soon. Dr. Bowry claimed that one reason she hadn't started yet was because of lack of space to store the split specimens, which didn't seem to make any sense as there are two Revco freezers available. Because the cost of repair of the freezer was \$5,000 we declined to fix her defective freezer.

(3) Dr. David Koech - Clinical Research Center

I met with Dr. Koech Friday, June 7, and thoroughly enjoyed my meeting. He is, I believe, a very sharp individual who it appears knows how to collaborate with overseas scientists (Americans) in a way that is mutually beneficial. His recent publications certainly suggest this.

I discussed the pertussis vaccine situation and the possibility of using a new Wyeth a cellular vaccine and discussed the possibility of looking at vaccine efficacy. He also told me that to get information on pertussis and surveillance that I should see Dr. Muite, who is in the Ministry of Health and is the manager of the expanded program on immunization (EPI). The director of this program, who I also should see, is Dr. Siongok.

We then discussed other aspects. Dr. Koech also said that she could do all the nutrition CRSP required immunology in his laboratory including the T-cell subsets without having to freeze lymphocytes and send them to California. He felt his laboratory could serve a quality control function for Embu. He apparently has the monoclonal antibodies and is well automated; he showed me a printout of T-cell subset studies. He also let me know in so many words that he thought Dr. Bowry was unlikely to do the various immunodiffusion studies. Although we didn't discuss it specifically, I believe he would be happy to be the full immunology collaborator in place of Dr. Bowry. Certainly I believe he would check the T-rosettes by the monoclonal antibody method on a subsample of our specimens.

He also said that we could store specimens in his -70 freezer.

A follow-up to the immunology situation is that Professor Bwibo, the Kenyan P.I. officially dismissed Dr. Bowry and formally invited Dr. Koech to join as the Kenyan immunologist. It is his technician David Eha whom Dr. Stiehm trained last summer (1983) when David was on loan to Dr. Bowry.

(4) Dr. Peter Tukei

Dr. Tukei is a virologist who runs the program in the Medical Research Center of KMRI. He is involved in major rapid viral diagnosis studies, comparing rapid methods with standard culture technics. He clearly knows what he is doing, and also has gotten reagents from the New Castle group and also from

people in the United States. I believe he would very much like to collaborate and do the laboratory work if we could get going a specimen collection system from our subjects when they are ill, particularly with diarrheal and respiratory disease. We would be interested in sending stool specimens and nasopharyngeal swabbings.

I am very impressed with Dr. Tukei and would like to pursue the rapid diagnosis of illnesses in our study subjects, if at all possible. I scheduled a meeting with him for Monday, the 18th, following my meeting with Dr. Koech.

(5) Dr. Muite, Dr. Siangok, Ministry of Health

On Friday afternoon I went to the Ministry and found that Dr. Muite, the manager of the expanding program on immunization was out, so I saw the director, Dr. Siangok instead.

We discussed the problem of pertussis immunization. He feels that less than 50 percent of the children are being immunized and that there is clinical pertussis, but he didn't know the exact rate.

(6) Visit to Embu and Project Site

Monday, June 11, the driver picked me up and took me to Embu arriving there about 10:00 a.m. I met with Dr. Eric Carter in the morning, and we discussed the principles and realistic aspects of the functional measure of immunity.

First of all, I reexamined the measles immunization situation to see if there was any way, retrospectively, to see if we could look at measles antibody titers on the 18-month blood and get something out of that. However, the vaccine histories apparently are not that good, so that this doesn't seem worthwhile.

We then discussed at length the use DPT as a functional measure of immunity. We spent quite a bit of time talking about the possibility of the Wyeth vaccine studies and some of the difficulties relating to that. Basically, the problems relating to a study with a new vaccine for efficacy relate to the need for a surveillance group, the relatively short time left in the present study, the need for a sizable grant from Wyeth, and a need for a quick approval from Wyeth and also from the Ministry. If we could get going by November, which would probably be possible, but optimistic, this would only give us at most a hundred newborns introduced into the study that could be immunized. Since the study ends in the end of '85, this would give us almost no follow-up in some and perhaps nine months at most in others. Therefore, for a decent follow-up, we would have to extend surveillance in this group as well as a control group after this study, and this would be expensive.

Therefore, we will concentrate only on DPT as a measure of immune function using the regular government DPT vaccine, and follow-up. Eric and I discussed this from two aspects. The first is whether we get the vaccine and immunize all the children or, secondly, should we just have them immunized in the regular clinic, but find a way to get them to the clinics. There are pros and cons to both. If we immunize, then the infants are likely to be reimmunized when they go to the clinics for other reasons. What this hyperimmunization will do and how many will get it I think is an important problem.

Probably the best solution will be to have our nurses give DPT, 3 immunizations by 5-6 mos. and measure pertussis antibody response in the blood sample. The project should issue clinic immunization cards so that the clinic staff does not reimmunize the infants. This will be settled in July.

Monday afternoon July 11 I spent in the laboratory with Wilson Mogisha and Sammy. First of all, I was impressed with both of them and in particular Wilson. He appears to be an adequately trained technologist who had a good feel for the subject. They ran some quality control on the E-rosettes that day, and I think that Wilson seems very competent. There was a problem; with dust that got into the specimens, and the white cells had clumping due to the dust particles. Wilson was able to figure this out and recognized it as a problem. I reviewed the laboratory work in general and the procedures and the results all seem quite reasonable. We discussed the plans for freezing some cells, for shipping to UCLA (or to Nairobi) for quality control purposes.

Morbidity Data Collection

Tuesday, June 12, I spent in the field with Dr. Amrullah Khelghati, who is the UCLA field physician with the project. In addition, there was a temporary Kenyan pediatrician. We started out at the Kararumo clinic where I met the nurses and we held a discussion about the work. At noontime, we saw a couple of study children who were quite sick. One boy seemed to have malaria and the nurse took a thick smear for malaria and we treated for malaria. We visited all four cluster centers and the community nurses in each. We also went out and visited some houses with an enumerator and this was quite an experience. While in one house we were asked to come over to another house, and there was a woman who was obviously quite sick with a temperature of 40.8 C° and shaking chills. A diagnosis of malaria was made and she was started on Chlorquine. She was to be checked the rest of that day by the enumerator and then seen the next day by the nurse.

We went over the enumerator's reports and the coding process. It appears to me that the enumerators were doing the job, as well as the nurses. The problem in which illnesses that were ongoing at the time of one visit were not recorded at all in the next visit, seemed to me to have a relatively simple answer. This is that the enumerators, prior to their visit, would review in the office the previous week's sheets and make a notation of all the continuation illnesses. After they initially asked if the people had been sick for the week before, if they said nothing about the previous illness, then they could ask specifically about it. This would not require taking the old sheets out to the field, nor would it require making a new month-long recording sheet.

Apparently, all of March has been coded. I'm not sure whether Dr. Khelghati has checked these over yet. April seems to be well on the way. But again, he hasn't checked these all over. It looks to me that morbidity data is being fairly well compiled for this type of study under the circumstances.

Morbidity Data Collection and Coding - Recommendations

1. Dr. Khelghati should review "Physician's Instructions: Morbidity for Weekly Coding." Several present difficulties are covered in the instructions.

2. Coding Problems.

- A. Coding is being done by the full month, not by four week period, as intended.
- B. The original plan to code four weeks by visit day is a good one and should be done starting at the end of the month, even if the backlog isn't caught up.
- C. Blocks 13 and 14 are not being entered, but should be if done as in 2B above. These blocks refer to the day the four week period ends and no coding is done.
- D. Blocks 15 and 16 are being used for month of data, rather than end of four-week period as appeared under "C".
- E. Treatment section on the report form has seven entities, but only six boxes. At present the "no treatment" category has been eliminated. Since things don't line up, there could be problems of miscoding. We could add boxes (107,108) for No Treatment category.
- F. Continuing illness is presently being done incorrectly (see page 3, Physician's instructions).

3. Problem With Week-To-Week Continuation of Illness.

- A. Khelghati's monthly form is one answer, except that we still have a problem at the end of the month. Also, the monthly form is a radical change for the enumerators and, in my opinion, will confuse Recall (R) from observation (O). I don't think the monthly record as proposed by Dr. Khelghati, is a good idea.
 - B. The alternative is to use present weekly forms but to have the enumerator review the preceeding week's form and record on a separate "working" form all continuing illness so that the endpoint of these illnesses can be specifically asked about during the visit.
4. In general, it seems that present data system (enumerator-nurse) is working fairly well. However, the physician should review records daily with the nurses. The doctors are leaving the field too early!
5. Dr. Neumann was concerned about the diagnosis of diarrhea. It seems to be diagnosed satisfactorily but Dr. Khelghati has not been using the specific WHO definition. I did not check nurses on this.

RECOMMENDATIONS

A. FUNCTIONAL MEASURE OF IMMUNITY

1. A vaccine efficacy study has many problems, the most important of which is lack of time. Therefore, we should start a routine DPT and/or polio program immediately so that we can get antibody data from the six-month blood specimen.
2. Two plans: either could be acceptable (Plan one - we immunize; Plan two - we get subjects to clinics for immunization).
 - a. Plan One. Advantages and Disadvantages
 1. We can be sure all children get vaccine in time for six-month blood to reflect uniform response. We use our own or Government supplied potency tested vaccine.
 2. The problem -- children may get additional doses in the routine health system.
 - b. Plan Two. Advantages and Disadvantages
 1. Children will not get extra doses.
 2. Will take great effort to get children to clinics on time to be fully immunized by six-month blood.
 3. The vaccine cold chain may be a problem
 4. Logistics and transport problems would abound if we undertake getting infants to the clinic from so farflung an area.

B. VERIFICATION OF ILLNESS

1. Original study had plans to use rapid viral diagnosis for respiratory syncytial virus and rotovirus. Money for this seems to be short. Peter Tukei has already done excellent work in this area, and it is my understanding that if we could collect the specimens, he would like to collaborate. Frank Loda, from the University of North Carolina will be joining him next month and possibly could consult. In addition to Tukei's present rapid diagnostic methods, we could also include chlamydia for eye disease although this is expensive (\$7.00). Chlamydia is an important pathogen.

C. IMMUNOLOGY

1. Change from Dr. Bowry to Dr. Koech as the latter immunologist not only is welcome but essential (already accomplished by Prof. Bwido)
2. T-cell studies can be checked by Dr. Koech using his monoclonal methods. We could still do our own checking as well for a while to see if UCLA's laboratory agrees with Dr. Koech's lab.
3. Ulrike Ochs will be able to work in Dr. Koech's laboratory and also in Embu.