

Postcard to: Professor Hellbrugge
Kinderpoliklinik der
Universitat Munchen
Munchen, Germany

February 27, 1964

Dear Doctor Hellbrugge:

The reprints which you sent contain much interesting material related to various fields in which we are working. Thank you for sending them. We are glad to have them for reference.

I assume that your various questions concerning Tables have been already answered by Dr. Bayley.

Sincerely yours,

Leona M. Bayer, M.D.

KINDERPOLIKLINIK DER
UNIVERSITÄT MÜNCHEN

Direktor: Professor Dr. G. Weber

8 München 15, den 6.12.1963
Pettenkoferstraße 8a – Telefon 558471

Mrs.
Leona M. Bayer M.D.
Presbyterian Medical Center
Clay & Webster Sts.

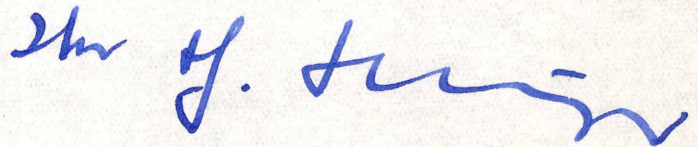
S a n F r a n c i s c o 15/California
U S A

Sehr geehrte Frau Dr. Bayer!

Vielen Dank für Ihre Karte vom 3.12.1963. Ich habe Ihnen und Frau Dr. Bayley einzeln geschrieben, weil ich hoffte, daß wenigstens einer dieser Briefe Sie erreichen wird, zumal ich keine genaue Anschrift von Ihnen hatte und somit an den Verlag schrieb. Sie erhalten in der Anlage eine Abschrift des Briefes an Frau Dr. Bayley und ebenfalls mit getrennter Post einige Sonderdrucke.

Ich freue mich, auf diesem Wege mit Ihnen in Verbindung gekommen zu sein, da ich mich auch seit längerem mit Fragen über Wachstum und Entwicklung beschäftigt habe, und hoffe, daß diese Verbindung weiter aufrecht erhalten bleibt.

Mit verbindlichen Grüßen



Prof. Dr. Th. Hellbrügge

3.12.1963

Mrs.
Nancy Bayley Ph.D.
Chief, Section on Early Development
Laboratory of Psychology
Nat'l. Institute of Mental Health

Department of Health, Education, and Welfare
Public Health Service, National Institutes
of Health
Bethesda 14, Maryland
U S A

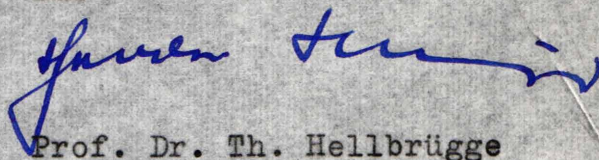
Sehr geehrte Frau Dr. Bayley!

Für Ihren Brief vom 27.11.1963 möchte ich mich herzlich bedanken. Kurz zuvor kam bereits eine Antwort von Frau Dr. Leona Bayer. Ich bin nun froh, daß auch mit Ihrem Brief meine letzte Frage geklärt zu sein scheint:
Skeletal Age 7,9 bedeutet demnach nicht 7 und 9/10 Jahre, sondern 7 Jahre und 9 Monate; auf Seite 229 wäre demnach Skeletal Age 6,10=6 Jahre und 10 Monate?

Ich hatte soeben die Tabellen von Inch in cm umrechnen lassen, weil ich gern Ihre wertvolle Arbeit den deutschsprachigen Ärzten zugänglich machen möchte.

Mit verbindlichen Grüßen

Ihr


Prof. Dr. Th. Hellbrügge

P.S. Mit getrennter Post erlaube ich mir, Ihnen einige Sonderdrucke zu überreichen

UNIVERSITY of WASHINGTON
SCHOOL OF MEDICINE
DEPARTMENT OF MEDICINE
SEATTLE 5

Medical Genetics

Hubert -
January 15, 1963

Dear Dr. Baye,

It was pleasant to have
met you at the Winkelstein's
at Strain Beach. Upon returning here
I asked Dr. Reich's contingent if they
had purchased your and Dr. Bailey's
volume and they admitted they had.

Reference Card
The most recent issue of
Clinical Research (11: 74 (1963)) contains
an abstract on growth in children with
Edwards' malformation which may interest you.

My best regards to your

"Rochester - alumnus" husband

Cordially,
Frederick Hecht

file
in conference
(H)

SAN FRANCISCO ACADEMY OF HYPNOSIS

affiliated with

The AMERICAN SOCIETY of CLINICAL HYPNOSIS
The SOCIETY for CLINICAL and EXPERIMENTAL HYPNOSIS

N E X T M E E T I N G

PAIN

Panel

Vincent W. Cangello, M.D. (Cancer)
Herbert E. Owens, D.D.S. (dental)
Irving Schwartz, M.D. (intractable)
Charles Wellington, M.D. (obstetrical)

8:00 P.M.

March 28, 1963

The Bay View Savings and Loan Association Auditorium
Palm Avenue and Geary Boulevard
San Francisco

SKyline 2 9995
For meeting only

Each panelist will speak for ten minutes.
Questions from the floor will follow.

ANNOUNCEMENT

A course in elementary hypnotic techniques will start in April. It will consist of ten or twelve weekly sessions conducted by the members of the Academy. The tuition fee will be minimal. Details at this March meeting.

Announcements of meetings henceforth will be sent only to Members and Associate Members. Applications for membership may be obtained by contacting one of the numbers below.

Contact numbers for the course and the Academy:

San Francisco: PR5 1001
WE1 0211

Oakland: TE4 4282
452 1988

SAN FRANCISCO ACADEMY OF HYPNOSIS

affiliated with

The AMERICAN SOCIETY of CLINICAL HYPNOSIS
The SOCIETY for CLINICAL and EXPERIMENTAL HYPNOSIS

Application for Membership

Membership requirements: (1) A holder of a M.D., D.D.S., or Ph.D. or equivalent (in psychology) degree. (2) Membership in the American Medical Association, American Dental Association or American Psychological Association. (3) Sponsorship by a Member of SFAH. (4) Evidence of competency in clinical or investigative fields of hypnosis to qualify for (full) Member. (5) Associate Members are required to obtain competency in the field of hypnosis before December 31st one full year following their election.

Please print or type.

Name _____ Birth place _____

Address _____ Birthdate _____

City and State _____ AMA-ADA-APA (Please circle)

Training: M.D.-D.D.S.-Ph.D.-other _____ (Please circle)

Name and address of institution granting degree _____

_____ Date _____

Other special training (other than in hypnosis) _____

*

Training and experience in hypnosis _____

*

ASCH-SCEH (Please circle one or both if applicable) *Use extra sheet if necessary. Please give dates and be as complete as possible.

\$10.00 (Initiation fee and dues) enclosed.

Date _____

Signature _____

Degree _____

FOR CREDENTIALS AND MEMBERSHIP COMMITTEE ONLY					
Classification	AM	M	H	Comment	Signature
Committeeman					
Committeeman					
Chr. Comm.					
Final action SFAH Sec'y.					

February 1, 1962

Dr. Orrin Harris
Chairman, Committee for the Creation of a Division
of Child Health and Human Development
National Institute of Health
Bethesda 14, Maryland

Dear Doctor Harris:

Ever since President Kennedy's inauguration we have been reading about the interest of the Administration in child health and human development. Recently, Dr. Nancy Bayley gave me your name as being Chairman of the Committee considering the creation of a Division concerned with this area of health.

At the Presbyterian Medical Center, we have a Youth Clinic whose staff is unusually alert to the growth and constitutional aspects of adolescent medicine, and unusually well qualified to study them. We would be much interested to know about the present status of the proposed division, and whether there is any way we could coordinate our work with its projected programs.

We will greatly appreciate any information you can give us.

Sincerely yours,

Leona M. Bayer, M.D.
Youth Clinic Staff
Associate Clinical Professor of Medicine

LMB:R

November 30, 1961

Iowa Child Welfare Research Station
University of Iowa
Iowa City, Iowa

Gentlemen:

Please send me two paper height scales, C.O.D., to this address. I have in mind the scales used in growth institutes: inches on the left, centimeters on the right. If you have scales for the bottom 100 cm., I would like those also. I understand they are \$1.50 each. Thank you.

Sincerely yours,

Leona M. Bayer, M.D.
Youth Clinic

LMB:R

Henry Ford Hospital

DEPARTMENT OF PEDIATRICS

DETROIT 2, MICHIGAN

JOSEPH A. JOHNSTON, M.D.
PHILIP J. HOWARD, M.D.
HARRY O. DAVIDSON, M.D.
BRENTON M. HAMIL, M.D.
GORDON MANSON, M.D.

Leona Bayer, M. D.
Presbyterian Medical Center
Clay and Webster Streets
San Francisco 15, California

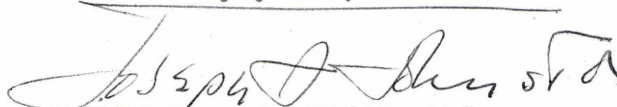
April
18
1961

Dear Doctor Bayer:

The reprint on the testosterone study is exhausted. I am sending along a few others bearing on the subject.

The reference to the testosterone article is as follows:
Factors Influencing Retention of Nitrogen and Calcium in
Period of Growth, VII, Effect of Methyl Testosterone,
Am.J. Dis. Child. 74:52, July, 1947.

Sincerely yours,



JOSEPH A. JOHNSTON, M.D.

Pediatrician-in-Chief

JAJ:vd
enclosures 3

April 29, 1961

Joseph A. Johnston, M.D.
Pediatrician-in-Chief
Henry Ford Hospital
Detroit 2, Michigan

Dear Doctor Johnston:

Thank you for the reprints and the additional reference.

It was a great pleasure to meet you at the Denver Conference and to hear your wise observations on so many aspects of adolescent medicine. You confirmed my belief that one of the best ways to understand the 10 - 20 decade, is to live through it with enough young people!

Sincerely yours,

Leona M. Bayer, M.D.

LMB:R

464 COLERIDGE AVENUE
PALO ALTO
CALIFORNIA

March 20, 1960

Leona M. Bayer, M.D.
San Francisco - Stanford Hospital
Clay and Webster Streets
San Francisco 15, California

Dear Doctor Bayer:

Forgive me the delay in my reply, but this is the result of my really heavy job at the hospital, which even precludes much correspondence.

We are going away for a short and much-needed holiday in a week's time, followed by another trip I must make. This, plus my having to be on duty occasional evenings and weekends leaves me little energy for extra-curricular things.

If I give up the half day which it would take to give a talk some place, it would mean I would have to squeeze out extra time for this in the short evenings at my disposal. I have felt that while I am on this job I must be very careful in taking on any extra commitments.

You were kind to send me a reprint of your paper which is among a number of things I am waiting to read.

I regret very much my inability at this time to undertake other things, but hope you will understand.

Sincerely yours,

George Hogle

George H. Hogle, M.D.

GHH:na

*Perhaps we can meet personally
though sometimes.*

G.H.

file H

February 12, 1960

George Hogle, M.D.
San Mateo Community Hospital
San Mateo, California

Dear Doctor Hogle:

I am so pleased to have "tracked you down", as Doctor Balint suggested. Now I am writing to ask if you think your busy schedule would allow you to meet with our newly organized Youth Clinic Staff some Wednesday, perhaps in March or April. We could make it either from 11 to 12, or at noon, whichever is the more feasible for you.

Under separate cover I am sending you a copy of the same reprint which I sent to Dr. Balint, and which caused him to think you might be interested in some professional contact.

Sincerely yours,

Leona M. Bayer, M.D.

LMB:R

phones - San Mateo Hospital 7Inside 1-1361
r. Davenport 6-8014
Coleridge St
Palo Alto, Calif.

SAN FRANCISCO-STANFORD HOSPITAL

XX

November 12, 1959

Dear Harold and Mary:

Your set of reprints arrived at a most opportune time. This Saturday I am taking part in an Adolescence Seminar, talking on the subject of, "Varieties and Significance of Growth Patterns in Adolescence". Mary's papers, and hers with Mussen, gave me just the material I need.

Thanks for having me on your mailing list.

Cordially,

Leona M. Bayer, M.D.

LMB:R

Harold E. Jone, Ph.D.
Mary C. Jones, Ph.D.
Institute of Human Development
University of California
Berkeley, California

JONES, Harold & Mary

Nov. 21, 1957

Dear Dr. Bayer -

Many thanks for your note and for initiating the invitation for me to talk at The Endocrine Clinic. I was very happy about the session there, and enjoyed talking with you again.

Your summary is excellent. I have suggested a few minor changes. Let me explain each one. (1.) 150 refers to the total number of human subjects studied; only about $\frac{1}{3}$ of them were in the pilot survey; I'm sorry if I gave the wrong impression.

(2.) The hydrocortisone elevation in new situations seems worth mentioning explicitly because it is quite striking.

(3.) We would like to study aldosterone too, and hope to, but there are no definite plans yet. The other 3 hormones are definite.

Once again, thanks for your kindness.

All best wishes,

David Hamburg

Psychosomatic News from Stanford University Hospitals.

November 20, 1957.

From: Leona M. Bayer, M.D.

To: Sam Nelken, M.D.

On November 20, 1957, the Stanford Endocrine Clinic heard a lively and persuasive presentation of psychosomatic relationships when David A. Hamburg discussed "Psychological Stress and Adrenal Cortical Function". Dr. Hamburg is this year at the Center for Advanced Study in the Behavioral Sciences, consolidating some work in which he has previously collaborated with various co-workers. His report concerned mainly the results of experimentation on primates in Walter Reed Hospital, and of observations on human subjects in Michael Reese Hospital. As a psychiatrist, his share has been the collection and evaluation of psychological data. This has then been correlated with physiological data independently derived.

Dr. Hamburg first described a pilot survey on ~~some 150~~ patients in crisis and recovery. Based on the ideas of stress developed by Selye, and on newer methods of establishing plasma hydrocortisone blood levels, this exploration established the general fact that hydrocortisone levels are higher in patients in distress than they are in normal controls.

Subsequent observations on both monkeys and men permitted the following inferences:

1. Fear leads to increased hydrocortisone levels, and such a physiological response will recur over periods of time, at least as long as 25 weeks.

2. New situations - such as transfer to a new laboratory or admission to a hospital - are in themselves anxiety producing, and tend to be associated with elevated hydrocortisone levels.

3. Behavioral responses and adrenal responses tend to be related.

Further observations are contemplated on the simultaneous behavior of ^{hydrocortisone,} aldosterone, epinephrine and norepinephrine.

NOV 23 1957

*rec'd back from Hamburg & corrections passed
onto Nelken by plane*

✓
CENTER FOR ADVANCED STUDY IN THE BEHAVIORAL SCIENCES

202 Junipero Serra Boulevard • Stanford, California

DAvenport 5-0026

October 4, 1957

Dr. Leona M. Bayer
Stanford University School of Medicine
2398 Sacramento Street
San Francisco, California

Dear Dr. Bayer:

Thank you very much for your invitation to meet with your group at the Stanford Endocrine Clinic. I am very appreciative of this opportunity and would welcome the comments and suggestions of your group since it would help me in planning my future research.

During the past few days I have been trying to figure out the best time for the meeting, since it so happens that the next few weeks present a particularly heavy schedule for me, including two trips to the East Coast. Therefore I am afraid the original date you suggested, November 6, would not work out. Indeed, I shall be out of town at that time. I would suggest Wednesday, November 20, if this is agreeable with you. For a title I would suggest "Psychological Stress and Adrenal Cortical Function". I should appreciate hearing from you as to whether this date and title will be satisfactory.

Once again, many thanks for your invitation. I look forward to meeting you.

Sincerely yours

David A. Hamburg

David A. Hamburg, M.D.

DAH:db

Oct.5, 1957

Dear Doctor Hamburg:

Title and date both excellent: we shall look forward to hearing you speak to us Wednesday morning at 11:15 o'clock in the Endocrine Clinic on "PSYCHOLOGICAL STRESS AND ADRENAL CORTICAL FUNCTION".

We hope you will be our guest for lunch after clinic, which would give us an opportunity for some informal exchange of ideas. If you plan to come by train, one of us could meet you at the station. Another possibility is that Dr. Mark Krupp would be glad to give you a ride up from Palo Alto earlier in the morning, if that would be convenient. He will contact you to make arrangements. There is plenty of time for details.

Sincerely yours,

Leona M. Bayer, M.D.

David A. Hamburg, M.D.
Center for the Advanced Study in the Behavioral
Sciences, Stanford, California

cc: Francis S. Greenspan, M.D.

September 27, 1957

David A. Hamburg, MD
Center for Advanced Studies in the Behavioral Sciences
202 Junipero Serra Blvd.
Stanford, California

Dear Doctor Hamburg:

The staff of the Stanford Endocrine Clinic is very pleased at the prospect of your coming to tell us about some of your recent psychosomatic research on stress problems. Will Wednesday morning, November 6, 11 a.m. be a convenient time for you? If this is not possible, any subsequent Wednesday in November would be agreeable.

Since our group is particularly interested in the cortico steroids, you might wish to phrase your title with this in mind.

I look forward to hearing from you, and to hearing more about your interesting observations.

Sincerely yours,

Leona M. Bayer, MD
Assoc. Clinical Professor of Medicine

LMB:LG
cc; Francis S. Greenspan, MD

Hamburg, David A.

Nov. 20, 1957

PATIENT'S NAME:

HISTORY NUMBER:

^{± 1949}
Selye - stress in rats - lying down - loud noise } → adrenal hypertrophy

Nelson & Samuels 1952 - Hydrocortisone in Plasma.

First survey in man - crisis & recovery - vs plasma Hydrocortisone levels
normal 12-13 mcg %
acute distress ± 20 mcg % ± 150 patients
both controls & patients studied on several occasions.

1953 } animal experimentation - Walter Reed
started } human " - Michael Reese

Animal Work - offers more freedom to observer - better control of subject
parameters - nervous system most similar to man.

role of cortex in relation to neuroendocrine control.

Hydrocortisone - normal 35 mcg %.

Level always goes up, reverses diurnal variation, whenever
a new situation presents.

Highest on Monday, definitely lower on weekend.
"Scaring" - by clicker → electric shock. Very terrified
5 mins.

Fear continues even after shock is removed - i.e. just
turn clicker 5 mins on, then off, etc.

Hydrocortisone - rises 40 mcg in 2 hours (25-60 mcg rise)
similar to rise with ACTH in graded doses

Trained to avoid shock by pressing lever at appropriate
intervals: "Conditioned avoidance" Not terrified.

Looks like "junior executive"

Adrenal response & behavioral response continued to ± 2 weeks

PATIENT'S NAME:

HISTORY NUMBER:

Continued

Similar experiments including epinephrine & norepinephrine
epinephrine rise drops out, while nor-e continues.

Human Observations confirm the rise in Hydrocortisone during stress
even over a long time.

Venning - Aldosterone rises under stress - Med student exam
low anxiety - sl. change
mod " - mod "
high " - high "

Independence of Physiological from Psychological Data is
very IMPORTANT - account of human capacity
for self perception.

Human Observations

anxiety - anger - depression

Rated by 2 "screen" observers, 2 interviews

Finally a "consensus" rating checked against physiological
Experienced observers correlated very well.

Stress - ① ~~using~~ interview of probing related into known problems

② measuring perception of time

③ measuring their social perception.

During first getting acquainted day, before stress
neurotic patients show much more reaction than
normal controls (soldiers)

Psychosomatic News from Stanford University Hospitals.

November 20, 1957.

From: Leona M. Bayer, M.D.

To: Sam Nelken, M.D.

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Subsequent observations on both monkeys and men permitted the following inferences:

1. Fear leads to increased hydrocortisone levels, and such a physiological response will recur over periods of time, at least as long as 25 weeks.
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3. Behavioral responses and adrenal responses tend to be related.

Further observations are contemplated on the simultaneous behavior of aldosterone, epinephrine and norepinephrine.

Psychosomatic News from Stanford University Hospitals.

November 20, 1957.

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To: Sam Melken, M.D.

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November 20, 1957

Miss Millicent L. Hathaway, Nutrition Specialist
United States Department of Agriculture
Agricultural Research Service
Institute of Home Economics
Washington 25, D. C.

Dear Miss Hathaway:

Thank you for sending me your reference bulletin on
"Heights and Weights of Children and Youth in the
United States". I am pleased both with the way in
which my material is used, and with its overall
contents and composition.

This little publication will be a real treasure
house of reference material.

Sincerely yours,

Leona M. Bayer, M.D.

LMB:R

UNITED STATES DEPARTMENT OF AGRICULTURE
AGRICULTURAL RESEARCH SERVICE
INSTITUTE OF HOME ECONOMICS
WASHINGTON 25, D. C.

HUMAN NUTRITION RESEARCH DIVISION

NOV 4 1957

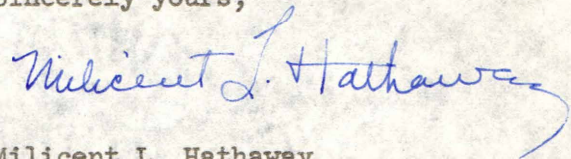
Dr. Leona Bayer
Stanford University
School of Medicine
2398 Sacramento Street
San Francisco 15, California

Dear Dr. Bayer:

The enclosed copy of our reference bulletin on "Heights and Weights of Children and Youth in the United States" is being sent to you in appreciation of your cooperation in contributing data for it. This supercedes the preliminary draft sent to you previously, which should now be destroyed.

As a follow up of this publication work is underway on a companion reference on heights and weights of adults in the U.S.

Sincerely yours,



Millicent L. Hathaway
Nutrition Specialist

Enclosure

March 15, 1956

Thomas H. Holmes, M.D.
Associate Professor of Psychiatry
University of Washington
Seattle 5, Washington

Dear Doctor Holmes:

I have just sent one of your reprints
to an interested medical student, and
would very much like to have a
replacement.

The reprint is: "The Relationship of
Stress, Adrenocortical Function, and
Tuberculosis", The American Review
of Tuberculosis, Vol. 60, No. 3,
March, 1954.

Cordial greetings,

Leona M. Bayer, M.D.

LMB:R

HOLMER, file

PAUL HOLMER, M. D.
14 RANCHERIA ROAD
KENTFIELD, CALIFORNIA

April 20th

Dear Dr. Bayer:-

You certainly are a very quick arranger! This is to confirm. You may count on me for May 19th - Wednesday at 11³⁰ a.m.

It occurs to me that I would rather not refer to my office as President of the Psychoanalytic Society in the announcement. Why not just say - member S.F. Psychoanalytic? The other may seem pretentious.

I may not be able to take advantage of your invitation to lunch since I must be back in Marin Co for a 1³⁰ hour.

Sincerely, Paul Holmer

October 8, 1946

Miss Joan Havel
1515 Arch Street
Berkeley, California

Dear Miss Havel:

Today I was able to make arrangements with Dr. Suzanne Reichard to work on the psychosomatic study with me at Stanford. Since she has had a great deal of clinical experience in related problems, I feel this is a most fortunate opportunity for our clinic.

I am writing you immediately so that you will not keep time open. At the same time I want to thank you very much for coming to see me about the project, and to wish you success in your plans for a PhD.

Sincerely yours,

Leona M. Bayer, M. D.
Assistant Clinical
Professor of Medicine

LMB:R

PAUL HOLMER, M. D.
FOUR-FIFTY SUTTER
SAN FRANCISCO 8, CALIFORNIA

August 28, 1945

Leona M. Bayer, M. D.
2233 Post Street
San Francisco, California

Dear Dr. Bayer:

I am sorry I was so long in getting these pictures to you, as I had promised. Unfortunately, I did not date the pictures, but I recall that they were taken just one year apart. You will easily be able to tell which ones are the "before" and which ones are the "after" pictures. This boy was treated with testosterone propionate, beginning with rather large doses of 25 milligrams three times a week and gradually tapering off to 25 milligrams once a week. The boy's whole emotional attitude changed and his voice changed from a very high-pitched squeak to a normal bass voice. He became much more stable, even without much in the way of psycho-therapy, which was impossible because of his extreme resistances.

Very truly yours,

Paul Holmer

Paul Holmer, M. D.

PH:cp

October 23, 1945

Dr. Paul Holmer
450 Sutter Street
San Francisco 8

Dear Dr. Holmer:

I have the slides of your problem boy in my car, ready to return to your office on my next visit to 450 Sutter.

Meanwhile, I thought you'd be interested to know that Dr. Bayley and I went over the pictures with our new criterea. In spite of the wonderful improvement, the second set of photos still shows many evidences of femininity in ourline and surface modeling, especially from the waist down.

Thank you again for sending me these pictures.

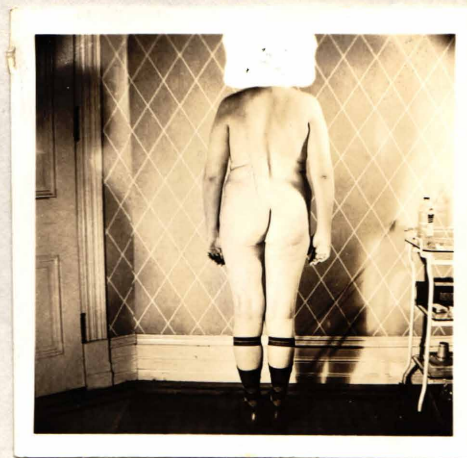
Sincerely,

Leona M. Bayer, M. D.

B:R

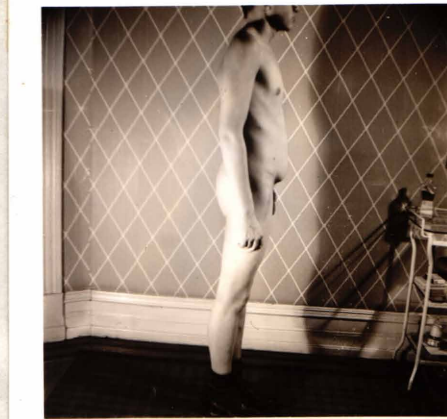
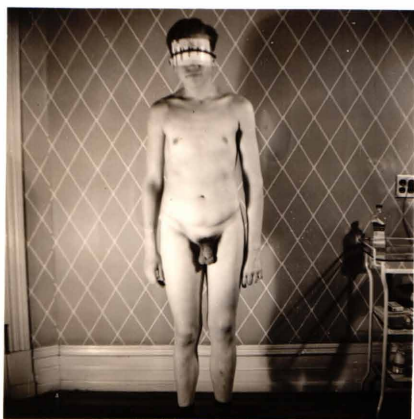
Dr. Holmes Case

Jan 1940



Rx. 25 mg. testosterone 3x week; then 2x week, then 1x week.

Dec 1940



February 28, 1950

Doctors A. Iliff, H. H. Gordon, W. R. Bell
Departments of Human Growth and Pediatrics
University of Colorado Medical Center
Denver, Colorado

Dear Doctors:

I would appreciate very much receiving a reprint of your recent article on Basal Metabolic Rate in Children, Pediatrics, December, 1949. Also, if the original standards are still available, as published in the Journal of Pediatrics, 23:1, 1943, I would also like to have the reprint containing them.

Sincerely yours,

LMB/rkg

Leona M. Bayer, M. D.

Judith S. Kestenberg, M. D.

21 EAST 87TH STREET

NEW YORK 28, N. Y.

LE 4-6011

January 8, 1955

Dr. Leona M. Bayer
2233 Post Street
San Francisco, Calif .

Dear Dr. Bayer:

I am sending you a copy of my manuscript
"Vicissitudes of Female Sexuality". I am sorry
for the delay but I had no manuscript and had to
wait until one had been returned. When you have
finished with it, will you kindly return it to me.

With every good wish for a happy New Year, I
remain,

Sincerely yours,

Judith S. Kestenberg
D.S.

May 12, 1955

Judith S. Kestenberg, M. D.
21 East 87th Street
New York 28, New York

Dear Doctor Kestenberg:

When your manuscript "Vicissitudes of Female Sexuality" reached me, I was involved in getting together a manuscript of my own for a "Handbook on Evaluation of Growth and Development". So I put your paper aside temporarily, not expecting that it would be May before I would finally read it. I do hope this delay in its return has not inconvenienced you. Thanks very much for sending it.

Reading it now, I am again impressed with the logic of your theory of female sexual development, although I miss the many case illustrations that enlivened your December presentation. It seems to me that, especially in the area of infantile development, all first hand observations such as yours are gold, and form an important bulwark against the danger of assuming that when new hypothesis fit in with Freud's brilliant contentions, they are therefore substantiated.

Your manuscript is coming to you under separate cover, along with two reprints of my own. As you will see, one of these is based on observations, but the other is almost pure speculation.

Sincerely yours,

Leona M. Bayer, M. D.

LMB:R

Name
and No.

LILLY - INSULIN, mixed
QANTS

THE LILLY RESEARCH LABORATORIES

ELI LILLY AND COMPANY
INDIANAPOLIS 6, IND., U. S. A.

April 30, 1948

Leona M. Bayer, M.D.
Department of Medicine
Stanford University School of Medicine
2398 Sacramento Street
San Francisco, California

Dear Dr. Bayer:

After talking with my colleague, Dr. F. B. Peck, on his return from San Francisco, I dictated a letter to you yesterday afternoon. Before it could be typed however, this morning's mail brings your letter of April 28th. I am very much interested in your experience with diethylstilbestrol for inhibition of growth. It seems to me that your observation that A.D. began to grow again as soon as diethylstilbestrol was discontinued is a strong indication that the effects of the drug do not persist beyond its administration. Doses of this size will, of course, stimulate development of all the genital tissues, including the endometrium, and prolonged administration is likely to induce endometrial hyperplasia and irregular bleeding. Since menstruation cannot be considered abnormal at eleven years of age, it is my suggestion that a patient such as this be given progesterone periodically if she shows a tendency to bleed irregularly. The administration of 10 mg. progesterone intramuscularly for three doses on alternate days will produce the secretory phase which will be followed by true menstruation. Treatment of this kind at intervals of four to six weeks should prevent hyperplastic changes.

Your letter raises a very interesting question; namely, whether different estrogens have comparatively different quantitative effects on different tissues. Of course, the simplest concept is that if estrogen A has x degree of effect on the endometrium and y degree of effect on vaginal mucosa, and if estrogen B has $2x$ effect on the endometrium, then estrogen B will have a $2y$ effect on vaginal mucous membrane. It is entirely possible, however, that estrogen B might have a y effect on the vaginal mucosa or even a $3y$ or a $10y$. These are questions which are very difficult to investigate for the reason that the results cannot be transferred from one species to another but have to be established separately for each species. As a matter of fact, the subject deserves, in my opinion, much more attention than it has been given.

The question as it relates to your problem is this. Can you find an estrogen which will have a high inhibiting power against the anterior pituitary and a low stimulating power on the endometrium? No one has yet brought forth such a compound very definitely, and no other estrogen has been shown to have an advantage over diethylstilbestrol with regard to this proportion.

Dr. Leona M. Bayer
Stanford University School of Medicine
San Francisco, California

Estriol is a very weak estrogen all around. It does not produce bleeding because it has practically no stimulating effect on the endometrium. I do not believe it has any significant inhibitory effect on the anterior pituitary either. It is, in fact, impossible to state the comparative potency of estriol and diethylstilbestrol. Animal assays differ by several thousand percent, and there is no reason to believe that any of them have any direct bearing on human potency. We market estriol in capsules of .06, .12, and .24 mg. We would not be able to supply it in larger capsules, but we would be willing to send you a supply for trial if you think it worth-while. I would not know what dosage to suggest. I personally think that its use will be a waste of time, but I would not set that up as a final opinion.

Dr. Peck brought up the question of estrogenic therapy in young girls tending to cause later sterility. I think the best answer to that is the promptness with which normal spontaneous menstrual function is resumed after diethylstilbestrol therapy has been discontinued. Dr. Fancher told me that his girls almost invariably had their first menstrual period about six weeks after discontinuing diethylstilbestrol. This corresponds very well with the theoretical consideration that the effect of the drug stops as soon as it is discontinued. What has been your experience in girls past the menarche?

I am very much interested that two of your patients have no significant inhibition of growth. Until larger doses have been tried, one can make no certain predictions as to risks. I should not like to treat very young children with large doses of estrogen over a long period of time, but after a girl reaches twelve or thirteen, I see no objection to a careful trial. Of course, all new therapy -- and some old -- carries a certain amount of unpredictable risk.

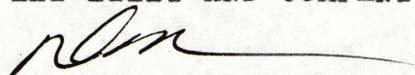
Have you run into any trouble with nausea on the 5 mg. daily dosage? I think you might on the 10 mg. We have found pyridoxine hydrochloride rather effective in preventing nausea from estrogens.

Perhaps after receiving this letter you will have additional comments. I would be interested to hear in more detail about the entire menstrual history of the three girls who have received diethylstilbestrol. I might then have additional comment myself.

I see no good prospect of a trip to California before the A.M.A. meets there next. If I come, I shall certainly get in touch with you. Are you going to be in Chicago for the meetings in June?

With kindest regards.

Yours very truly,
ELI LILLY AND COMPANY


D. C. Hines, M.D.
Medical Department

ELI LILLY AND COMPANY

INDIANAPOLIS 6, U.S.A.

April 22, 1947

Leona M. Bayer, M.D.
Department of Medicine
Stanford University School of Medicine
2398 Sacramento Street
San Francisco, California

Dear Leona:

I am very much interested in your letter of April 15th on your experience in treating overly tall adolescent girls.

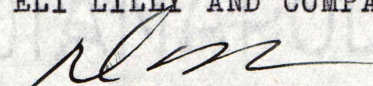
I frankly do not see any real danger in increasing the doses of diethylstilbestrol to 5 mg. I do believe, however, that at this dosage level there may be a few instances of irregular uterine bleeding even though the administration is continuous. Whereas unexpected bleeding might be alarming in a woman of menopausal age, I do not see why it need be a cause of concern in this age group, particularly if the patient and her mother are prepared for it. However, I have no assurance that you will see any sizeable incidence of this sort of thing.

It seems to me that with the analogy of pregnancy there is no reason to fear continuous estrogenic administration at high levels for periods of nine months, and I see no reason why one year would not be equally safe; however, I do think that continuation without interruption for much longer than one year would bring the patient into rather unknown territory in which there is no basis for prediction of exactly what may happen -- if anything.

I appreciate very much your letting me know what is happening in this study, and I will be very much interested in hearing about further progress. I expect to attend the Endocrine Meeting in Atlantic City the first part of June, and perhaps we can have a visit then.

With kindest regards.

Yours very truly,
ELI LILLY AND COMPANY


D. C. Hines, M.D.
Medical Department

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April 28, 1948

Dr. Don Carlos Hines
Eli Lilly and Company
Indianapolis 6, Indiana

AIRMAIL

Dear Don:

Here is another report on the treatment of tall girls, and another request for advice.

There are now three youngsters between eleven and thirteen years, whom I have had on continuous dosage of diethyl stilbestrol, 5 mgs. daily for varying lengths of time. Two of them had no significant inhibition of growth nor improvement in height prediction. One girl (A.D.), however, stayed right at 65.5 inches during the whole nine months of treatment, and her height prediction dropped from 70 to 68 inches. Since stopping medication she is growing again at her old rate. This girl, as well as the others, had several menstrual periods even while she was on continuous diethyl stilbestrol, none excessive but a little disturbing to me!

These are the questions I want to ask you: Do you think another preparation might have less tendency to stimulate bleeding? Sevringhaus suggested estriol. Do you have this available in comparable dosage forms so that it could be tried? I know your commercial tablets are small, but maybe you would have another form for experimental use. Would you advise trying it? Would you be interested in supplying enough for treatment in two or three girls?

With regard to diethyl stilbestrol, have you had reports from other clinics which would throw more light on risks and dosages? If I am going to continue with it, I would like to prescribe up to 10 mg. per day. There is a premenarchial, eleven year old girl (M.L.) whose height prediction is 71 inches, on whom I would like to start treatment next week. There is also the question of resuming treatment on A.D. after a suitable interval.

Thank you again for any wise words you may have. I hope you come out here this summer, so I can show you some records.

Cordially,

Leona M. Bayer, M. D.

LMB:R

April 15, 1947

Dr. Don Carlos Hines
Eli Lilly and Company
Indianapolis 6, Indiana

Dear Don:

You will remember our correspondence with regard to the treatment of two tall girls.

Among the youngsters I have under observation, I now have two on whom I think I see some results. One of them is on 3 mg. diethyl stilbestrol daily; in the other, I have just increased the dose to 5 mg. per day. Both are 11 years old. Menarche in both supervened after the first cyclic administration of the estrogen, but I have now started both on continuous medication, thinking that especially in these younger girls it is better to suppress the cycle entirely.

Do you see any danger in upping the dose to 5 mg. per day? There have been no toxic symptoms. I am doing rectal examinations every two months to check on uterine size. Do you suggest any other safeguards? Do you suggest a time limit beyond which it would be unwise to continue uninterrupted medication, as six months or one year?

Incidentally, I find that the calcium and vitamin D is not well liked, and I think, anyhow, results will depend on the effectiveness of the stilbestrol rather than on collateral aids.

Thank you for your continuing interest.

Sincerely,

Leona M. Bayer, M. D.

LMB:R

December 17, 1946

Dr. Don Carlos Hines
Eli Lilly and Company
Indianapolis 6, Indiana

Dear Don:

Your letter of December 6 is a great help. Thank you. I am immediately stepping up the diethylstilbestrol dosage, as you suggest. Your comments about gastrointestinal symptoms and about the unimportance of inhibiting menstruation are also very apt.

I'm glad to know you think well of Dr. Fancher's work. We have corresponded, and he sent me a recent reprint.

The only exception I would take to your advice is about thyroid. There is a good deal of published data and also some evidences from my own cases to show that thyroid has even more effect in speeding maturation than in stimulating growth. In fact, that is its great danger in dwarfism. However, I'll watch the effects critically, and will report to you as things progress in general.

Sincerely,

Leona M. Bayer, M. D.

LMB:R

Dr. Bayer

AIRMAIL

November 26, 1946

Dr. Don Carlos Hines
Eli Lilly and Company
Indianapolis 6, Indiana

Dear Don:

Here we are with another project with which we would like your advice and help.

Too tall girls are coming for treatment in increasing numbers, especially since the recent "Life" story on Dr. Nancy Bayley's growth studies. With Dr. Bailey's prediction tables, we have a good instrument for measuring whether or not we are able to influence adult stature. Progress is charted by frequent height readings and bone age x-rays every six months at least. So far, results are inconclusive.

The treatment program has been tentatively and cautiously developed. At present, in adolescent girls, either before or after the menarche, I am giving:

Thyroid, where the BMR or Blood Cholesterol indicate it.

Diethyl stilbestrol (Lilly), 1 mg. every night from the 1st to the 24th day of the cycle.

Prothone, 10 mg. every night from the 20th to the 24th day of the cycle, where it is necessary to keep the menses regular.

Vitamin D with Dicalcium Phosphate (Lilly), 2 tablets 3 times daily, i.e., about 4,000 units of D per day.

Do you have any comments on this plan? The rationale is, of course, both to foster skeletal maturation and perhaps also to depress growth hormone production or action. Would you have any suggestions concerning dosages? Would you think it advisable to try larger doses of either D or the Diethyl stilbestrol? I have talked this over with Dr. Hanzlik, and it appears it's all a stab in the dark.

There is also a slight possibility that one of the men on a post-war research fellowship would try out treatment possibilities on some laboratory animal, perhaps mice. If this should materialize, do you think Lilly might supply the medication?

I hope this is not too far out of your field of interest. I shall appreciate hearing from you.

Sincerely,

Leona M. Bayer, M. D.

LMB:R

ELI LILLY AND COMPANY

INDIANAPOLIS 6, U.S.A.

December 6, 1946

Dr. Leona M. Bayer
Stanford University
School of Medicine
2398 Sacramento Street
San Francisco, California

Dear Leona:

I have been out of town and consequently have not been able to answer your letter of November 26 on the treatment of tall girls.

Of course I heard the paper which you and Dr. Nancy Bayley gave at the Meeting of the Association for the Study of Internal Secretions last summer. I saw the story in the magazine, LIFE, and I am not surprised that it has created a great deal of interest.

Do you know Dr. J. K. Fancher of Atlanta, Georgia? He is a very competent endocrinologist and is particularly interested in children. He usually attends the endocrine meetings. Some years ago he was very much interested in this matter of checking growth in overly tall adolescent girls. His technic was to administer rather large doses of estrogen, sufficient to inhibit completely the output of gonadotropin. Of course, menstruation was suppressed in these girls, but it invariably returned six weeks after cessation of therapy. Of course, you have gotten around this amenorrhea by giving pranone for a few days each four weeks. Dr. Fancher also gave rather large doses of calcium by mouth and 1,000 units of vitamin D daily as aids in the closure of the epiphysis. It was his observation that he could not check growth unless he removed milk completely from the diet.

I have had no personal experience with the treatment of this condition. Judging from what is known of the effects of the various endocrine preparations in animals, I am inclined to agree in general with your line of attack, but I have some suggestions. I am not certain that 1 mg. of diethylstilbestrol is a sufficiently large dose. I would suggest that if the girls do not stop growing promptly, the dose might be doubled or tripled. As you know, diethylstilbestrol is not toxic.

Even on 3 mg. a day I do not believe many young girls will have gastro-intestinal disturbances. If they do, I suggest the administration of 50 to 100 mg. vitamin B₆ daily by mouth for a week or two, and if this does not prevent nausea, the concomitant administration of 50 to 100 mg. thiamin chloride for the same period.

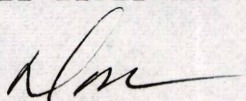
It seems to me, in view of Dr. Fancher's experience, your suggested dosage of vitamin D is adequate. In my opinion, the pranone serves no function other than to induce bleeding. Of course, this may be good psychotherapy and may avoid alarm on the part of the patient's mother over her amenorrhea. I personally believe it would be much wiser not to give any of these girls thyroid. As you know, one of the most striking features of hypothyroidism in children is the lack of growth. All the work on animals also indicates that thyroid is a potent growth-stimulating substance. It apparently does not lead to closure of the epiphyses, and of course closure of the epiphyses is what is desired in these patients.

If you are going to do some studies in animals, we would like to have the opportunity of providing the material for treatment. Of course, we sometimes have our supply difficulties in these times so that I can make no blanket promise without having some idea of the substances and quantities required.

You may be interested in the attached bibliography. While it is probably not complete, it may save you some time.

I am very much interested in this subject, and I hope you will keep me informed of the progress of your work.

Very truly yours,
ELI LILLY AND COMPANY


D. C. Hines, M. D.
Medical Department

dm

THOMAS R. MC LIN, M. D.

450 SUTTER STREET - SUITE 2340

SAN FRANCISCO 8, CALIF.

OCTOBER THE ELEVENTH
NINETEEN FORTY-FIVE

DEAR DOCTOR PECK,

I HAVE GONE OVER YOUR CORRESPONDENCE WITH DOCTOR BAYER WITH GREAT INTEREST. I HAVE BEEN USING MIXED INSULIN IN THE CONTROL OF DIABETES FOR A LITTLE MORE THAN TWO YEARS, AND DURING THAT TIME I HAVE FOLLOWED FORTY THREE CASES; FOUR CASES ARE AT PRESENT UNDER OBSERVATION AND IN THE PROCESS OF BEING BROUGHT UNDER CONTROL ON MIXED INSULIN IN THE OUTPATIENT CLINIC OF THE STANFORD UNIVERSITY HOSPITAL. IT HAS BECOME OUR POLICY TO USE MIXED INSULIN IN ALL CASES IN WHICH DO NOT GET GOOD CONTROL ON PROTAMINE ALONE; NO NEW CASES ARE BEING STARTED ON GLOBIN OR ANYOTHER INTERMEDIATE INSULIN, AND MOST OF THOSE WHO WERE PREVIOUSLY ON GLOBIN ARE NOW ON OTHER THERAPY.

IT HAS BEEN OUR EXPERIENCE IN THE CLINIC WITH MIXED INSULIN (AND THIS EXPERIENCE HAS CONFIRMED MY PREVIOUS FINDINGS) THAT THERE IS NO ONE MIXTURE WHICH IS SUITABLE FOR ALL INDIVIDUALS. ONE PATIENT STABILIZED ON A MIXTURE CONTAINING THIRTY-TWO UNITS OF CRYSTALLINE WITH FOUR UNITS OF PROTAMINE ZINC INSULIN. AT THE OPPOSITE EXPTREME IS A YOUNG MAN WHO STABILIZED ON A MIXTURE OF TWENTY EIGHT UNITS OF CRYSTALLINE WITH TWENTY UNITS OF PROTAMINE ZINC.

OUR ROUTINE IN THE USE OF MIXED INSULIN IS AS FOLLOWS: THE PATIENT IS STARTED ON PROTAMINE ZINC INSULIN ALONE [AND THE DOSE VARIED AS NECESSARY TO OBTAIN A NEGATIVE BEFORE BREAKFAST SPECIMEN. CRYSTALLINE INSULIN IS THEN GIVEN THREE TIMES A DAY BEFORE MEALS AS SEPARATE INJECTIONS ACCORDING TO A SLIDING SCALE BASED UPON EITHER THE BENEDICT'S OR THE CLINITEST REACTION. WHEN CONTROL OF THE GLYCOSURIA HAS BEEN ESTABLISHED WITH SEPARATE INJECTIONS IN THIS MANNER THE PATIENT IS THEN CHANGED OVER TO MIXED INSULIN. THE INITIAL DOSE OF MIXED INSULIN GIVEN AS A SINGLE INJECTION BEFORE BREAKFAST IS SET AT APPROXIMATELY EIGHTY-FIVE TO NINETY PERCENT OF THE TOTAL UNITAGE PREVIOUSLY REQUIRED

THOMAS R. McLIN, M. D.

450 SUTTER STREET - SUITE 2340

SAN FRANCISCO 8, CALIF.

PAGE 2

OCTOBER 11, 1945

TO ACHIEVE CONTROL WITH SEPARATE INJECTIONS OF THE TWO KINDS OF INSULIN. THE TWO TO ONE MIXTURE IS USED INITIALLY IN THOSE CASES WHERE THE RATIO OF CRYSTALLINE TO PROTAMINE WAS RELATIVELY LOW; THE THREE TO ONE IN THOSE CASES WHERE THE RATIO WAS RELATIVELY HIGH. AFTER THE PATIENT HAS BEEN ON THE MIXED INSULIN FOR THREE TO FOUR DAYS THE AMOUNT OF PROTAMINE IN THE MIXTURE IS ADJUSTED AGAIN SO THE SPECIMEN BEFORE BREAKFAST IS JUST NEGATIVE. THE CARBOHYDRATE IN THE DIET IS THEN ADJUSTED SO THAT THERE IS APPROXIMATELY THE SAME AMOUNT OF SPILLAGE AFTER EACH MEAL. THE CRYSTALLINE ZINC IN THE MIXTURE IS THEN ADJUSTED AS NECESSARY TO ACHIEVE NEGATIVE OR FAINTLY POSITIVE TESTS BEFORE LUNCH, BEFORE SUPPER, AND AT BEDTIME. FOLLOWING THESE BASIC PRINCIPLES WE HAVE ACHIEVED QUITE GOOD RESULTS, ALTHOUGH AS I HAVE SAID BEFORE, THE RELATIVE PROPORTIONS OF INSULIN IN THE MIXTURE VARIES MARKEDLY FROM ONE PATIENT TO ANOTHER.

THERE HAS BEEN SOME DIFFICULTY WHEN THE PATIENT FINISHES ONE BOTTLE OF PROTAMINE ZINC INSULIN AND HAS TO CHANGE TO A NEW BOTTLE IN THAT IN MAKING THE CHANGE OVER TO A NEW BOTTLE OF INSULIN, CONTROL OFTEN IS LOST SO THAT THE RELATIVE PROPORTIONS OF INSULIN IN THE MIXTURE MUST BE CHANGED. I HAVE ASSUMED THAT THE CHANGE IN THE RATIO OCCURRING WHEN A NEW BOTTLE OF PROTAMINE IS STARTED IS DUE TO ONE OF TWO FACTORS: EITHER THE AMOUNT OF EXCESS PROTAMINE IN THE BOTTLE VARIES FROM ONE LOT TO THE NEXT, OR THERE IS SUFFICIENT VARIATION IN THE PH OF THE INSULINS TO EFFECT THE FINAL PH OF THE MIXTURE SIGNIFICANTLY. AS I UNDERSTAND IT, THE RELATIVE PROPORTION OF FREE TO FIXED INSULIN IN ANY MIXTURE IS DEPENDENT UPON TWO FACTORS; ONE, THE RELATIVE CONCENTRATION OF INSULIN IN EACH FORM (AN INCREASE IN THE AMOUNT OF FREE INSULIN IN A MIXTURE WILL INCREASE THE AMOUNT OF INSULIN WHICH IS BOUND TO A FIXED QUANTITY OF PROTAMINE); AND TWO, THE PH OF THE MIXTURE.

I ASSUME THAT FOR COMMERCIAL PURPOSES IT IS NOT NECESSARY TO HOLD

THOMAS R. McLIN, M. D.

450 SUTTER STREET - SUITE 2340

SAN FRANCISCO 8, CALIF.

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OCTOBER 11, 1945

THE PH OF CRYSTALLINE INSULIN WITHIN NARROW LIMITS IN AS MUCH AS THE PRIME REQUISITE IS THAT THE PH OF THE CRYSTALLINE INSULIN BE KEPT LOW ENOUGH TO GUARANTEE THE STABILITY OF THE SOLUTION. LIKEWISE, I ASSUME THAT WITH PROTAMINE ZINC INSULIN IT IS NOT NECESSARY TO CONTROL THE EXCESS OF PROTAMINE PRESENT WITHIN NARROW LIMITS BUT RATHER ONLY NECESSARY THAT THERE BE SUFFICIENT EXCESS PRESENT TO INSURE THAT ONLY AN INCONSIDERABLE PROPORTION OF THE INSULIN IN THE MIXTURE SHALL BE IN THE FREE STATE. HOWEVER, I THINK IT WOULD BE HIGHLY VALUABLE FROM THE STANDPOINT OF MAKING A MIXTURE WITH DEFINITE CHARACTERISTICS TO HAVE A CRYSTALLINE INSULIN WHOSE PH IS RIGIDLY CONTROLLED AND A PROTAMINE INSULIN IN WHICH THE EXCESS OF PROTAMINE IS KEPT WITHIN NARROW RIGIDLY CONTROLLED LIMITS. INSULINS WITH THESE CHARACTERISTICS WOULD GREATLY FACILITATE ACCURATE ADJUSTMENT OF MIXED INSULIN. IN ADDITION I THINK IT WOULD BE WELL IF POSSIBLE, TO HAVE SUFFICIENT BUFFERING OF THE PROTAMINE ZINC INSULIN TO INSURE THAT THE PH OF THE RESULTANT MIXTURE WOULD BE NEUTRAL OR ALKALINE. I AM AWARE THAT FREE INSULIN IS UNSTABLE AT THIS PH BUT IN AS MUCH AS THE TIME INTERVAL BETWEEN MAKING THE MIXTURE AND USING IT IS SO SMALL THIS SHOULD NOT PROVE OF GREAT CONSEQUENCE.

THE DISTRIBUTION OF CRYSTALLINE INSULIN IN AN OVERSIZE BOTTLE SO THAT MIXTURES CAN BE MADE EASILY BY THE EXTEMPORANEOUS ADDITION OF THE PROPER AMOUNT OF PROTAMINE ZINC MIGHT BE ADVANTAGEOUS, PARTICULARLY WITH THOSE INDIVIDUALS WHO HAVE DIFFICULTY IN GRASPING THE TECHNIQUE OF MAKING THE MIXTURE WITHIN THE SYRINGE; HOWEVER, IT HAS BEEN MY EXPERIENCE THAT MOST PATIENTS WHO REQUIRE MIXED INSULIN HAVE NO REAL DIFFICULTY IN LEARNING TO MAKE THE MIXTURE IN THE SYRINGE AT THE TIME OF INJECTION.

TO SUMMARIZE: IT HAS BEEN OUR EXPERIENCE THAT EXTEMPORANEOUS MIXTURES OF CRYSTALLINE ZINC AND PROTAMINE ZINC INSULIN GIVE EXCELLENT RESULTS

THOMAS R. MCLIN, M. D.

450 SUTTER STREET - SUITE 2340

SAN FRANCISCO 8, CALIF.

PAGE 4

OCTOBER 11, 1945

IN THOSE CASES NOT CONTROLLABLE WITH PROTAMINE ALONE; THAT RIGID CONTROL OF THE PH OF THE CRYSTALLINE ZINC INSULIN, AND OF THE EXCESS OF PROTAMINE ZINC INSULIN WOULD FACILITATE THE MAKING OF THE MIXTURES ACCURATELY AND REPRODUCIBLY; AND THREE, THAT THE DISPENSING OF CRYSTALLINE ZINC INSULIN IN AN OVERSIZE BOTTLE WOULD PROVE OF VALUE IN SOME CASES.

WE APPRECIATE THE OPPORTUNITY OF WORKING WITH YOU ON THIS PROJECT. ANY SUGGESTIONS YOU MIGHT HAVE REGARDING OUR WORK HERE WOULD BE APPRECIATED.

SINCERELY,

F.B. PECK, M.D.
ASSOCIATE DIRECTOR
MEDICAL DIVISION
LILLY RESEARCH LABORATORIES
INDIANAPOLIS 6, INDIANA

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/
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THE LILLY RESEARCH LABORATORIES

ELI LILLY AND COMPANY
INDIANAPOLIS, IND., U. S. A.

October 2, 1945

Dr. Leona M. Bayer
Stanford University Hospitals
Clay and Webster Streets
San Francisco 15, California

Dear Dr. Bayer:

Many thanks for the comments in your letter of September the twenty-fifth. Since you are in position to make some further studies in your clinic along with Dr. McLin, I am taking the liberty of sending two additional special preparations for comparison with the material you have already studied. One of these is NP50, lot T-1716, which contains slightly more protamine than the NP42 preparation, lot T-1846. It is the product that Dr. MacBryde has reported on so enthusiastically.

The other material is right in line with your own suggestion. It consists of an oversized vial containing 10 cc. of Iletin (Insulin, Lilly) and enough space to permit the addition of several cc. of Protamine Zinc Insulin. Thus a mixture may be readily prepared which may be altered to fit individual circumstances and yet which will be under proper supervision. Addition of the Protamine Zinc Insulin is facilitated by using an extra sterile needle to serve as an exhaust vent and by turning the vial on its side to avoid splashing and excess frothing and foaming. I will be very much interested in your experience with this method.

As far as adjustment of the pH values of Protamine Zinc Insulin and any of the modified preparations, whether crystalline or amorphous, little can be done to bring Protamine Zinc Insulin to an acid pH like Insulin. It results in a clear preparation but one having a different time-activity very similar to that of Globin Insulin. To distribute Insulin made from crystalline sources at the same pH as Protamine Zinc Insulin (7.2) would be impractical since the stability of free Insulin is only about

Dr. Bayer
page 2

one-tenth at pH 7.2 what it is in the acid range below the iso-electric point. As a matter of fact, this is one of the problems that has held back the distribution of special modifications such as NP50 and NP42 since they are adjusted to 7.2 and contain some unprecipitated Insulin.

The shipment will contain twenty vials of NP50 and thirty oversized vials, lot W-1833. Should you need additional material, please do not hesitate to get in touch with us.

Again thanking you for your kind co-operation.

Very truly yours,

ELI LILLY AND COMPANY



F. B. Peck, M. D.
Associate Director
Medical Division

FBP:MW

September 25, 1945

F. B. Peck, M. D.
The Lilly Research Laboratories
Eli Lilly and Company
Indianapolis 6, Ind.

Dear Dr. Peck:

In answer to your letter of September 19, I think I can best summarize our experience with modified insulins by stating our conclusions, namely:

- 1) That the optimum proportion of protamine to crystalline insulin necessarily varies with each patient, the severity of his diabetes, his living routine, etc.
- 2) For this reason we feel that it is perhaps better not to market another intermediate type of insulin but that instead:
- 3) We would like to see the making of extemporaneous mixtures simplified by attention to the following factors:
 - a) Standardization of Protamine so that a constant amount of protein exists in every bottle. Adjusted mixtures for every patient could thereby be reliably reproduced, as is not now always the case.
 - b) Standardization of Protamine and crystalline insulins to the same pH.
 - c) The marketing of an empty vial of about 30 cc size, in which mixtures could easily be made and stored by the patient.

Dr. McLin who is now in our clinic has taken a special interest in this problem for several years and is now taking the main interest in it in our clinic. He will send you a summary within the next few days.

I hope this note is helpful to y

orking on this problem.

Sincerely,

Dr. Leona M. Bayer
Endocrine Clinic

THE LILLY RESEARCH LABORATORIES

ELI LILLY AND COMPANY
INDIANAPOLIS, IND., U. S. A.

September 19, 1945

Dr. Leona M. Bayer
Stanford University Hospital
Clay & Webster Streets
San Francisco, California

Dear Dr. Bayer:

During the past year data have continued to accumulate which indicate that the most generally useful of the specially modified Insulin series are those preparations having a time-activity in the range of the products designated NP50, lot T-1716; NP42, lot T-1846; and the 2:1 mixture, either extemporaneously admixed or premixed in vials.

As a guide to further evaluation, your opinion regarding the comparative place of these or any other special modifications will be extremely helpful. If actual comparative data are not available, please let me have at least a brief summary of your experience thus far. These data will be needed by the fifteenth of October in order that they may be tabulated for presentation to the Insulin Committee.

Many thanks for your kind cooperation.

Very truly yours,

ELI LILLY AND COMPANY


F. B. Peck, M. D.
Associate Director
Medical Division

FBP:MW

THE LILLY RESEARCH LABORATORIES

ELI LILLY AND COMPANY • INDIANAPOLIS 6, IND., U. S. A.

July 23, 1945

Dr. Leona M. Bayer
Stanford University Hospitals
Clay and Webster Streets
San Francisco, California

Dear Dr. Bayer:

This will acknowledge your letter of July seventeenth to Dr. Peck. Dr. Peck is out of the city and your letter is being held for his attention upon his return about August first.

Very truly yours,

ELI LILLY AND COMPANY

Mary Halvey
Secretary to Dr. F. B. Peck

THE LILLY RESEARCH LABORATORIES

ELI LILLY AND COMPANY
INDIANAPOLIS, IND., U. S. A.

July 31, 1945

Dr. Leona M. Bayer
Stanford University Hospitals
Clay and Webster Streets
San Francisco, California

Dear Dr. Bayer:

Thank you for your letter of July seventeenth which was received during my absence from the city. There is one statement in it that suggests that I may have given you the wrong impression regarding the stability of these various combinations. That is the one to the effect that since stability is very desirable probably a neutral rather than an acid preparation is preferable. As a matter of fact the acid preparations of Insulin are far more stable than those in the alkaline or neutral zone. For example, the Insulin in the supernatant of some of the buffered combinations is only one-tenth as stable as the product which is below the isoelectric point. Thus the clear or acid preparations would be ideal in so far as stability alone is concerned. At the present time we have no neutral modifications having a span of action of 14 - 18 hours. One of these was prepared a year or so ago and tested clinically, but abandoned owing to its inability to cover the entire twenty-four-hour period satisfactorily. It appears that the most desirable action is one incorporating some over-lapping. The latter effect makes it possible for the patient to handle a breakfast of reasonable size without undue hyperglycemia, and it can be obtained with a mixture of two to three parts of Insulin to one part of Protamine Zinc Insulin, or by a buffered combination ranging between 0.4 or 0.5 mg. of protamine per 100 units of Insulin.

Under separate cover we are forwarding a half dozen vials of specially modified Protamine Zinc Insulin, NP42. It is a product of this type. We will be very much interested in your observations.

Very truly yours,

ELI LILLY AND COMPANY


F. B. Peck, M. D.
Associate Director
Medical Division

FBP:MW

July 17, 1945

Dr. F. B. Peck, Associate Director
Medical Division
The Lilly Research Laboratories
Eli Lilly and Company
Indianapolis 6, Indiana

Dear Dr. Peck:

I have waited until now to answer your letter of June 20th because I wanted to talk over this insulin problem with some of the other workers in the clinic. We have come to the conclusion that what we need for most of our patients is one of the longer, rather than the shorter acting modifications. Also, since stability is very desirable, probably a neutral, rather than an acid preparation is preferable.

Therefore, if you make up any neutral modifications with an action span of 14 - 18 hours, we will be very grateful for an opportunity to try out such a preparation. Meanwhile, we will keep the last lots which you sent us, T-1934 and T-1900, on hand in case a suitable patient comes along for their use.

Sincerely yours,

Leona M. Bayer, M. D.
Assistant Clinical Professor
of Medicine

B:R

THE LILLY RESEARCH LABORATORIES

ELI LILLY AND COMPANY
INDIANAPOLIS, IND., U. S. A.

June 20, 1945

Dr. Leona M. Bayer
Stanford University Hospitals
Clay and Webster Streets
San Francisco, California

Dear Dr. Bayer:

Many thanks for your letter of June fourteenth with the attached summary of progress of the case of Mrs. D. N. who was treated with specially modified Protamine Zinc Insulin, NP42.

Since NP42 does not appear active enough in the afternoon, it might be worthwhile to employ a still shorter acting modification. With this in mind I am sending four vials each of AP175, lot T-1934, which you received early in the year, and AP125, lot T-1900, a still more rapidly acting modification. Both of these are acid modifications and as a matter of fact most of the evidence thus far indicates that they act too briefly to occupy a particularly useful zone. The same observation has applied to the buffered modifications containing less than 0.4 mg. of protamine per 100 units. Considerable work was done with NP31 which was discarded for this reason and supplies are no longer available. Unfortunately these shorter acting modifications do not span the night period with enough intensity to control the night rising blood sugar level even though they might work pretty well during the daytime.

I will be very much interested in your continued observations.

Very truly yours,

ELI LILLY AND COMPANY



F. B. Peck, M. D.
Associate Director
Medical Division

FBP:MW

June 14, 1945

Dr. F. B. Peck
Associate Director, Medical Division
The Lilly Research Laboratories
Eli Lilly and Company
Indianapolis 6, Indiana

Dear Dr. Peck:

Enclosed are Dr. Windsor Cutting's notes on the use of NP42 during pregnancy. You will note, control was less successful than with Crystalline alone. Knowing your general attitude on the matter of new insulin mixtures, I imagine this is a not unacceptable report!

My six year old child is still thriving on the mixture, and I will send you more about her after the summer.

Sincerely,

Leona M. Bayer, M. D.
Assistant Clinical Professor
of Medicine

B:R
Encl.

Mrs. D. N.

June 8, 1945

Diet approximately 2000 calories, non-pregnant; 2500 calories, pregnant.
150 gr. to 200 gr. CHO

Diabetes controlled as follows: (u. of insulin)

	<u>AM</u>	<u>Noon</u>	<u>PM</u>	<u>Control</u>
Age 19	PZI 60 Cryst 15			Fair control; diet not careful
Age 20	PZI 40			
Pregnancy	Cry. 10	Cryst. 10		Poor control in spite of careful diet; reactions and glycosuria
I early				
Pregnancy	Globin 50			Good control.
late.				
Age 21	Globin 45			Reasonable control
	Cryst. 10			
Age 22	Globin 38			Afternoon reactions
Pregnancy	Cryst. 15			
II. Early				
Pregnancy	Lilly 70			Afternoon hyperglycemia
middle	"42"			
Pregnancy	Cryst. 40		Cryst. 30	Excellent
late.				

Conclusion: Globin too active in afternoon, "42" not active enough, when either
given so early AM shows perfect control.

THE LILLY RESEARCH LABORATORIES

ELI LILLY AND COMPANY
INDIANAPOLIS 6, IND., U. S. A.

March 28, 1945

Dr. Leona M. Bayer
Stanford University Hospitals
Clay and Webster Streets
San Francisco, California

Dear Dr. Bayer:

Thank you for your recent letter regarding the six year old child whose case has apparently responded well to specially modified Protamine Zinc Insulin, type NP42. We will be glad to furnish additional material for this case as well as the other one, and I am sending under separate cover ten additional vials. When the supply is depleted, please let us know.

Since the quantity of material available is so small, we are dependent for data on relatively few observers, and consequently your comparisons between the effects of this product and other forms of management will be particularly helpful.

Many thanks for your kind cooperation.

Very truly yours,

ELI LILLY AND COMPANY


F. B. Peck, M. D.
Associate Director
Medical Division

FBP:MW

AIRMAIL

March 23, 1945

Dr. F. B. Peck, Associate Director
Medical Division
The Lilly Research Laboratories
Eli Lilly and Company
Indianapolis 6, Indiana

re: modified insulins.

Dear Dr. Peck:

The little six year old about whom I wrote you is started on N. P. 42, and, according to reports by mail, is doing extremely well. Instead of making an experimental shift now, I would really prefer to continue with the same preparation, especially since the child has been through several acute severe upper respiratory illnesses which have complicated the picture.

Also, we have under observation, a young woman now pregnant for the second time, on whom we have a record since adolescence. We would like to try her on N. P. 42.

Would it therefore be possible for you to supply us with enough material to carry these two patients along for the next months? The child requires about 20 units per day, the young woman up to 80.

Thank you very much for your cooperation.

Sincerely yours,

Leona M. Bayer, M. D.
Assistant Clinical Professor
of Medicine

B:R

THE LILLY RESEARCH LABORATORIES

ELI LILLY AND COMPANY
INDIANAPOLIS 6, IND., U. S. A.

January 30, 1945

Dr. Leona M. Bayer
Stanford University Hospitals
Clay and Webster Streets
San Francisco, California

Dear Dr. Bayer:

Thank you for returning the experimental material cards with your signature. Under separate cover we are forwarding a shipment consisting of four vials NP42, lot T-1846, four vials AP175, lot T-1934, and two vials AH38, lot T-1844.

Since the patient is already taking separate injections of 16 units Protamine Zinc Insulin and eight units of unmodified Insulin, I believe it would be worthwhile to start with NP42 as suggested in your letter. As a standard for comparison, you might then try AP175 and AH38, and also another period using an ordinary extemporaneous mixture in about the proportions of two parts of Insulin to one part of Protamine Zinc Insulin. I have a number of cases that have had about the same doses as your patient when given separately, that have responded very satisfactorily to this procedure by simply reversing the proportion of each product given. Thus with separate injections she now takes 16 units of Protamine Zinc Insulin and 8 of Insulin made from zinc-Insulin crystals, which might be reversed to 8 of Protamine Zinc Insulin and 16 of the unmodified preparation. Not infrequently in our experience that change may be made without any disturbance whatsoever in control.

We very much appreciate your kind co-operation and will be much interested in your observations.

Very truly yours,

ELI LILLY AND COMPANY


F. B. Peck, M. D.
Associate Director
Medical Division

FBP:MW

January 23, 1945

Dr. F. B. Peck, Associate Director
Medical Division
The Lilly Research Laboratories
Indianapolis 6, Ind.

Dear Dr. Peck:

Thank you for your letter of January 15th. Herewith are the signed cards.

The immediate case for which I want to have a modified insulin is a little six year old girl who is now stabilized on separate simultaneous injections in the morning, of 16 P. Z. I. and 8 crystalline. It sounds as though, with N. P. 42, one injection might suffice. Or do you recommend one of the other modifications?

Please send me enough for one month of whatever you think would be the most suitable mixture. I will try it after one month on the present regime, and will, of course, be glad to send records on this and other cases.

Very truly yours,

Leona M. Bayer, M. D.

B:R
Encl.

THE LILLY RESEARCH LABORATORIES

ELI LILLY AND COMPANY
INDIANAPOLIS 6, IND., U. S. A.

January 15, 1945

Dr. Leona M. Bayer
Stanford University School of Medicine
Stanford University Hospitals
Clay and Webster Streets
San Francisco, California

Dear Dr. Bayer:

Your recent letter has been referred to me by Dr. Hines and we want to express our regret that the modification reported on by MacBryde recently is still not being distributed for clinical trial. This product, however, is only one of a series and from the manufacturing viewpoint it is not considered to have sufficient stability in its present state to be a practical addition to the armamentarium. Nevertheless it will keep satisfactorily in small lots and if proper precautions are taken during its storage. As a matter of fact free Insulin at the pH of this preparation is only about one-tenth as stable as it is in the official preparation.

However, there are some other modifications which have been undergoing investigation in co-operation with the Toronto Insulin Committee for sometime past and at present we are particularly interested in three of them. If you are in position to supply clinical reports of comparisons, we will be glad to make these available and should other modifications later be distributed, these can be added to the group. The ones which now appear most promising are designated as follows: AP175, lot T-1934; NP42, lot T-1846; and AH38, lot T-1844. The capital letters indicate the type of the preparation; "A" referring to an acid pH and "N" referring to a product buffered to about 7.2. The latter is, of course, in precipitated form; whereas, the former products are all clear. The letter "P" designates protamine as the modifying agent, while "H" refers to histone. The figures indicate the amount of the agent; thus, 175 indicates 1.75 mg. of protamine per 100 units of the Insulin. NP42 is of the same general type as the material Dr. MacBryde has reported on but it contains a little less protamine. The modification he has been using contains 0.5 mg. of protamine per 100 units.

AP 175	acid protamine (1.75 mg per 100 u)
NP 42	neutral protamine (0.42 mg per 100 cc)
AH 38	acid histone (38 mg per 100 cc)
	Mac Bride (50 mg per 100 cc)

INDIANAPOLIS

Dr. Bayer
page 2

Enclosed is an experimental material card for your signature which permits us to comply with the Food and Drug Administration in respect to the shipment of products for investigational use only.

Your co-operation in this study will be greatly appreciated.

Very truly yours,

ELI LILLY AND COMPANY



F. B. Peck, M. D.
Associate Director
Medical Division

FBP:MW

1

Dr. Bayer

THE LILLY RESEARCH LABORATORIES

ELI LILLY AND COMPANY
INDIANAPOLIS 6, IND., U. S. A.

January 11, 1945

(AIR MAIL)

Dr. Leona M. Bayer
Stanford University School of Medicine
Stanford University Hospitals
Clay and Webster Streets
San Francisco, California

Dear Leona:

Your letter of January 9th arrived this morning. I am very sorry that we are not able to send you any of the modified Protamine Zinc Insulin that Dr. MacBryde has been using. Dr. Peck tells me, however, that he has available some other modified Insulins which may meet your needs. I am, therefore, going to refer your letter to him and I know that he will do everything possible for you.

With kindest personal regards,

Yours very truly,
ELI LILLY AND COMPANY



D. C. Hines, M.D.
Medical Department

ek

AIRMAIL

January 9, 1945

Dr. Don Carlos Hines
Eli Lilly and Company
Indianapolis 6, Indiana

Dear Don:

After we came back from Chicago, ^{Dr. Cutting} wrote to Dr. Peck and asked for some modified Protamine Zinc Insulin as both you and Dr. MacBryde had suggested. At that time Peck wrote that it was only available to special clinics, so we did not get any.

Now that MacBryde's article has come out in the Journal of Clinical Endocrinology we are more than ever eager to try the new insulin, and have certain specific cases in whom we think it would be very appropriate. Especially, I am now regulating a little six year old girl with newly developed diabetes in whom I think regulation might be possible with only one injection daily, of modified Protamine Zinc Insulin.

Do you think some of this material could be available to us for use and study? If we could only have enough for one case, I would like to have enough for one month's trial on the little girl; about thirty units daily are needed. The material can be billed and sent to me at Stanford. The family is able to pay regular charges.

Thank you for anything you can do about this.

Sincerely,

Leona M. Bayer

B:R

THE LILLY RESEARCH LABORATORIES

ELI LILLY AND COMPANY
INDIANAPOLIS 6, IND., U. S. A.

June 17, 1946

Leona M. Bayer, M.D.
Stanford University School of Medicine
2398 Sacramento Street,
San Francisco, California

Dear Dr. Bayer:

Thank you for your letter of June 10, 1946.

Under separate cover we are forwarding another fifty oversized vials of Iletin (Insulin, Lilly), U-80. We will be very much interested in the analysis of your experience.

Very truly yours,

ELI LILLY AND COMPANY



F. B. Peck, M. D.
Associate Director
Medical Division

FBP:ELL

June 10, 1946

Dr. F. B. Peck
Eli Lilly and Company
Indianapolis 6, Indiana

Dear Dr. Peck:

I have temporarily misplaced our correspondence, but you will recall that you supplied us with some oversized vials for the study of the newer insulin mixtures in patients of the Stanford Endocrine Clinic. We have used up our supply and would greatly appreciate having another two or three dozen vials.

Dr. MacLin is at present working on an analysis of our experience which has been, in general, very satisfactory.

Sincerely yours,

Leona M. Bayer, M. D.
Assistant Clinical Professor
of Medicine

LMB:R

THE LILLY RESEARCH LABORATORIES

ELI LILLY AND COMPANY
INDIANAPOLIS, IND., U. S. A.

November 13, 1945

Dr. Leona M. Bayer
2233 Post Street
San Francisco 15, California

Dear Dr. Bayer:

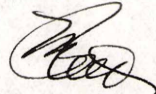
In reply to your recent letter we are forwarding two cartons of 10 vials each of the oversized vials of Iletin (Insulin, Lilly), lot W-1833. If it will facilitate matters for you to receive a regular monthly allotment, please do not hesitate to request it.

There is one point in particular which requires clarification. This is the question of who shall make such a mixture. We need additional experience in the application of this method to the group of diabetic patients in general. There is, of course, a hazard of contamination of such a multiple dose vial in the hands of a poorly trained patient.

Nevertheless the vials should be useful if for no other purpose than in providing different combinations for study and comparison. Your data will be very helpful.

Very truly yours,

ELI LILLY AND COMPANY



F. B. Peck, M. D.
Associate Director
Medical Division

FBP:MW

November 6, 1945

Dr. F. B. Peck
The Lilly Research Laboratories
Eli Lilly and Company
Indianapolis 6, Indiana

Dear Dr. Peck:

The oversized Iletin vials which you sent to me to Stanford Hospitals, seem to be a great help in the making of insulin mixtures. Would it be possible for you to send me ten more such vials to my office at the above address.

I would greatly appreciate having this material to try on a few of my patients now making their own daily mixtures. I could also use these records for study.

Thank you again for your cooperation.

Sincerely yours,

Leona M. Bayer, M. D.

B:R

6.8.45

Mrs. Dorothy Hodge

Diet approx 2000 cal nonpregnant; 2500 cal pregnant. 150 gm
+ 200 gm
CHO

Diabetes controlled as follows: (N. Insulin)

		AM	Noon	PM	Control
Age 19	PZI	60			
	Crypt	15			

fair control; did not
careful

Age 20

pregnancy I
early

PZI 40
Crypt 10

Crypt 10

poor control in
spite of careful
diet; reactions
and glycosuria
good control

pregnancy
late

globin 50

Age 21

globin 45
Crypt 10

reasonable control

Age 22

pregnancy II
early

globin 38
Crypt 15

afternoon reactions

pregnancy
middle

hilly 70
"42"

afternoon hyperglycemia

pregnancy
late

Crypt 40

Crypt 30 excellent

Conclusion: globin too active in afternoon, "42" not active
enough, when both given so early AM
shows perfect control.

Name
and No.

LILLY - INSULIN, mixed
QANTS

SAN FRANCISCO-STANFORD HOSPITAL

XX
XX

XXXXXXXXXX
XXXXXXXXXXXXXX

December 10, 1959

Jacob P. Kahn, M.D.
3261 Clay Street
San Francisco 15

Dear Jay:

This note has a triple purpose, only two-thirds of which is "ulterior".

First, congratulations on your election as head of San Francisco-Stanford Psychiatry. This is completely disinterested! !

Second, I do hope you keep on working with our Youth Clinic. I have high hopes for our potential, and on the basis of Ernst's enthusiasm about working with you in a group setting, I would like especially to have your cooperation in our efforts.

Third, the dates of the Jewish Community Center series, "Understanding the Teen Ager", are Wednesdays, February 26 to March 16, inclusive. You could have any evening you prefer, if you will only agree to prefer one! The topic that occurs to me, is for you to close the series with a very informal discussion of something like: "When and How can Psychiatry Help"? Weill, Wolff and Bayer will cover the rest. As I mentioned on the phone, I promised an answer to the Jewish Community Center by Monday, December 14.

Cordially,

Leona M. Bayer, M.D.

LMB:R

CONSULTANT IN:
INDUSTRIAL MEDICINE
IN-PLANT MEDICAL SERVICE

Christopher Leggo, M.D.
3838 ALAMEDA
MENLO PARK, CALIFORNIA

MEDICAL ADMINISTRATION
WORKMEN'S COMPENSATION
INSURANCE

March 16, 1956

Dr. Leona M. Bayer
Stanford University School of Medicine
Clay and Webster Streets
San Francisco, California

Dear Dr. Bayer:

I am enclosing the reprints for which you asked. I very much appreciate your interest.

I am also enclosing a recent reprint on a subject which may be of very little, if any, interest to you.

With best regards.

Yours sincerely,

Chris Leggo

CL:EB

KOETS

MEMO

February 26, 1946

To: Dr. Koets
From: L. M. Bayer, M. D.

During the war years, research on problems immediately connected with the emergency have taken precedence over every other kind of research. Now that there is time again to spend on more general problems, a revived interest in clinical endocrinology is evident in both the medical and gynecological departments. Since it is clear to all of us that a good biochemical laboratory must be the backbone of any research program in this field, many of us are eager to see such a laboratory developed.

even clinical practice
Many of us also appreciate the gratuitous and generous help you have offered us thus far, and hope that your work will be stabilized and recognized as a regular part of our medical school set-up.

August 8, 1944

Dr. M. M. Kunde
116 So. Michigan Avenue
Chicago, Illinois

Dear Dr. Kunde:

With regard to your ten year old child, I am glad to suggest to you our present plan of treatment.

First, we survey the patient by taking exact measurements of height, sitting height, and shoulder and pelvic breadths. Laboratory work includes bone age and basal metabolic rate. If the bone age is at least moderately retarded, and the BMR not definitely high, we proceed about as follows:

1. Adequate diet, with special emphasis on high protein.
2. Vitamin supplements of A, B complex, and D.
3. Thyroid to tolerance, beginning with one grain daily, U. S. P., and increasing by one grain every two weeks. We maintain this tolerance dose for three months and note the effect by exact monthly measurements of height.
4. At present, we are not using any growth hormone, but are trying out testosterone as a growth stimulant. In the female, special search must be made for any masculinizing effects. The whole plan is still altogether experimental, but has seemed helpful several times in boys on the following schedule: Methyl testosterone - 10 mg. tablets

1 tablet 3 times a day for 3 month period.

This is in addition to the tolerance dose of thyroid and is also followed for three months, at monthly intervals. At the end of this time, there should be a reevaluation of all measurements, bone age, and basal metabolic rate, and, on the basis of results, a further program should be worked out. In any case, the testosterone should not be given for longer than three months without a minimum of one month's rest period.

I hope these suggestions will be helpful to you.

Very truly yours,

Leona M. Bayer, M. D.
Endocrine Clinic

B:R

August 8, 1944

Dr. M. M. Kunde
116 So. Michigan Avenue
Chicago, Illinois

Dear Dr. Kunde:

With regard to your ten year old child, I am glad to suggest to you our present plan of treatment.

First, we survey the patient by taking exact measurements of height, sitting height, and shoulder and pelvic breadths. Laboratory work includes bone age and basal metabolic rate. If the bone age is at least moderately retarded, and the BMR not definitely high, we proceed about as follows:

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2. Vitamin supplements of A, B complex, and D.
3. Thyroid to tolerance, beginning with one grain daily, U. S. P., and increasing by one grain every two weeks. We maintain this tolerance dose for three months and note the effect by exact monthly measurements of height.

4. At present, we are not using any growth hormone, but are trying out testosterone as a growth stimulant. In the female, special search must be made for any masculinizing effects. The whole plan is still altogether experimental, but has seemed helpful several times in boys on the following schedule: Methyl testosterone - 10 mg. tablets

1 tablet 3 times a day for 3 month period.

This is in addition to the tolerance dose of thyroid and is also followed for three months, at monthly intervals. At the end of this time, there should be a reevaluation of all measurements, bone age, and basal metabolic rate, and, on the basis of results, a further program should be worked out. In any case, the testosterone should not be given for longer than three months without a minimum of one month's rest period.

I hope these suggestions will be helpful to you.

Very truly yours,

Leona M. Bayer, M. D.
Endocrine Clinic

B:R

M. M. KUNDE. M. D.
SUITE 1000
116 SO. MICHIGAN AVENUE
CHICAGO, ILLINOIS

Aug 4/44.

Dr. Leona M. Bayle,
Stanford Univ.

Dear Dr. Bayle:-

I have a true pituitary dwarf in my practice, age 10, female, very normal mentally but only about the ht. of a 4 year old child. I have tried for 2 years all growth hormone with disparaging results. Can you please advise me as how to obtain your new Growth Hormone. Please let me hear from you soon.

M. M. Kunde M.D.
116 So. Michigan Ave. Chicago

March 15, 1956

Dear Doctor Leggo:

I have just sent away some of your reprints to interested friends. One is Dr. Marechek, now connected with the Ford Foundation Center for Advanced Studies in the Behavioral Sciences. He is an economist with an interest in the behavioral aspects of industrial groups. Another is Dr. Reichard, now working on an Old Age study in connection with Industry.

The purpose of this note is to ask for replacements, and to let you know that you might hear from these individuals. Meanwhile, greetings.

Cordially,

Leona M. Bayer, M.D.

Reprints:

Fundamentals of Human Behavior in Industrial Medicine
Invite the Professor for Dinner
Employment of the Aging

October 8, 1946

Mrs. Maria Levison
2249 College Avenue
Berkeley, California

Dear Mrs. Levison:

Dr. Suzanne Reichard has agreed to work with me on the psychosomatic project at Stanford. I am delighted about it, and appreciate the interest of all my psychological friends in Berkeley in helping me find a co-worker.

Meanwhile, I wish you continued joy in your present status, up to and beyond its successful outcome.

Cordially,

Leona M. Bayer, M.D.

LMB:R

September 27, 1946

Dr. Rolf Luft
Department of General Pathology
The Caroline Institute
Stockholm, Sweden

Dear Dr. Luft:

Thank you for sending the reprints. We
were especially glad to have the study
on Treatment, which we had not previously
seen.

Sincerely yours,

Leona M. Bayer, M. D.
Assistant Clinical Professor
of Medicine

LMB:R

July 9, 1946

Dr. Rolf Luft
Department of General Pathology
The Caroline Institute
Stockholm, Sweden

Dear Dr. Luft:

Many of us at Stanford Hospital have greatly enjoyed reading your fine study on "Hirsutism, Cushing's Syndrome and Precocious Puberty", published in the Acta Medica Scandinavica, Supplementum CXLIX, 1944.

We would greatly appreciate having three or four reprints of this article for reference. We will be glad to pay whatever expenses are involved.

Sincerely yours,

Leona M. Bayer, M. D.
Assistant Clinical Professor
of Medicine

LMB:R

August 22, 1944

Dr. E. Kirk Lyon
Leamington, Ontario
Canada

Dear Dr. Lyon:

With regard to the child about whom you wrote to me August 10th, I note that the height and weight, as you quoted them, would make him about the size of an average three year old. This is, of course, a very marked retardation and one would be skeptical of making a very significant improvement in his status. Besides the fact that the epiphyses are open, it would be helpful to have a more exact evaluation of the bone age by comparison of hands and knees with a suitable standard such as Todd's.

In any case, with undescended testicles and general sexual retardation, our treatment at present would be to give a chorionic gonadotrophic hormone on a treatment schedule similar to that which you would use in any standard case of undescended testicles. The average dose in such cases is about 500 International Units, three times per week, and must be given with the usual precautions. Besides that, we proceed about as follows:

1. Adequate diet, with special emphasis on high protein.
2. Vitamin supplements of A, B complex, and D.
3. Thyroid to tolerance, beginning with one grain daily, U. S. P., and increasing by one grain every two weeks. We maintain this tolerance dose for three months and note the effect by exact monthly measurements of height.

The chorionic gonadotrophic hormone is given in addition to the thyroid. A real evaluation of all measurements, bone age, and basal metabolic rate should be made every three to six months, and at that time a further program worked out.

Concerning growth hormone extracts, per se, our experience with them has not been very encouraging. There are several commercial extracts available. These are put out by Armour, Parke Davis, and Schering, all of which are standardized to a potency of about ten rat units per cc. Two to three cc., three times a week for three month periods, has been tried.

I hope these suggestions will be helpful to you.

Very truly yours,

Leona M. Bayer, M. D.
Endocrine Clinic

B:R

E. KIRK LYON, M.B., F.A.C.S.

LEAMINGTON, ONTARIO

August 10, 1944

Dr. Leona M. Bayer,
Stanford University School of Medicine,
San Francisco, Calif.

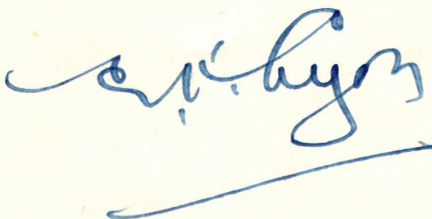
Dear Doctor Bayer:

Dr. Kunde, of Chicago suggested that I write you to obtain the latest information on growth hormone. I have under my care a very interesting case of Levi-Lorraine syndrome. The child is 10 years of age, in third grade at school, growth was normal till 3 years of age, since then no progress. His height is 38", his weight 35 lbs., both testicles are undescended, the penis is small and infantile. Otherwise he is a well proportioned mentally alert child. X-ray of the skull shows a normal size sella turcica and films of the pelvis, arms and legs show the epiphyses to be open. His B. M. R. is normal. Will you kindly advise me what growth hormone you are using and in what dosage?

Thanking you in advance, I am,

Yours sincerely,

EKL/L

A handwritten signature in blue ink, appearing to read "E. K. Lyon", with a long horizontal flourish underneath.