THE BERNHARD BARON MEMORIAL RESEARCH LABORATORIES
QUEEN CHARLOTTE'S MATERNITY HOSPITAL
GOLDHAWK ROAD, LONDON, W.6

Director: J. MURRAY, M.D., F.R.C.O.G. Tel. No. Riverside 4666

27th November, 1961.

Dr. I.H. Gosset, F.R.C.P.,
Children's Physician,
General Hospital,
Northampton.

Your ref: IHG/PMP.

Dear Dr. Gosset,

Thank you for your letter of October 29th and your kind comments.

I was interested in your theory that jaundice of prematurity has occurred in "waves" at different times in different localities and I am sure Dr. Norman will also be interested. As you say it would be most valuable if the cause of these epidemics could be traced. I cannot say that I have been aware of any sustained period during which a high incidence of markedly jaundiced premature babies has been observed at Queen Charlotte's. It is possible, however, that a detailed analysis of our records over the past seven years or so might reveal such a period.

I agree that in the investigational stage the use of a considerable range of shades was essential; but now that the correlation between shade and pigment levels has been found and the limitations of the instrument established, I think, for some at least, the omission of shades No's. 1 & 5 would simplify the construction and the use of the icterometer. Of course as you point out if a daily comparison is made between icterometer readings and the chemically determined pigment level then a greater number of shades is a help, but I was thinking primarily of the use of the instrument as a screening test in the hands of the paediatrician.

Your disapproval of the use of the icterometer in the small hospital, I feel, cut out one of its uses. Ideally, I agree that all premature babies should be transferred to a Premature Unit, but this is not always possible and it is here that the icterometer could be a useful indication of those that should be moved for treatment of jaundice. In fact, if I understand you correctly, you only transfer a jaundiced baby from a peripheral unit if the icterometer reading is 3 or over, although I imagine you are referring here to any baby not

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necessarily a premature.

Thank you again for your detailed answer to my letter and your interesting remarks.

Yours sincerely,

C.R.J. Ruthven

C.R.J. Ruthven,
Biochemist.

IHG/PMP. October 29th, 1961.

Dear Mr. Ruthven,

It was unfortunate that your letter of May 23rd arrived at a time when I was particularly busy because it meant that I put it on one side and it seems to have ended up at the bottom of a pile. I am very sorry to have kept you waiting so long but here at last are my observations.

In the first place, may I thank you once again for the interest you have shown in the icterometer and for the painstaking work you have done with it. I do not know of anyone else, except the Birmingham people, who have taken the trouble to make detailed tests with it, and I am most grateful to you for letting me know the results.

I am glad to find that by and large you have been able to confirm that the icterometer is of some value. I am interested to see that your graph contains relatively fewer cases in the higher ranges than mine did. We had an epidemic of fairly deeply jaundiced babies at the time when my graph was made and hence it was easy to get enough readings of four or five on the scale. Nowadays we should have more difficulty over this. In talking to other paediatricians and listening to papers read at meetings I am quite certain that the "waves" of jaundice exist. We had ours 4 or 5 years ago and so, I think, did Beryl Corner at Bristol. Birmingham have been having a wave this summer at Sorento. They have been doing a lot of exchanges on Prems. whereas we have not exchanged a jaundice of prematurity for over 18 months. I suspect these waves are related to drugs used by the Obstetricians on the mothers but we were never able to track down the offending substance in our own cases.

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We were not using sulphonamides or large doses of Synkavit nor were the babies in contact with mothballs. Have you come across these waves of jaundice? At the peak of our wave we had to exchange 17 babies in one month and only two or three of them were Rhesus babies. It would be very nice to know what lay behind it all in case it starts happening again.

Turning now to the various points in your letter.

I agree that the lightest stripe No.1. is not much use and could probably be omitted. As a matter of fact, my original scale had an even lighter stripe (No.0.) which was intended to correspond to non-jaundiced skin but we omitted it quite early on. I find the nursing staff seem to like to have No.1. for their day-to-day charting so I have not so far abolished it.

Shade No.5 could, as you say, be abolished on the grounds that a serum bilirubin would be done anyway at that level, but we do find it useful for our day-to-day charting and we also find that there are some babies whose serum bilirubin is still below the threshold even when their skin matches No.5. (you can see this from the graph in my original article. We do bdlirubins on all these babies, of course, but we like to be able to chart them by their scale readings as well.

As to the reliability of the icterometer as a guide to the day-to-day trend in bilirubin level, all I claimed was that: "The serum bilirubin levels and icterometer readings do, infact

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tend to rise and fall together," and I still think that is a fair statement. I agree that one does sometimes get results such as you mention but I do not think that these are very significant because, 1) in most hospitals there is in any case a margin of error in serum bilirubin estimations, and 2) strictly speaking it is the tissue bilirubin rather than the serum bilirubin which matters in the production of kernicterus, and the icterometer may well give a betteridea of the tissue level than the laboratory does.

You suggest that the icterometer will prove particularly popular in the smaller hospital without adequate pathological facilities, but I have grave doubts as to whether such a hospital ought to be dealing with premature babies at all. In this area if a premature baby is born in one of the G.P. Units at the periphery it is transferred as soon as possible to the Premature Baby Unit at the main centre so there is no real need for the peripheral Units to use the icterometer at all. If I am called to see a jaundiced baby at one of these Units I do, of course, bring my icterometer with me but I only use it as a screening test when I get there and transfer the baby to the central Unit if the icterometer reading is 3 or over.

From discussion with my colleagues I would say that the icterometer is mainly being used to cut down the number of pricks that premature babies have and to cut down the load on the pathological laboratory, and there seems to be general agreement that it saves quite a lot of work. I have not heard of anyone using as a sole guide to exchange transfusion.

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Thanking you once again for the interest you have shown and for the very careful work that you have done in calebrating the icterometer and with apologies for taking such a very long time to reply to your most interesting and stimulating letter.

Yours sincerely.

I.H.Gosset, F.R.C.P.
Children's Physician.

Mr.C.R.J.Ruthven,
The Bernhard Baron Memoral Research Laboratories,
Queen Charlotte's Maternity Hospital,
London.W.6.

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Dear Mr Ruthven

Your letter of 23rd May on your experiences with the Interometer is of the greatest interest to me and I am flattered to find that you have done so much work on it. I intend to do my best to answer your questions in detail soon, but I hope you will forgive me if I wait a bit. My opposite number has been away for the past 3 weeks and I have been fully occupied with the extra work.

As soon as things settle

down again I will get down to it, and write to you when I have had more time to consider the points you have raised.

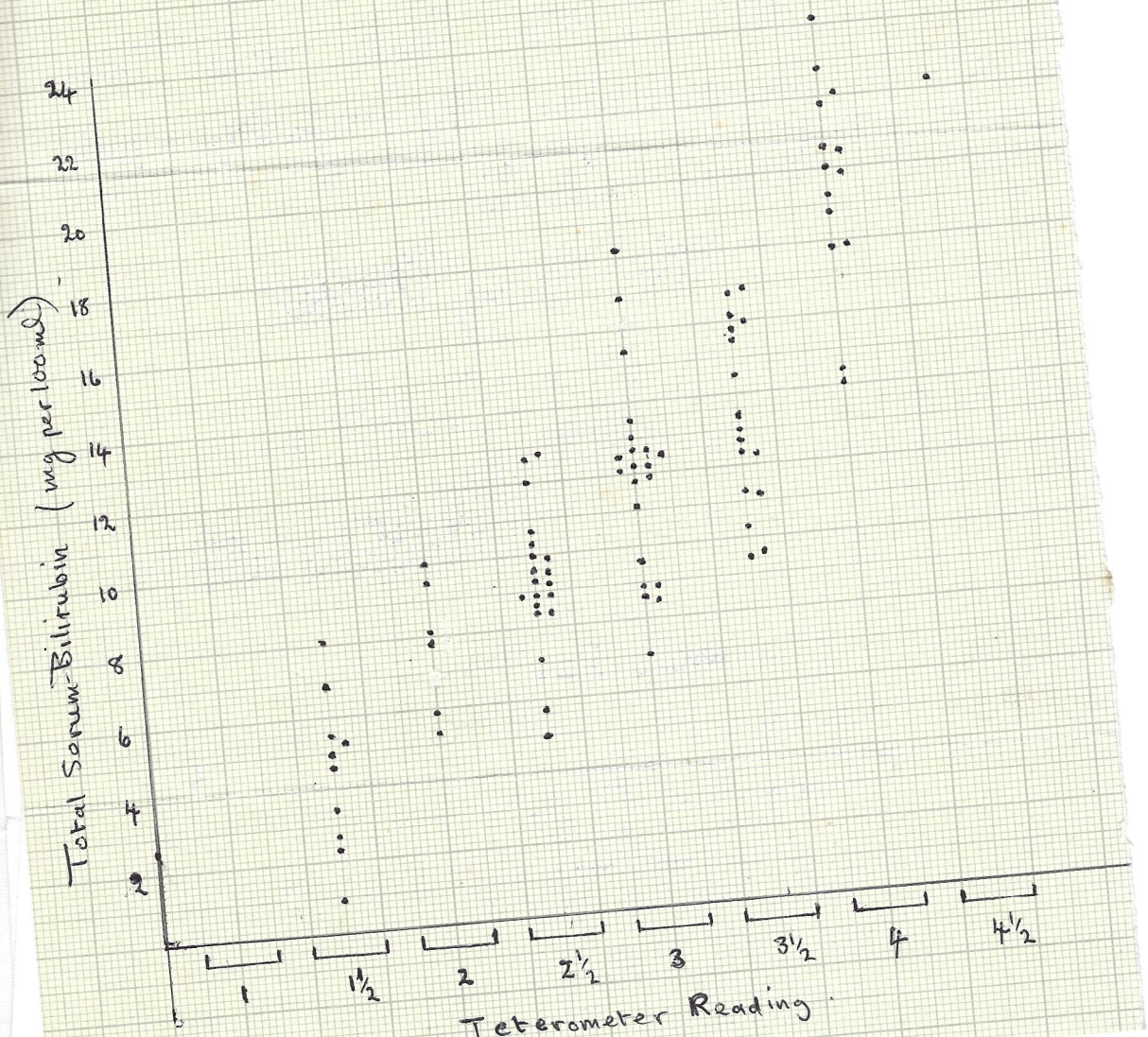
With many thanks

Yours sincerely

W. S. Gosset.

C R J Ruthven Esq
Biochemist
Queen Charlotte's
Maternity Hospital
London W6.

Icterometer readings compared with total serum-bilirubin levels (estimated by method of Lathe & Ruthven (1958) J. clin Path 11 155) Each dot indicates one reading. Ninety readings are shown.



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23rd May, 1961.

Dr. I.H. Gosset, M.A., B.M. Oxon. M.R.C.P.,
Consultant Paediatrician,
Northampton General Hospital,
Northampton.

Dear Dr. Gosset,

Following your publication in Lancet last year (Lancet i, 87, 1960) describing the use of an icterometer to assess the degree of neonatal jaundice, Dr. A.P. Norman gave me a similar instrument and asked me to carry out a trial with it at Queen Charlotte's Hospital. This we have done, and at Dr. Norman's suggestion, I am writing to give you our results.

We have compared 90 icterometer readings with the corresponding serum-bilirubin levels, determined by a modification of the Malloy & Evelyn technique. The results have been plotted on a scatter graph, as in Fig. 3 of your Lancet article. They represent data from 30 different babies, ranging from isolated values on single babies, to as many as 10 serial determinations on one infant. Most of the observations and serum-bilirubin determinations have been made by one operator, therefore our results must be influenced by the ability of this operator to match colour shades and to do so consistently. We felt, however, that it would be under such conditions that the icterometer would most frequently be used, whether by paediatrician or laboratory technician. Naturally the icterometer reading was made before the serum-bilirubin level was known.

The graph, which I enclose, is essentially similar to the one that you published. Like yours, it shows that fairly small variations in bilirubin level may be detected statistically from a considerable number of readings, but that, as you point out, the level cannot be reliably predicted from a single icterometer reading. It would seem, and this I think is also shown by your graph, that the greatest inaccuracy arises in assessing pigment levels below 7 mg. per 100 ml. Clinically this level is not of importance and perhaps suggests that the shade No.1 might be omitted from the range. Possibly a case might also be made for omitting shade No.5, for as you state

and our figures endorse, any pigmentation even corresponding to shade No.3½ should signify the need for the immediate determination of the serum-bilirubin level.

In our hands we did not always find the icterometer a reliable guide for the day to day trend in bilirubin level. For example, we had one case in which the bilirubin varied only by 0.7 mg./100 ml. over three days, being lowest on the last, while the respective icterometer readings were 2½, 2 and 3. In another case, a drop in the icterometer reading was recorded from one day (reading 3½) to the next (reading 3) while the serum level had actually risen (from 15.5 to 18.2 mg./100 ml.). Also we have had a number of instances in which the daily icterometer readings on a baby were assessed the same over several days while a variation in pigment level ranging from 3 to 4 mg./100 ml. was recorded during the period. Such discrepancy might be sufficient to mask quite a considerable daily rise in level.

We expect that the icterometer will prove particularly popular in the smaller hospital without adequate pathological facilities. In our view any icterometer so used should be calibrated against the serum bilirubin level, over probably at least 30 determinations, the latter made by some reliable standard technique. The icterometer readings should be made by the operator or operators who intend to use the instrument. We also feel that the use of the icterometer should be restricted to that of a screening tool to supplement the assessment of the depth of jaundice made clinically. We hope there would be no temptation to use the instrument as a sole guide to exchange transfusion, a use which you of course do not recommend.

These comments are based on our experience with the icterometer which is slight compared with yours or the Birmingham group, but which perhaps corresponds to that of the majority of other users. We would be interested to hear how others have found the instrument and also would be grateful to have your guidance on the points that we have raised.

Yours sincerely,

C.R.J. Ruthven,
Biochemist.