WFSOM

Women Faculty of the School of Medicine
Case Western Reserve University

Our mission: Professional Development, Advocacy, Networking
Welcome to the 2015 WFSOM Spring Dinner

Special Guest
Francine Kaufman, MD
WFSOM Officers

• President: Karen R. Horowitz, MD

• Vice President: Amy Hise, MD, MPH

• Secretary: Mathilde H. Pioro, MD

• Immediate Past President: Usha Stiefel, MD
Steering Committee Members

- Agata Exner, PhD
- Amy Hise, MD, MPH
- Anne Matthews, R.N., PhD
  Chair, Awards Committee
- Claudia Hoyen, MD
- Corrilynn Hileman, MD, MS
- Karen R. Horowitz, MD, FACP
- Kristian Baker, PhD
- Mathilde H. Pioro, MD
- Miriam Rosenthal, MD
- Phyllis Nsiah-Kumi, MD
- Reena Mehra, MD, MS, FCCP
- Ronda Mourad, MD
- Stephanie Harris, PhD, RDN, LD
- Sumita Khatri, MD MSc
- Usha Stiefel, MD
Self-evident Truths

Women in Academics

Women in Medicine

Women in Leadership
## School of Medicine

### Women Faculty

<table>
<thead>
<tr>
<th>Year</th>
<th>Full Time</th>
<th>Adjunct/Clinical</th>
</tr>
</thead>
<tbody>
<tr>
<td>1979</td>
<td>135 (9% of the Faculty)</td>
<td>135 (9% of the Faculty)</td>
</tr>
<tr>
<td></td>
<td>113 Professors</td>
<td>31 Professor</td>
</tr>
<tr>
<td></td>
<td>160 Associate</td>
<td>35 Associate</td>
</tr>
<tr>
<td></td>
<td>563 Assistant</td>
<td>322 Assistant</td>
</tr>
<tr>
<td></td>
<td>27 Senior Instructors</td>
<td>81 Senior Instructors</td>
</tr>
<tr>
<td></td>
<td>45 Instructors</td>
<td>117 Instructors</td>
</tr>
<tr>
<td></td>
<td>35.6% of Faculty</td>
<td>40.5% of Faculty</td>
</tr>
</tbody>
</table>
Getting Better

What is a master but a master student? And if that's true, then there's a responsibility on you to keep getting better and to explore avenues of your profession.

Neil Peart (*Drummer and Lyricist for the band Rush*)
Special Guests

Nazha Abughali, MD
Nathan Berger, MD
Sosamma Berger, PhD
Robin Bissell
Robert Bonomo, MD
Mark Chance, PhD
Colleen Croniger, PhD
Susan Friemark, MA, LPC
Susan Fuehrer, MBA
Nancy Johnson, MD

Margaret Larkins-Pettigrew, MD
Shannon Lundeen, PhD
Lina Mehta, MD
Marilyn Mobley, PhD
Lynda Montgomery, MD, Med
Susan Padrino, MD
Suzanne Rivera, PhD, MSW
Siu Yan Scott, MNO, LSW
Lynn Singer, PhD, MeD
Mamta Singh, MD, MS
Opening Event: Networking Mixer

Gloria Steinem at CWRU

in support of

Flora Stone Mather Center for Women

September 9, 2014
Programs

• **WFSOM *Inspiring Women* Series:**
  Lectures to inspire us by women who inspire us-
  topics include leadership, career development,
  research, work-life balance

• **WFSOM Catalyst for Change Series**
  Workshops on networking, career development
  and increasing your professional impact at the
  university and beyond.
WFSOM Programs 2014-15

• ELAM Workshop  
The Executive Leadership in Academic Medicine Program Susan Nedorost, MD

• Dr. Robin Jump Reflections on AAMC Early Career Development Program for Women

• WFSOM/AMWA Fall Wine and Cheese Mixer  
  Program Chair: Usha Steifel, MD
Inspiring Women Series

Charis Eng, MD, PhD

Mentoring Roundtable

Networking, building relationships, learn the game (oenophile), be a mentor to others

December 2, 2014
Stop trying to be excellent, start working toward accomplishing something meaningful to you...

January 14, 2015
Inspiring Women Series

Leslie Walker, MD

Successful Self Care for Women Professionals
February 4, 2015
2015 FACULTY LUNCHEON TOOLKIT SERIES

January 20  Building a Lab Team
February 17  Faculty Service Opportunities
March 17    Promotion & Tenure
April 21    Conflict Management
May 19      Negotiating Your Way Forward
June 16     Protecting Your Intellectual Property
July 21     Time Management
August 18   Authorship
September 15 Promotion & Tenure
October 20  Intercultural Communication
November 17  Improving Supervision Skills
December 15  Enhancing Professional Visibility Using Social Media
CWRU
Flora Stone Mather Center for Women

- Overwork
- Women, Find Your Voice!
- Helping Faculty Find Work-Life Balance: The Path Toward Family-Friendly Institutions
- How to Avoid Being Marginalized

Shannon Lundeen, PhD
Director, Flora Stone Mather Center for Women
Assistant Professor of Bioethics

Susan Freimark, MA
Associate Director of Faculty Leadership Programs
WFSOM Website

• www.cwru.edu

• Follow us on Twitter:
  CWRU WFSOM @wfsom
WOMEN FACULTY of the SCHOOL OF MEDICINE

The mission of the Women Faculty School of Medicine organization at Case Western Reserve University is to provide:

1. Professional Development opportunities for women faculty in the School of Medicine.
2. Advocacy on behalf of women in academic medicine at CWRU and affiliates.
3. Networking among women and leaders in academic medicine to promote academic, professional, and personal growth.

Follow us on Twitter

CWRU WFSOM @wfsom 30 Apr
A time-off policy to increase residents' utilization of health care services. - PubMed - NCBI
ncbi.nlm.nih.gov/m/pubmed/25354...

CWRU WFSOM @wfsom 30 Apr
Favorites Article addresses #burnout in #scientists in #AcademicMedicine pdfs.journals.lww.com/academicmedi...
Acknowledgements

Barb Juknialis  
Bioethics

Halle Lewis  
Finance & Planning

Patty Urbon  
Faculty Affairs & HR

Joyce Helton  
Faculty Affairs & HR
Future Programs: Fall 2015

• WFSOM/CWRU Career Development Opportunities Fair
• 7 Habits of Highly Effective Jr. Faculty
• Preparing for a New Leadership Position: Onboarding Strategies for Success
• Negotiation Skills Workshop
• Op Ed Writing Workshop
Cleveland Clinic
Women Professional Staff Association

Women in Healthcare Forum
September 19, 2016
Rochelle Rosian, MD
Catherine Boyle, Program Manager
Promotions
# Promotions to Assistant Professor

<table>
<thead>
<tr>
<th>Faculty Name</th>
<th>Department</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soozan Abouhassan</td>
<td>Anesthesiology &amp; Perioperative Medicine</td>
<td>UH</td>
</tr>
<tr>
<td>Jaina Amin</td>
<td>Psychiatry</td>
<td>UH</td>
</tr>
<tr>
<td>Tracy Bartone</td>
<td>Anesthesiology &amp; Perioperative Medicine</td>
<td>UH</td>
</tr>
<tr>
<td>Jen Bohon</td>
<td>Nutrition</td>
<td>SOM</td>
</tr>
<tr>
<td>Katya Chiong</td>
<td>Anesthesiology &amp; Perioperative Medicine</td>
<td>UH</td>
</tr>
<tr>
<td>Danette Y. Conklin</td>
<td>Psychiatry</td>
<td>UH</td>
</tr>
<tr>
<td>Mirela A. Dobre</td>
<td>Medicine</td>
<td>UH</td>
</tr>
</tbody>
</table>
Promotions to Assistant Professor

<table>
<thead>
<tr>
<th>Faculty Name</th>
<th>Department</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irina Korobkova</td>
<td>Psychiatry</td>
<td>UH</td>
</tr>
<tr>
<td>Marin K. Mannix</td>
<td>Anesthesiology &amp; Perioperative Medicine</td>
<td>UH</td>
</tr>
<tr>
<td>Nora K. McNamara</td>
<td>Psychiatry</td>
<td>UH</td>
</tr>
<tr>
<td>Krisztina Papp-Wallace</td>
<td>Medicine</td>
<td>VA</td>
</tr>
<tr>
<td>Allison H. Payne</td>
<td>Pediatrics</td>
<td>UH</td>
</tr>
<tr>
<td>Agne Petrosiute</td>
<td>Pediatrics</td>
<td>UH</td>
</tr>
<tr>
<td>Michelle Elizabeth Romero</td>
<td>Psychiatry</td>
<td>UH</td>
</tr>
<tr>
<td>Karen Tien</td>
<td>Psychiatry</td>
<td>UH</td>
</tr>
<tr>
<td>Andrea N. Trembath</td>
<td>Pediatrics</td>
<td>UH</td>
</tr>
<tr>
<td>Yan Yang</td>
<td>Neurology</td>
<td>UH</td>
</tr>
</tbody>
</table>
# Promotions to Associate Professor

<table>
<thead>
<tr>
<th>Faculty Name</th>
<th>Department</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Micheala Aldred</td>
<td>Molecular Medicine</td>
<td>CCLCM</td>
</tr>
<tr>
<td>Tracey Bonfield</td>
<td>Pediatrics</td>
<td>UH</td>
</tr>
<tr>
<td>Christine Hoga Booth</td>
<td>Pathology</td>
<td>CCLCM</td>
</tr>
<tr>
<td>Heather Broihier</td>
<td>Neurosciences</td>
<td>SOM</td>
</tr>
<tr>
<td>Nancy J. Cossler</td>
<td>Reproductive Biology</td>
<td>UH</td>
</tr>
<tr>
<td>Katharine A. Downes</td>
<td>Pathology</td>
<td>UH</td>
</tr>
<tr>
<td>Healther L. Gornik</td>
<td>Medicine</td>
<td>CCLCM</td>
</tr>
<tr>
<td>Rula A. Hajj-Ali</td>
<td>Medicine</td>
<td>CCLCM</td>
</tr>
<tr>
<td>Anna Maria Hibbs</td>
<td>Pediatrics</td>
<td>UH</td>
</tr>
<tr>
<td>Natalie Joseph</td>
<td>Surgery</td>
<td>MHMC</td>
</tr>
</tbody>
</table>
## Promotions to Associate Professor

<table>
<thead>
<tr>
<th>Faculty Name</th>
<th>Department</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sangeeta Tina Mahajan</td>
<td>Reproductive Biology</td>
<td>UH</td>
</tr>
<tr>
<td>Katharine E. Mason</td>
<td>Pediatrics</td>
<td>UH</td>
</tr>
<tr>
<td>Jennifer Michelle McBride</td>
<td>Surgery</td>
<td>CCLCM</td>
</tr>
<tr>
<td>Courtenay Moore</td>
<td>Surgery</td>
<td>CCLCM</td>
</tr>
<tr>
<td>Nora Nock</td>
<td>Epidemiology &amp; Biostatistics</td>
<td>SOM</td>
</tr>
<tr>
<td>Donna M. Plecha</td>
<td>Radiology</td>
<td>UH</td>
</tr>
<tr>
<td>Michelle Puchowicz</td>
<td>Nutrition</td>
<td>SOM</td>
</tr>
<tr>
<td>Marion J. Skalweit</td>
<td>Medicine</td>
<td>VA</td>
</tr>
<tr>
<td>Lan Zhou</td>
<td>Pathology</td>
<td>UH</td>
</tr>
</tbody>
</table>
## Promotions to Professor

<table>
<thead>
<tr>
<th>Faculty Name</th>
<th>Department</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jennifer R. Bailit</td>
<td>Reproductive Biology</td>
<td>MHMC</td>
</tr>
<tr>
<td>Elma D. Baron</td>
<td>Dermatology</td>
<td>UH</td>
</tr>
<tr>
<td>Leslie Anne Bruggeman</td>
<td>Medicine</td>
<td>MHMC</td>
</tr>
<tr>
<td>Margot S. Damaser</td>
<td>Molecular Medicine</td>
<td>CCLCM</td>
</tr>
<tr>
<td>Isabelle Deschenes</td>
<td>Medicine</td>
<td>MHMC</td>
</tr>
<tr>
<td>Lydia Furman</td>
<td>Pediatrics</td>
<td>UH</td>
</tr>
<tr>
<td>Veronique Lefebvre</td>
<td>Molecular Medicine</td>
<td>CCLCM</td>
</tr>
<tr>
<td>Cristina Magi-Galluzzi</td>
<td>Pathology</td>
<td>CCLCM</td>
</tr>
<tr>
<td>Theresa Torres Pizarro</td>
<td>Pathology</td>
<td>SOM</td>
</tr>
<tr>
<td>Marcia Rochelle Silver</td>
<td>Medicine</td>
<td>MHMC</td>
</tr>
<tr>
<td>Amy L. Wilson-Delfosse</td>
<td>Pharmacology</td>
<td>SOM</td>
</tr>
</tbody>
</table>
WFSOM Humanistic Values in Medicine Award

Rebecca Cooper-McCann

Tiffany Kenison
WFSOM Gender Equity Award

Pre Clinical Faculty Recipient:  
**Charles Malemud, PhD**

Clinical Faculty Recipient:  
**Jennifer Hanrahan, DO,MA**
WFSOM Awards: Mary Hellerstein
Junior Career Development Award Recipients

Jennifer Eads, MD
Erika Trapl, PhD
WFSOM Awards: Helen Evans
Mid-Career Development Award Recipients

Kristian Baker, PhD
Mamta Singh, MD
WFSOM Awards
Toyoko Yamashita Award Recipient

Usha Stiefel, MD
Congratulations to Dr. Jennifer Bailit on your acceptance to the ELAM class of 2015-16!
Congratulations!

FLEX: A Professional Development Program of the Women Faculty of the School of Medicine

- Executive Presence
- Networking
- Negotiation
- Time Management
- Presentation Skills
- Leading Relationships
- Personal Coaching
- Mentoring
- Self assessment
- Goal Setting
- Reflection
Goals of the FLEX Program

• Increase the number of women in leadership positions
• Empower women to pursue career opportunities with national and international presence
• Decrease the rate of attrition of high achieving women, thereby increasing the proportion of women at higher academic ranks
• Develop a leadership pipeline of skilled and qualified women
• Serve as a national model for other academic organizations
• Become a destination site for leadership development for faculty in other academic medical centers

The FLEX Program Team
Director: Sumita Khatri, MD
Program Manager: Billie C. Kyriakides   bxk223@case.edu

Sponsored by the Office of the Dean and the Women Faculty of the School of Medicine
Dr. Francine Kaufman

Advances Towards the Closed Loop
Francine Kaufman, MD

- Chief Medical Officer and Vice President
  Global Medical, Clinical & Health Affairs
  Medtronic Diabetes

- Distinguished Emerita Professor of Pediatrics and Communications
  Keck School of Medicine and Annenberg School of Communications -
  University of Southern California

- Member of the Institute of Medicine of the National Academies (2005)

- Chair of NIH funded studies on Prevention and Treatment of Type 2
  Diabetes in Youth (TODAY Trial)

- President, American Diabetes Association 2002-2003
Women in Medicine

Francine Ratner Kaufman, MD
Chief Medical Officer, VP Global Medical, Clinical and Health Affairs
Medtronic Diabetes
Distinguished Professor Emerita of Pediatrics and Communications
The Keck School of Medicine and the Annenberg School of Communications
University of Southern California and
Children’s Hospital Los Angeles
Discussion Points

• My Inspiration
• My Career Start
  – It was easier then
• Strategic Planning
• Career Shifting
• My Passion
• Giving Back
My Inspiration

1907

1921
I Didn’t Have a Career Plan – So I Raised My Hand

• The first week of my fellowship a young 21 year old woman with classic galactosemia was seen in our combined genetics/endocrine clinic with primary amenorrhea

• The department chair George Donnell asked who wanted to see her – I put up my hand

• That defined the next ten years of my life
I Needed A Mentor
I Told my Mentor my Passion was Diabetes

- Camp Chinnock in San Bernardino Mountains
- Started in 1978

3-4 IVs hanging to treat DKA every day

A hypoglycemic seizure every 36 hours

Regular and NPH animal insulin and only urine testing
Diabetes Camps
Haiti and Ecuador
My Team

• We did clinical, basic and public health research
• We cared for one of the largest pediatric diabetes patient populations
• We taught the next generation of pediatric endocrinologists
The STOPP T2 Trials

HEALTHY
A Middle School Program for Diabetes Prevention

2DAY
Treatment of Type 2 Diabetes in Youth

- Randomized clinical trial with a pre-randomization run-in period
  - 704 patients at 15 clinical centers
  - 3 treatment regimens
    - Metformin + Placebo
    - Metformin + Rosiglitazone
    - Metformin + Intensive Lifestyle Program
    - At treatment failure: Standardized approach to insulin initiation

- Primary outcome: time to failed glycemic control

- Inclusion criteria
  - Age 10 to 17 years
  - Duration of diabetes < 2 years
  - BMI ≥ 85th percentile
A Clinical Trial to Maintain Glycemic Control in Youth with Type 2 Diabetes

Proportion Free of Glycemic Failure

Failure rates:
- Metformin alone, 51.7%
- Metformin–rosiglitazone, 38.6%
- Metformin–lifestyle, 46.6%

Pairwise tests:
- Metformin–lifestyle vs. metformin–rosiglitazone, P=0.15
- Metformin alone vs. metformin–rosiglitazone, P=0.006
- Metformin alone vs. metformin–lifestyle, P=0.17

No. at Risk

<table>
<thead>
<tr>
<th>Months since Randomization</th>
<th>699</th>
<th>542</th>
<th>425</th>
<th>297</th>
<th>187</th>
<th>92</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin–lifestyle</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metformin–rosiglitazone</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metformin alone</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Prevention
The HEALTHY Study

Population-based intervention
School unit of randomization
Pilots and feasibility studies - 2003 - 2005
OGTT pilot, 1770 8th graders
- BMI ≥ 85th - 49.0%
- FBG ≥ 100 mg/dL - 40.5%
- Insulin ≥ 30 µU/mL - 36.2%
Primary outcome: Combined prevalence of overweight plus obesity

- 42 schools
  - ≥ 50% minority &/or ≥ 50% with free/reduced lunch
  - Comprehensive health screening, results sent to parents

- Intervention Schools
  - Environmental changes
    - Food service, PE
  - Behavior change
  - Communications and promotional campaign

OGTT pilot, 1770 8th graders
BMI ≥ 85th - 49.0%
FBG ≥ 100 mg/dL - 40.5%
Insulin ≥ 30 µU/mL - 36.2%
Prevention
The HEALTHY Trial RESULTS

- Reduction in percentage of overweight/obesity 4% in both groups
- Prevalence of obesity declined more in intervention schools (p=0.05)
- Significant reduction in intervention schools (p=0.04)
  - BMI z-score
  - Prevalence of large waist circumference
  - Fasting insulin fell

- In the overweight/obese subgroup (n=2292), intervention schools had significantly greater decreases than control schools in prevalence of:
  - Obesity (p=0.04)
  - Large waist circumference (p=0.03)
  - Insulin (p=0.04)
Diabesity: A Global Epidemic Results from the Collision of our Ancient Genes and our Modern Environment

It is due to the Fruits of Human Progress - our Collective Human Experience to Secure the Food Supply and Develop Energy Savings Devices

We Now Have to Re-Define Human Progress
Socio-ecological Model

Social Norms
Subculture
Sectors of Influence
Behavioral Settings
Individual Factors
Food & Beverage Intake
Physical Activity
Energy Intake
Energy Expenditure
Energy Balance
Obesity
Insulin resistance/deficiency
Diabetes

Home Communities
Health Care Access, Adherence
Schools and Child Care
Worksites

Age, Sex, SES, Race/Ethnicity
Culture
Psychosocial Factors - Stress
Genes, Gene-Environment Interactions
Intrauterine Environment

Built Environment
Government
Public Health
Agriculture
Education
Media
Land Use and Transportation
Communities
Foundations
Industry
Food Beverage Retail
Leisure and Recreation
Entertainment

Food & Beverage Intake
Energy Intake
Energy Expenditure
My interest in Diabetes Technology led me, in 2009, to become Chief Medical Officer and VP of Global Clinical, Medical and Health Affairs at Medtronic Diabetes
Kazakhstan

Diabetes Statistics:
- Diabetes Patients: 153,000
- T1 Children (1-9 years): 438 patients
- T1 Children (9-18 years): 1,099 patients
- T1 Adults: 11,438 patients
Defining the Future of the Closed Loop

**INFORM**
- Bolus Wizard
- Integrated System

**SUSPEND**
- Low Glucose Suspend
- Predictive Low Glucose Management

**DELIVER**
- Overnight Closed Loop
- Hybrid Closed Loop
- Artificial Pancreas

---

**How SmartGuard Works**

- Median
- 25th Percentile
- 75th Percentile

---

**Graphs**

- Sensor Glucose (mg/dL) vs. Time from the TS event (hr)
- How SmartGuard Works graph
- 120 Fixed Target graph
The Artificial Pancreas

1. Continuous Glucose Monitor
2. Computer-Controlled Algorithm
3. Insulin Pump
4. Patient Effect

My Passion
I Wandered

Public Health Efforts

Arogya World

The largest diabetes prevention mHealth program in the world

Proposition 71 Funded Stem Cell Research in California
Giving Back

Insulin for Life – Brings supplies to Children
Life for a Child – the IDF Program for Children

The IDF Life for a Child Program is currently helping over 12,000 CHILDREN AND YOUTH WITH DIABETES IN 43 COUNTRIES
The IDF Youth Leadership Program

- 100 young leaders from around the world in Dubai in 2011
- 140 young leaders from 73 countries in Australia in 2013
- Delegation to be at IDF 2015 in Vancouver
The Youth Leaders Dominated in Australia at IDF 2013
Work Pinwheel, a 360° Assessment of Your Priorities & Time Allocated to Each

- Travel
- Strategic Planning
- Meetings/Conference Calls
- Execution
- Talent Development & Coaching
- Project 6/Mission in Motion
- External/Competitive Research
- Administrative Tasks
- Firing/“Firefighting”
- Budget Management/AOP
- Working Across Business, Function, or Geography
- Administrative Tasks
- Professional Development (self)
Life Pinwheel, a 360° Assessment of Your Priorities & Time Allocated to Each

- Work
- Sleep
- Faith / Spiritual
- Down-Time / Relaxing
- Entertainment / Fun / Hobbies
- Household Chores
- Spouse / Partner / Other
- Kids / Family
- Friends
- Fitness
- Health
- Community Service
- Financial Well Being

Taking Care of Me

______________

______________
Some Best Practices

- Planning is key – be a good planner, be organized
  - Identify conflicts early
- Reach out to others for help/support
  - Realize you don’t have to do everything
- Set boundaries based on your goals and values
  - Limit weekend work, allow for fitness time, don’t use internet around your family, etc.
- Be technology enabled so you can work from anywhere to gain flexibility
- Deal with the guilt when you make tradeoffs
- Make aligned every day decisions about how you spend your time
  - Plan ahead, decide and stick to it
- Learn from others
  - Ask for advice/help, have an outlet to vent/share
- See work/life balance as a dynamic process that changes throughout your life/career
  - What is needed today will be different in 5 years, be prepared to adjust as your situation changes
MONITORING
DELIVERY
Career Choice
INSULIN Education
Training
Grants, Positions, Mentors, Support, Family
Education
Training
Career Choice
Our Perceptions

Drive, Balance

Family, Partners, Kids

Adjustments

Taking Chances

Sense of Self

Satisfaction
HYPERGONADOTROPIC HYPOGONADISM IN FEMALE PATIENTS WITH GALACTOSEMIA

Francis Ratner Kaufman, M.D., Maurice D. Kogut, M.D., George N. Donnell, M.D., Uve Gobbelmann, M.D., Charles Marx, M.D., and Richard Koch, M.D.

Abstract We evaluated gonadal function in 18 female and eight male patients with galactosemia due to transferase deficiency. Four were normal in the males, but 12 females had signs of hypergonadotropic hypogonadism. All female patients had a 46,XX karyotype, normochromic, normocytic red blood cells, and no anti-ovarian antibodies. The biologic activity of urinary gonadotropins was normal. Ultrasonography of the pelvis revealed that ovarian tissue was diminished or absent. Total estrogen increased in one of two patients after administration of human menopausal gonadotropin. The frequency of hypergonadotropic hypogonadism was higher in females in whom dietary treatment for galactosemia was delayed. Clinical course and mean erythrocyte galactose-1-phosphate and urinal galactolactone levels did not correlate with ovarian function.

We conclude that female patients with galactosemia have a high incidence of ovarian failure due to acquired ovarian atrophy. Galactose or its metabolites may be toxic to the ovarian parenchyma, particularly during the immediate neonatal period. (N Engl J Med. 1981; 304:994-8.)

GALACTOSEMIA, a disorder due to a deficiency of the enzyme galactose-1-phosphate (Gal-1-P) uridyly transferase (transerase), represents an inborn error in the major pathway of galactose metabolism. As a consequence of the transerase defect, galactose and its metabolites accumulate in various tissues in untreated children with this condition and result in hepatic, renal, lenticular, and neurologic abnormalities. Early diagnosis and institution of dietary treatment permit survival and good health over the long term.1-5 Many galactosemic women have been treated since early childhood and are now reaching childbearing age, and although their fertility rate is not known, several have born healthy children.6 Because hypergonadotropism was noted in one of our patients, we evaluated gonadal function in 26 patients who attended the Galactosemia Clinic at Children's Hospital of Los Angeles. This report describes the finding of hypergonadotropism with a strikingly high incidence in female patients with galactosemia. The results of our studies suggest that ovarian failure is due to a direct toxic effect of galactose or its metabolites on the ovarian parenchyma.

METHODS

The study group consisted of 26 patients (18 male, 14 female) with documented transferase deficiency who had been followed in the Children's Hospital Galactosemia Clinic since infancy. They were seen to 20 years of age at the beginning of this study. Three female patients over 15 years old were unavailable for participation. All patients had been on a galactose-restricted diet since diagnosis in infancy. At yearly visits to the clinic, erythrocyte levels of Gal-1-P were measured according to the method of Galacteros.8-10 And urinary levels of galactose were identified by thin-layer chromatography, according to the procedure of Weinsten-D and Segal.11 Ertrocytophraphy was performed with the standard technqiue, and immunofluorometric (IF) was determined with the Standard Biostat Inc. or Rhenokeratate for Children.

Neuroendocrine function was assessed according to the method of Tannen.13 Serum luteinizing hormone (LH), follicle-stimulating hormone (FSH), thyroxine, thyroid-stimulating hormone, estradiol, progesterone, and prolactin were measured by radioimmunoassay. Anti-ovarian antibodies were assessed by the indirect immunofluorescence technique with rabbit antiserum to human IgG. Chromosomal analysis was performed on peripheral blood lymphocytes with standard banding techniques. Gonadotropins in 24-hour urine collections were measured by mouse-urine weight. Ovarian size was assessed by ultrasonography of the pelvis.

Two patients (1 and 11) received human menopausal gonadotropin (Pergonal) by intramuscular injection, and their serum levels of immunoreactive estradiol and progesterone were measured daily by radioimmunoassay.14,15 Calculations of statistical significance of differences were performed with the chi-square method and Student's t test.8,16,17 These studies were approved by the Committee on Clinical Investigation of Children's Hospital of Los Angeles. Informed consent was obtained from the parents or their patients (or both) before the patients entered into the study.

RESULTS

Endocrine Function

Female Patients

Stage of puberty and hormonal levels are shown in Table 1. Twelve of 18 female patients had hypergonadotropic hypogonadism, five had primary amenorrhea, six had secondary amenorrhea, and one had oligomenorrhea. In the latter seven patients menstrual cycles had occurred between 12 and 15 years of age. Persistently elevated gonadotropins and low estradiol levels were evident six months after the initial testing in six of these seven patients. Four of the seven tested (Patients 1, 6, 8, and 12) had levels of urinary gonadotropins that were greater than 50 mIU per 24 hours. Patient 1 became pregnant at 26 years of age.

Patient 4 had apparently normal ovaries on abdominal exploration for galactoses at seven years of age and streak gonads on laparoscopy at 17 years of age. Ultrasonography of the pelvis did not visualize ovarian tissue in three patients (1, 3, and 6), and in two (8 and 12) only a small single ovary was detected. In Patient 1 serum estradiol was 54 pg per millilitel before a 10-day course of up to 900 IU of meno-

From the divisions of Endocrinology and Metabolism and Medical Genetics, Children's Hospital of Los Angeles; the Department of Pediatrics, USC School of Medicine; and the Departments of Obstetrics and Gynecology, LAC-USC Medical Center, USC School of Medicine. Address requests to Dr. Kaufman at the Division of Endocrinology and Metabolism, Children's Hospital of Los Angeles, 4650 Sunset Blvd, Los Angeles, CA 90027.

Supported in part by a grant (05592) from the National Institutes of Child Health and Human Development.

Reprinted from the New England Journal of Medicine
304:994-998 (April 23, 1981)
Family and Friends Matter Most
Thank You
For
Attending!