“THE NEW TRENDS”: THE PERICONCEPTIONAL PERIOD WHERE WE ARE & WHERE WE GO

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PREMISES

THE TRENDS

Prevalence of type 2 diabetes

DIAB-5344; No. of Pages 11

ARTICLE IN PRESS

DIABETES RESEARCH AND CLINICAL PRACTICE XXX (2011) XXX–XXX

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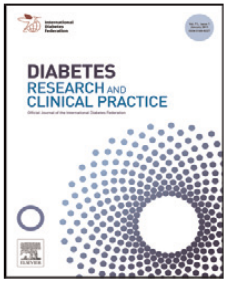
Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

ELSEVIER

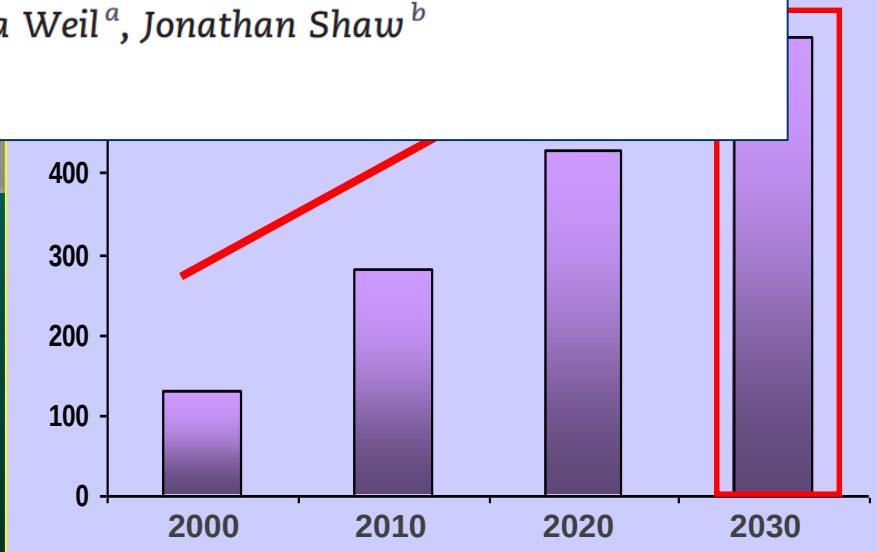
International Diabetes Federation



IDF Diabetes Atlas: Global estimates of the prevalence of diabetes for 2011 and 2030

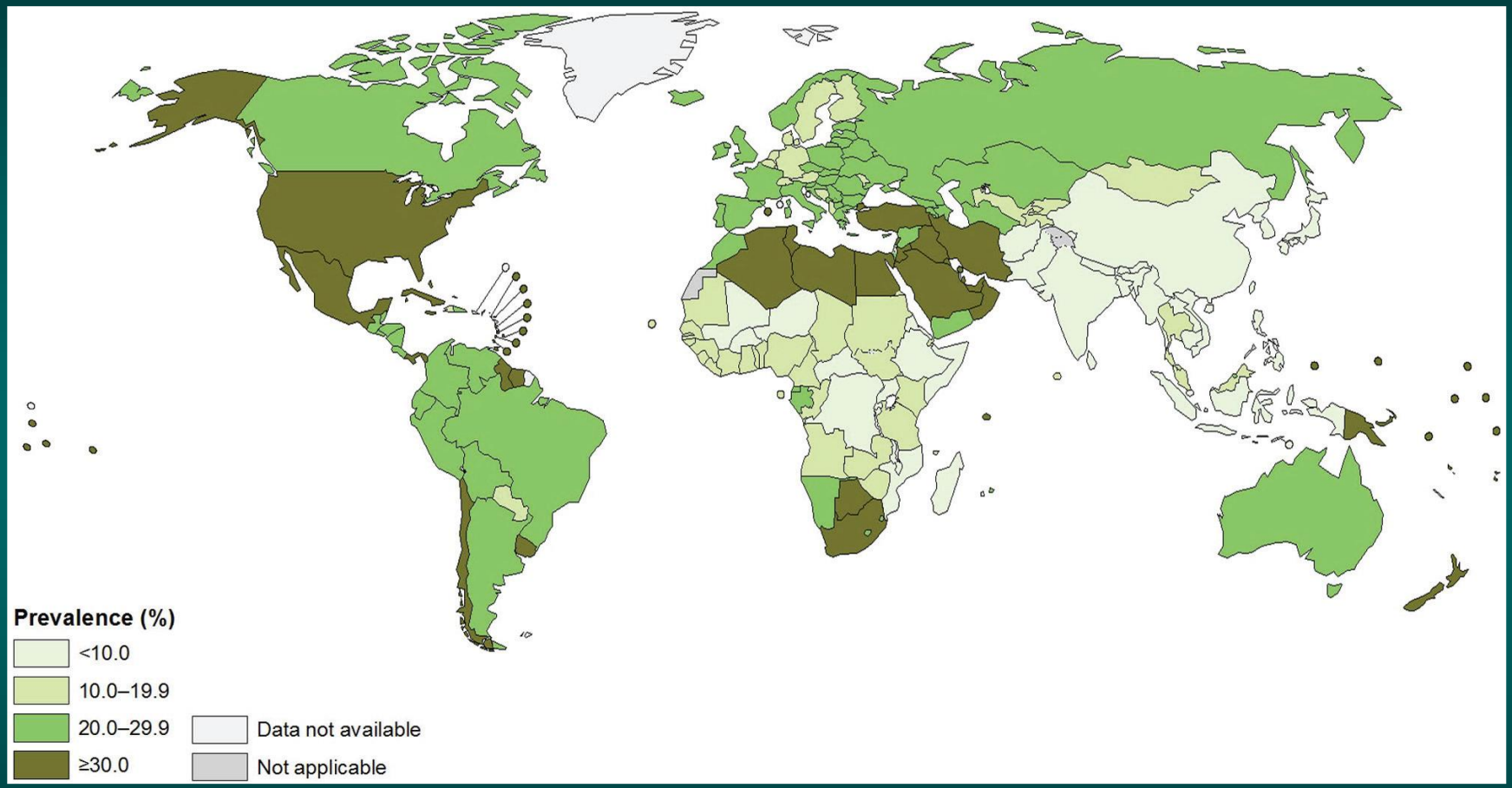
David R. Whiting [a,*], *Leonor Guariguata* [a], *Clara Weil* [a], *Jonathan Shaw* [b]

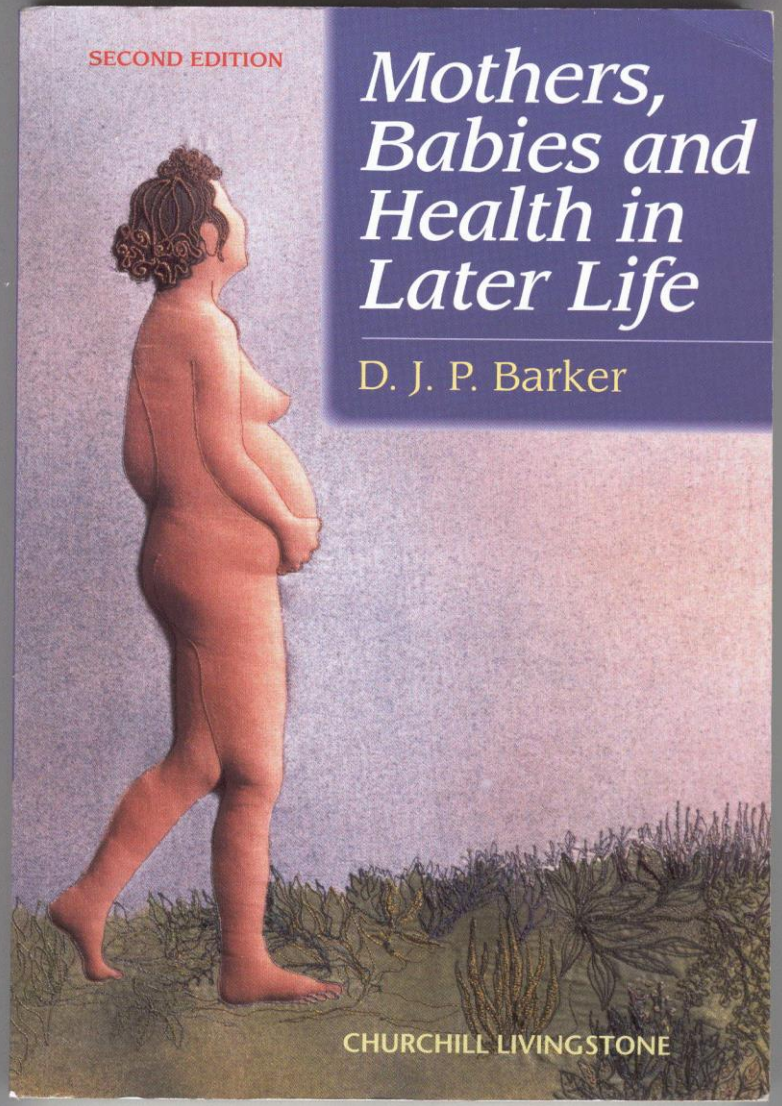
[a] *International Diabetes Federation, Brussels, Belgium*
[b] *Baker IDI Heart and Diabetes Institute, Australia*



IDF Diabetes Atlas, 2011

OBESITY


Prevalence (%)
<10.0
10.0–19.9
20.0–29.9
≥30.0
Data not available
Not applicable


SECOND EDITION
Mothers, Babies and Health in Later Life
D. J. P. Barker
CHURCHILL LIVINGSTONE

The Vicious Cycle - NCD Epidemic

The Great Obstetrical Syndromes

Obesity ,Diabetes, Metabolic Syndrome & Pregnancy

Pedersen & Freinkel Hypothesis

Diagnosis & Management

Abnormal Intrauterine Metabolic Environment

Programming & Imprinting Fetal - Neonatal

Insulin resistance Obesity

Pregnancy complicated with diabesity & Great Obstetrical Synd

Pre-Pregnancy Management

Childhood Obesity

Early T2DM Cardiovascular

Post-Pregnancy Management

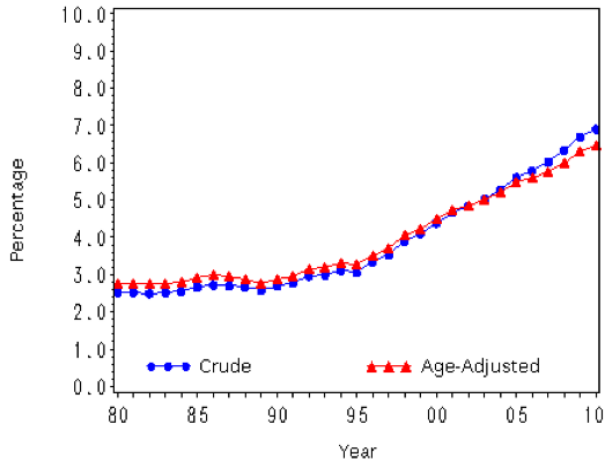
Adult Obesity

PCOS

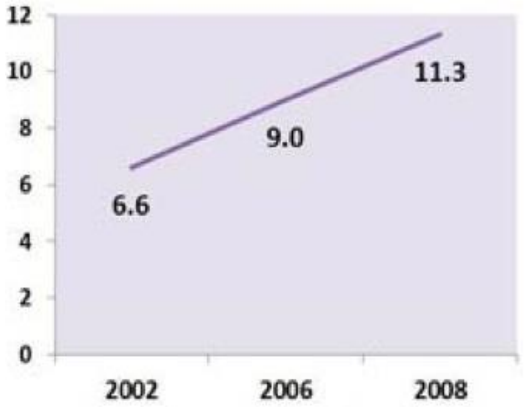
Early Metabolic syndrome

Should We Be Concerned?

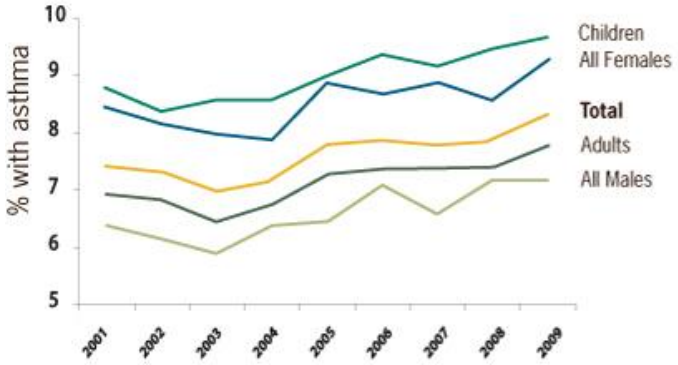
Increase in Diabetes (1980-2010)



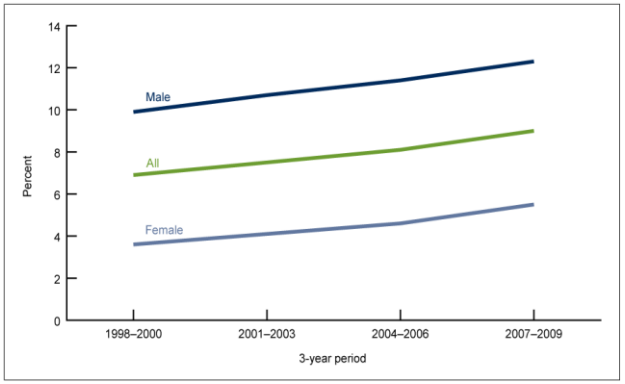
Increase in Autism Prevalence



Increase in Asthma

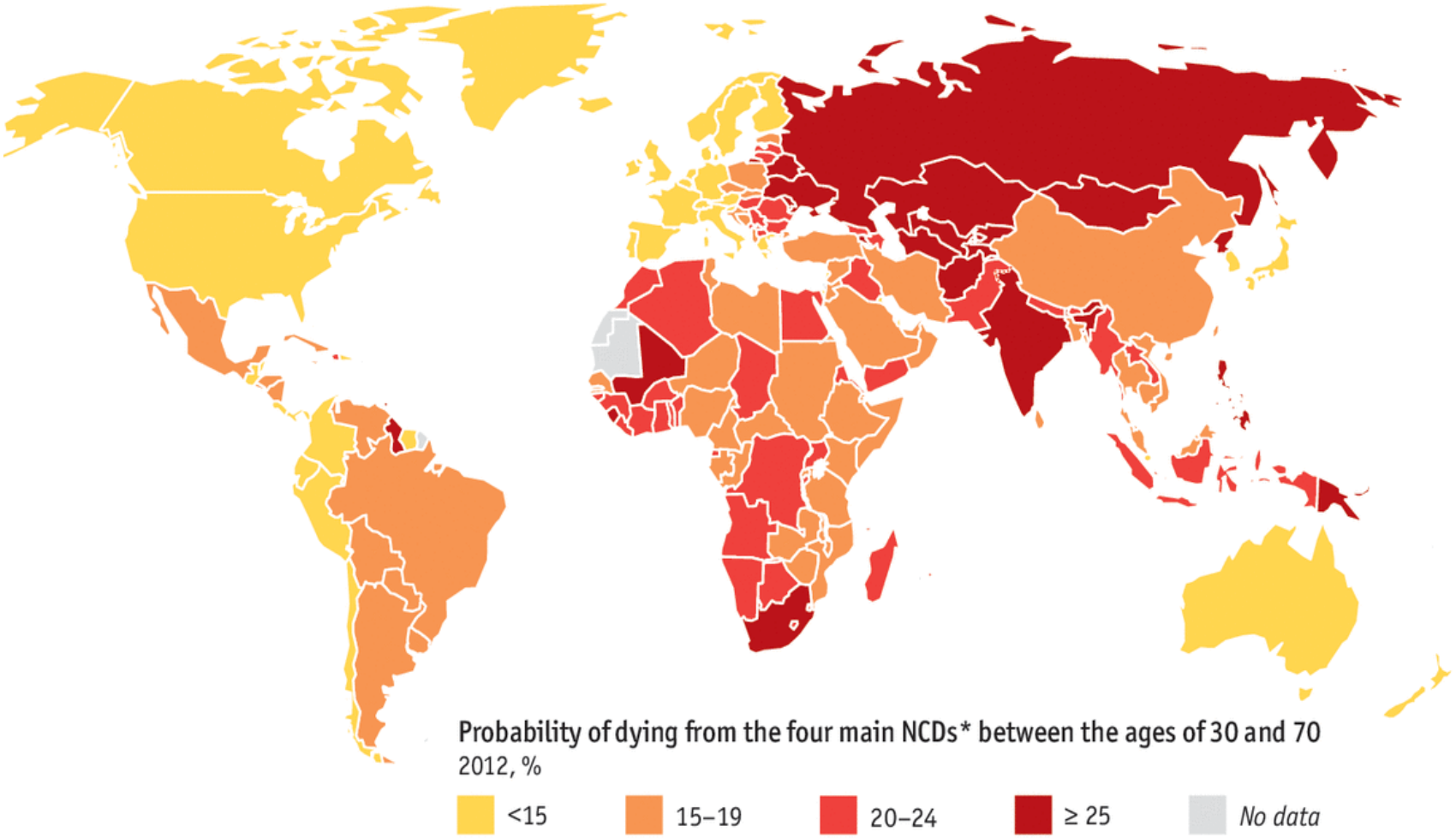


Increase in ADHD (hyperactive disorders)



Birnbaum: NIEHS, *Data from CDC / National Center for Health Statistics*

Probability of dying prematurely from non-communicable diseases



Source: WHO

*Non-communicable diseases: cardiovascular diseases, cancer, chronic respiratory diseases and diabetes

PARENTAL PRESSURE vs MEDICAL (IR)RESPONSIBILITY: THE DES STORY

This ad from a 1957 medical journal promoted the use of DES to prevent miscarriage.

 # DES was the first synthetic estrogen (USA).

 # Prescribed to nearly 5 millions women to prevent miscarriage between 1938 and 1970.

 # DES children (female) are at higher risk of vaginal and cervical dysplasia (Cancer ?) and uterine anomalies (Infertility, ectopic pregnancy, late miscarriage & Premature labour).

REMEMBER THALIDOMIDE!!!!!

Am J Epidemiol. 2014 Mar 1;179(5):536-44.

Chlordecone exposure, length of gestation, and risk of preterm birth.

Kadhel P, Monfort C, Costet N, Rouget F, Thomé JP, Multigner L, Cordier S.

Persistent organic pollutants have not been conclusively associated with length of gestation or with preterm birth. Chlordecone is an organochlorine pesticide that has been extensively used to control the banana root borer population in the French West Indies.

……These associations may result from the estrogen-like and progestin-like properties of chlordecone. **These results are of public health relevance because of the prolonged persistence of chlordecone in the environment and the high background rate of preterm births in this population**

THE EVIDENCES

The best example how periconception care can improve pregnancy outcome is supplementation with folic acid.

An increase in intake of folic acid among women planning a pregnancy was shown to prevent most neural tube defects.

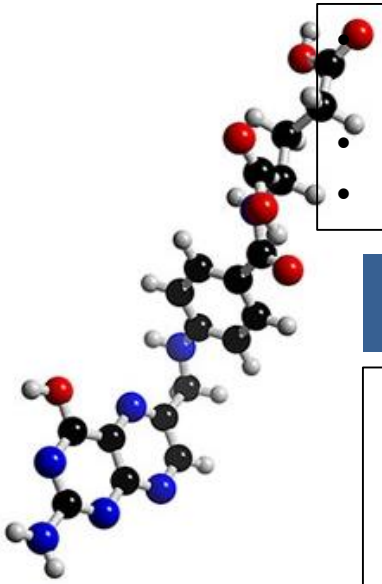
Understanding the problem

Folic acid and NTD

- **Folic acid (vitamin B9) is a water soluble vitamin that plays a fundamental role in the process of cell multiplication and in the formation of structural proteins and hemoglobin.**
- **Humans cannot synthesize folate; therefore, it has to be supplied to meet their daily requirements.**

Folate is the natural form and migth be supplied by diet

- Leafy vegetable such as spinach, aspatagus, turnip greens, lettuce, and some Asian vegetable
- Legumes such as dried or fresh beans, peas and lentils.
- Kidneys, liver and liver products contain high amounts of folate

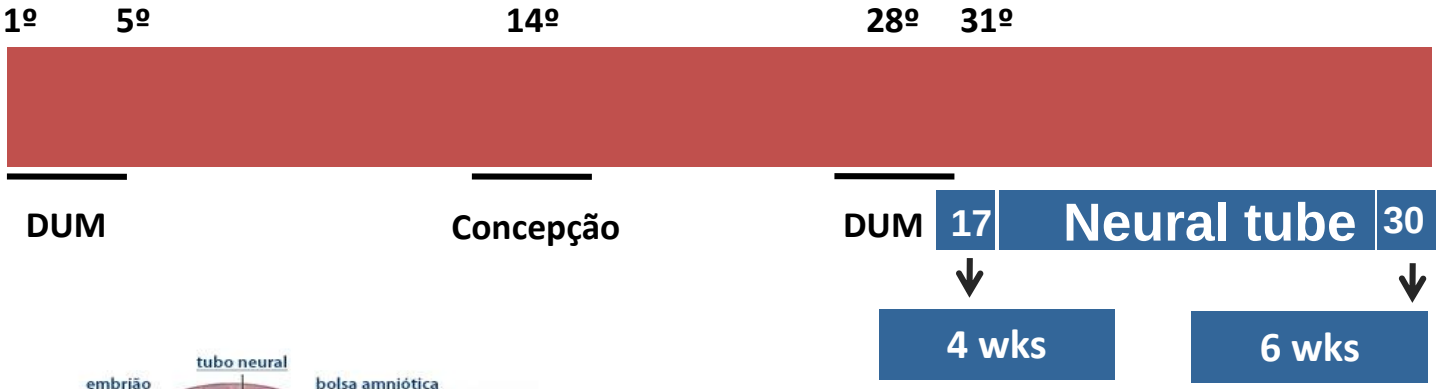


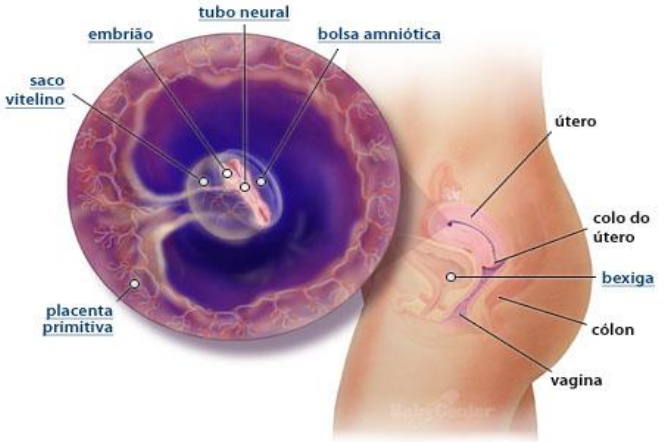
Folic acid is the synthetic form of folate

- Use as supplement or in food fortification
- Fortified grain products (pasta, cereal, bread); some breakfast cereal (ready-to-eat and others) are fortified with folate, sunflower seeds.
- Stable form

Understanding the problem

Neural tube development

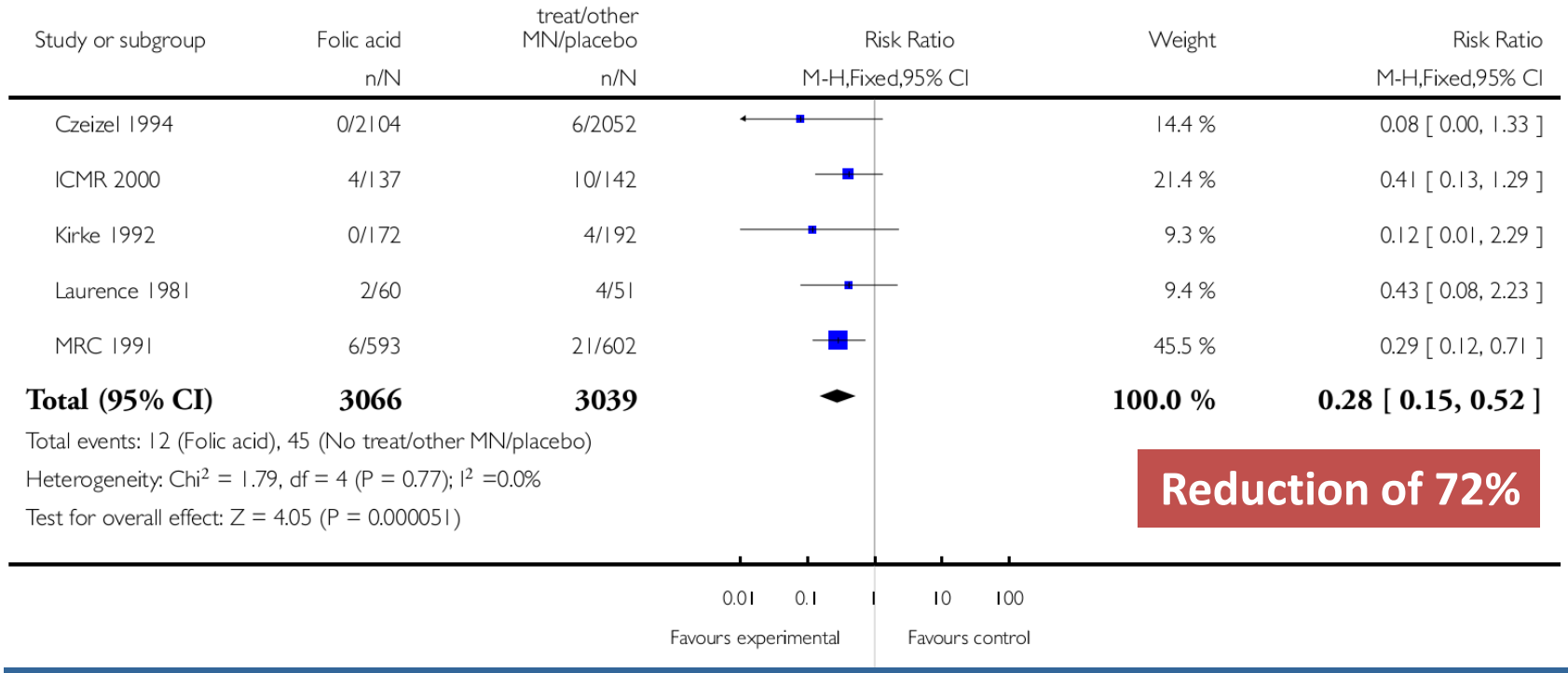




- **Up to 50% of pregnancies are unplanned,**
- **About 5-20% of all pregnant women start folic acid before pregnancy.**

THE COCHRANE COLLABORATION

Supplementation with folic acid versus no treatment/other micronutrients/placebo for NTD



Reduction of 72%

This review of five RCT, involving 6105 women (1949 with a Hx of a pregnancy affected by a NTD and 4156 with no Hx of NTDs), confirms that folic acid prevents the first and second time occurrence of NTDs.

De-Regil LM et al. Effects and safety of periconceptional folate supplementation for preventing birth defects. **Cochrane Database of Systematic Reviews** 2010, (10):CD007950

NTD Prevention

Folic Acid in the strategy for NTD prevention

- **Nutritional guidance**
- **Food fortification**
- **Periconceptional supplementation**
- **Folic acid in association with contraceptive pills**

First: RECOMMENDATION FOR LOW RISK POPULATION

All women who plans to become pregnant or all women at childbearing age without contraceptive method and who does not present risk factors for NTD utilize **400 micrograms (0.4mg)** of synthetic folic acid, beginning at least 30 days before the conception and to continue daily supplements throughout the first trimester of pregnancy (**II-1A**)

Expert panels suggest that supplemental intake in this population should range from 400 µg to 800 µg

Third: RECOMMENDATION FOR HIGH RISK POPULATION

Women who have NTD-affected previous pregnancy should be advised that synthetic folic acid supplementation at a dose of **4,000 mcg per day (4.0 mg)** is recommended. It should start at least 30 days before the conception and to continue daily supplements throughout the first trimester of pregnancy

In this group, it would be important; if possible, preconceptional genetic counseling with a physician specialized in medical genetics.

KEY ELEMENTS OF PERICONCEPTIONAL COUNSELING

- MEDICAL HISTORY
- GENETIC HISTORY
- REPRODUCTIVE HISTORY
- ENVIRONMENT & LIFESTYLE
- REPRODUCTIVE PERFORMANCE
- VACCINES AND IMMUNIZATION

Key Elements of Periconceptional Counseling

1

Medical history and medication review

- Diabetes: identify prior to pregnancy and optimize control
- Hypertension: avoid ACE inhibitors, angiotensin II receptor antagonist, thiazide diuretics
- Epilepsy: optimize control, folic acid, 5 mg/day
- DVT: switch from warfarin (Coumadin) to heparin
- Depression / anxiety: avoid benzodiazepines

Key Elements of Periconceptional Counseling

Genetic history

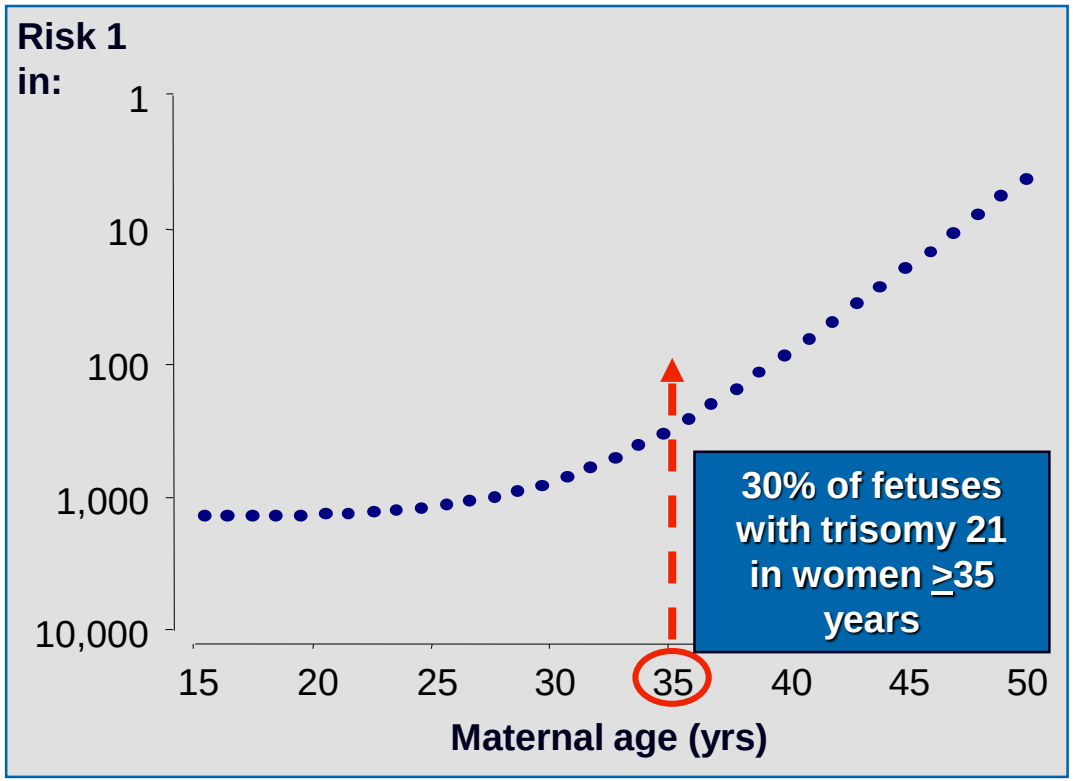
2

- Review family history of genetic issues
- Carrier screening (ethnic background): sickle cell anemia, thalassemia, Tay-Sachs disease
- Carrier screening (family history): cystic fibrosis, nonsyndromic hearing loss (connexin-26)

1970s

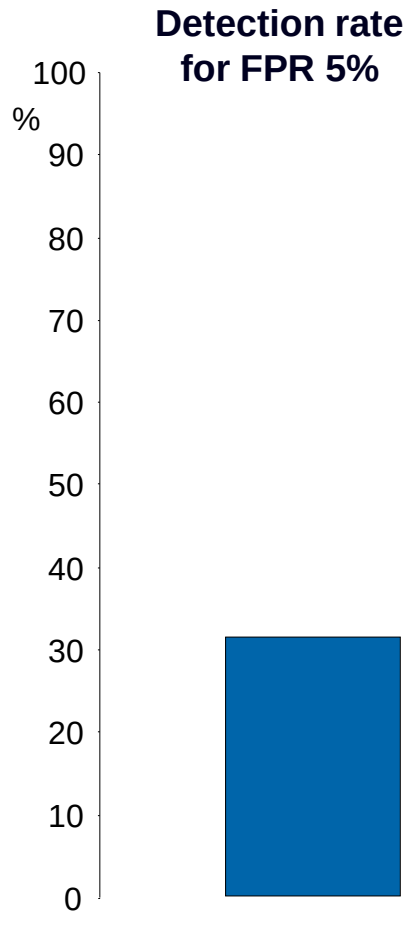
Screening for aneuploidies

Maternal age



In one-third of the Mongolian imbeciles in institutions the mothers were at the time of gestation approaching the climacteric period.

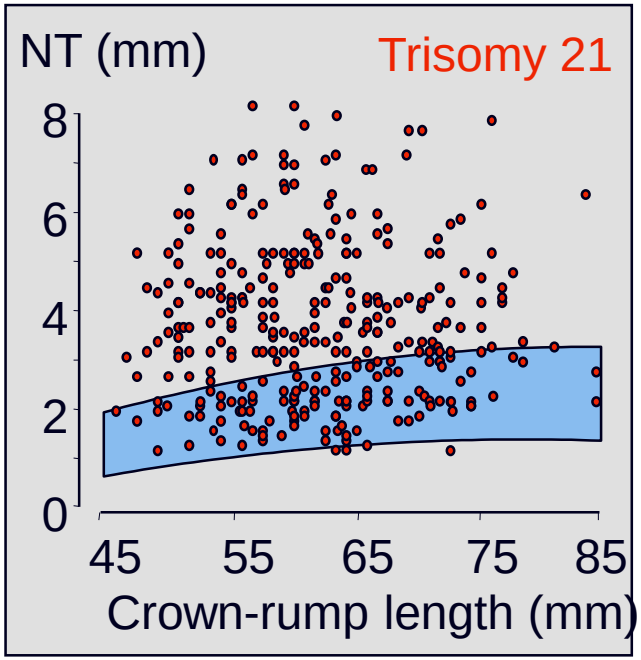
*Shuttleworth GE. Mongolian imbecility. Br Med J **1909**;2:661–5*

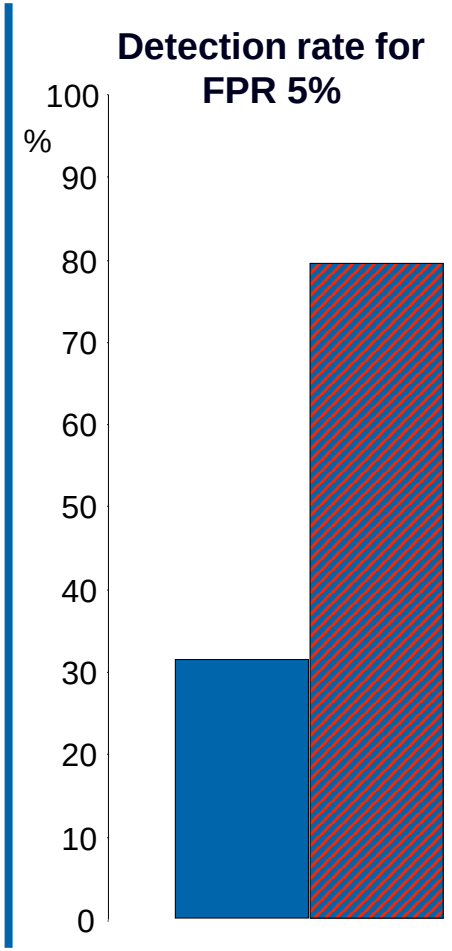


1990s

Screening for aneuploidies

Maternal age and fetal nuchal translucency





THE LANCET **1998;352:343-6.**

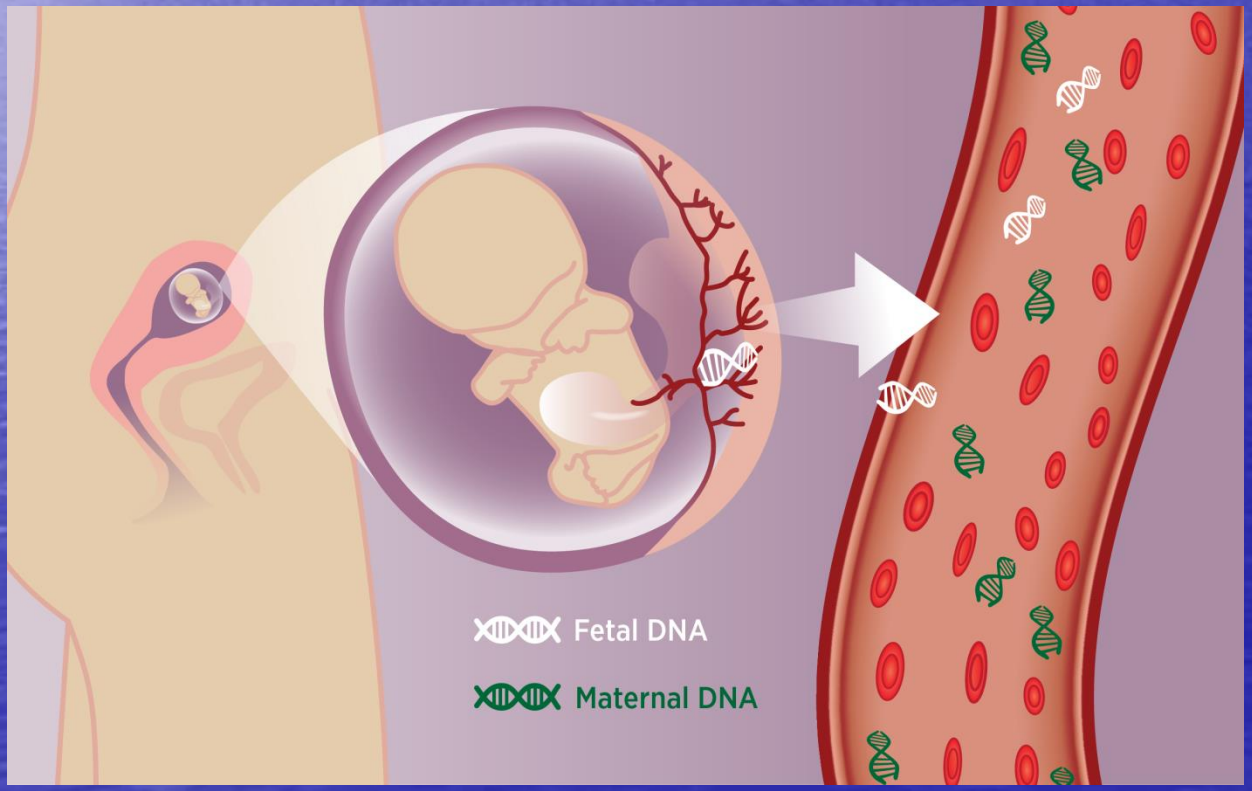
Snijders RJ, Noble P, Sebire N, Souka A, Nicolaides KH

Assessment of risk of trisomy 21 by maternal age and fetal nuchal-translucency thickness

96,127 singleton pregnancies, including 326 cases of trisomy 21: DR 77% for FPR 5%

Cell-free DNA in Maternal Blood

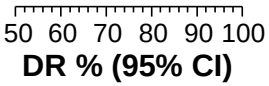
- Cell-free DNA (cfDNA) are short DNA fragments
- In pregnancy, cfDNA from both the mom and fetus are in maternal blood
- Amount of fetal cfDNA present is a small fraction of the maternal cfDNA

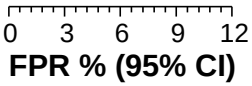


Cell free DNA test

Trisomy 21

Author	DR (95% CI)	Wt (%)	FPR (95% CI)	Wt (%)
Chiu *et al.*, 2011 [86]	100.0 (95.8 to 100)		2.06 (0.43 to 5.9)	1.52
Ehrich *et al.*, 2011 [39]	100.0 (91.0 to 100)		0.24 (0.01 to 1.4)	4.02
Palomaki *et al.*, 2011 [212]	98.6 (95.9 to 99.7)		0.20 (0.04 to 0.6)	11.87
Sehnert *et al.*, 2011 [13]	100.0 (75.0 to 100)		0.00 (0.00 to 10.3)	0.37
Ashoor *et al.*, 2012 [50]	100.0 (92.9 to 100)		0.00 (0.00 to 1.1)	3.45
Bianchi *et al.*, 2012 [89]	100.0 (95.9 to 100)		0.00 (0.00 to 0.9)	3.97
Jiang *et al.*, 2012 [16]	100.0 (79.4 to 100)		0.00 (0.00 to 0.4)	7.93
Lau *et al.*, 2012 [11]	100.0 (71.5 to 100)		0.00 (0.00 to 3.7)	1.02
Nicolaides *et al.*, 2012 [8]	100.0 (63.1 to 100)		0.00 (0.00 to 0.2)	14.54
Norton *et al.*, 2012 [81]	100.0 (95.6 to 100)		0.04 (0.00 to 0.2)	18.89
Sparks *et al.*, 2012 [36]	100.0 (90.3 to 100)		0.00 (0.00 to 2.8)	1.37
Zimmerman *et al.*, 2012 [11]	100.0 (71.5 to 100)		0.00 (0.00 to 2.7)	1.40
Guex *et al.*, 2013 [30]	100.0 (88.4 to 100)		0.00 (0.00 to 2.5)	1.52
	100.0 (90.5 to 100)		0.00 (0.00 to 1.0)	3.63
Nicolaides *et al.*, 2013 [25]	100.0 (86.3 to 100)		0.00 (0.00 to 1.8)	2.09
Song *et al.*, 2013 [8]	100.0 (63.1 to 100)		0.00 (0.00 to 0.2)	13.41
	97.4 (86.5 to 99.9)		0.00 (0.00 to 0.9)	4.20
Verweij *et al.*, 2013 [18]	94.4 (72.7 to 99.9)		0.00 (0.00 to 0.7)	4.83
Pooled analysis [809]	**99.0 (98.2 to 99.6)**	**100.0**	**0.08 (0.03 to 0.14)**	**100.0**





Screening for trisomy 21 1960-2017

	100,000 pregnancies			
	Trisomy 21 N=200		99,800 normal	
METHOD OF SCREENING	DR	Detected	False positive	
Maternal age	30%	60	5%	4990
Serum biochemistry at 16 wks	70%	140	5%	4990
Combined test at 12 wks	90%	180	5%	4990
Combined test PLUS at 12 wks	97%	194	3%	2994
Cell-free DNA	99.5%	**199**	0.08%	80

Good Clinical Practice Advice

FIGO COMMITTEE REPORT

Best practice in maternal–fetal medicine ☆

FIGO Working Group on Best Practice in Maternal–Fetal Medicine [1]

Screening for chromosomal abnormalities and non invasive prenatal diagnosis and testing

Maternal age has a low performance as a screening for fetal chromosomal abnormalities with a DR of 30-50% for FPR of 5-20%. Therefore, invasive testing for diagnosis of fetal aneuploidies should not be carried out by taking into account only maternal age.
Screening by analysis of cfDNA in maternal blood has a DR of 99% for trisomy 21, 97% for trisomy 18 and 92% of trisomy 13, at a total FPR of 0.4%.
Clinical implementation of cfDNA testing should preferably be in a contingent strategy based on the results of first-line screening by the combined test at 11-13 weeks' gestation

International Journal of Gynecology and Obstetrics 2015

Key Elements of Periconceptional Counseling

Reproductive and Gyn history

- Review prior pregnancy outcomes and counsel about recurrence
- Review prior gyn history
- Review history of PID or other tubal issues

Key Elements of Periconceptional Counseling

Living environment, diet, weight, food and medications

4

- Folic acid supplement (400 mcg routine, 1 mg diabetes/epilepsy, 4 mg previous neural tube defect)
- Assess weight, calculate BMI, advise optimal BMI
- Recommend regular exercise in moderation
- Avoid hyperthermia (hot tubs, overheating)
- Assess risk of nutritional deficiencies (vegan, pica, milk intolerance, calcium or iron deficiency)
- Avoid overuse of: vitamine A (limit to 3,000 IU per day) and vitamine D (limit to 400 IU per day)
- Limit caffeine to two cups of coffee or six glasses of soda per day
- Screen for domestic violence
- Household chemicals: avoid paint thinners and strippers, other solvents, pesticides
- Smoking cessation and avoidance of secondary smooking
- Screen for alcoholism and use of illegal drugs

Avoid anemia in pregnancy!

- **The results of a recent meta-analysis indicated a strong causal link between maternal iron-deficiency anemia and adverse birth outcomes. A strong association has been found between moderate to severe anemia at 28 weeks' gestation and the severity of intra- and postpartum haemorrhage, which cause 23% of maternal deaths.**

Lozano, R.Lancet Glob Health 2013;380:2095–2128.

Anemia in a big problem also for the NEONATE and for ADULT LIFE…

- There is mounting evidence that in infants iron deficiency anemia may produce long-lasting defects in mental development and performance that may further impair the child's learning capacity..

- defective myelination in iron deficiency anemia

…For the mothers who had severe iron deficiency during their first trimester *in utero*

- ***their babies*** experienced higher rates of cardiovascular morbidities and mortalities in their adult lives

Strategies to reduce the impact of iron deficit:

- ✓ **Prevention** (children, adolescents,schools, family, community, etc.)
- ✓ **Screening**
- ✓ **Supplementation**
- ✓ Delayed cord clamping at delivery
- ✓ Treatment
- ✓ Control

What are the solutions?

Supplementation

Food fortification

Dietary diversification

Control of infections that contribute to iron deficiency

Treatment

- **Prophylactic**: Supplement Fe – **40 mg** elemental Fe with Folinic Acid

- **Curative**: **200mg FeSo4** 3 times daily till Hb level becomes normal, then maintenance dose of 1 tab for 100 days

Key Elements of Periconceptional Counseling

5

Fertility review and optimization

- Assess for regular ovulation, signs of PCOS
- Luteal phase deficiency
- Discuss fertility after birth control
- Review frequency and timing of sexual intercourse

Preterm birth: reproductive system diseases

Polycystic ovary syndrome

Endometriosis

PCOS is associated with a higher risk of developing gestational diabetes, pregnancy-induced hypertension, pre-eclampsia and

preterm birth

Boomsma et al, Hum Reprod Update 2006

Increased risk of preterm delivery among women with endometriosis

Stephansson O et al., Hum Reprod 2010

Gravid women with adenomyosis were associated with increased risk of both spontaneous preterm delivery and PPROM

Juang CM, BJOG 2007

Key Elements of Periconceptional Counseling

Medical examination and testing: Immunization

6

- Test for infectious disease (e.g. HIV, syphilis)
- Hepatitis B immunization for at-risk patients
- Preconception immunizations (rubella, varicella)
- Counsel about avoidance of infections (e.g. toxoplasmosis, cytomegalovirus, parvosirus B19)
- Suggest a dental examination

Screening for infectious diseases

- Human immune deficiency virus (both in husband and wife)
- Syphilis (both in husband and wife)
- Hepatitis B antigen and antibody (both in husband and wife)
- Gonorrhea
- Chlamydia
- Testing for prior exposure to Parvovirus
- Testing for prior exposure to cytomegalovirus
- Testing for prior exposure to toxoplasma
- Testing for prior exposure to herpes (both in husband and wife)
- Testing for varicella immunity
- Testing for rubella immunity

Facts About Congenital CMV

- The most common congenital infection
- The most common cause of birth defects and childhood disabilities
- Every hour a child becomes permanently disabled because of congenital CMV
- One of the leading cause of cerebral palsy
- More disabilities than by Down syndrome, fetal alcohol syndrome or spina bifida

WHO, 2010

INTERVENTIONS

EARLY INTERVENTION

"better the evening before than the morning after"

- education
- awareness
- address risk factors

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International Journal of Gynecology and Obstetrics

journal homepage: www.elsevier.com/locate/ijgo

SPECIAL COMMUNICATION

International Federation of Gynecology and Obstetrics opinion on reproductive health impacts of exposure to toxic environmental chemicals☆

Gian Carlo Di Renzo [a], Jeanne A. Conry [b], Jennifer Blake [c], Mark S. DeFrancesco [b], Nathaniel DeNicola [b], James N. Martin Jr. [b], Kelly A. McCue [b], David Richmond [d], Abid Shah [d], Patrice Sutton [e], Tracey J. Woodruff [e,*], Sheryl Ziemin van der Poel [f], Linda C. Giudice [g]

[a] International Federation of Gynecology and Obstetrics, London, UK
[b] American College of Obstetricians and Gynecologists, Washington, DC, USA
[c] Society of Obstetricians and Gynaecologists of Canada, Ottawa, ON, Canada
[d] Royal College of Obstetricians and Gynaecologists, London, UK
[e] Program on Reproductive Health and the Environment, University of California, San Francisco, San Francisco, CA, USA
[f] World Health Organization, Geneva, Switzerland
[g] American Society for Reproductive Medicine, Birmingham, AL, USA

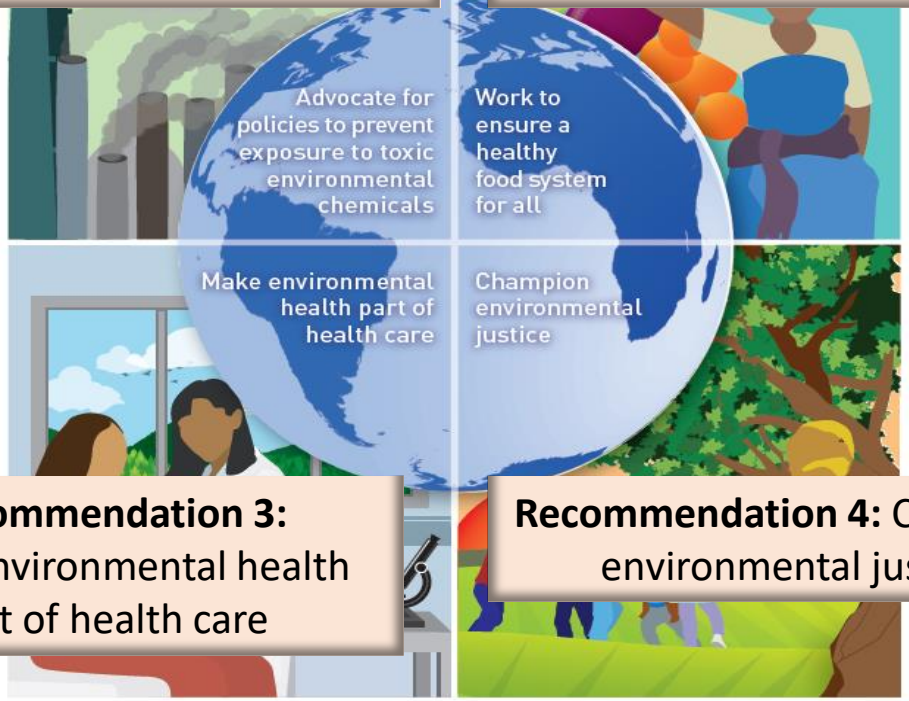
This seminal paper was published and distributed to 7000 participants at the FIGO Conference. It is a available for free down load.

INTERNATIONAL FEDERATION OF GYNECOLOGY & OBSTETRICS

Recommendations for Preventing Exposure to Toxic Chemicals

Recommendation 1: Advocate for policies to prevent exposure to toxic environmental chemicals

Recommendation 2: Work to ensure a healthy food system for all



Recommendation 3: Make environmental health part of health care

Recommendation 4: Champion environmental justice

- **Women and Children 14 times more likely to die than men in natural disasters**
- **Migration and movement from risky regions**
- **Changing distribution of pollutants: mercury, lead, persistent organophosphates and toxins**
- **Expanding Vectors: ZIKA, Dengue, Malaria**
- **Increased environmental temperatures associated with decreasing fetal weight**
- **Reports of gestational hypertension as a function of drinking water salinity and prolonged dry season**
- **Gender-based violence increases with disasters**
- **Association between preterm birth and particulate/sulfur based air pollution**

REFRAME PREGNANCY CARE

- **R**eproductive history
- **E**nviromental toxic chemicals and climate
- **F**olic acid (& inositol)supplementation
- **R**eview genetic history
- **A**ntioxidants and oxidative stress
- **M**edical preexisting conditions
- **E**valuate immunizations and infections

WE NEED TO

- MOVE TO PERICONCEPTIONAL PERIOD
- MOVE EARLY DIAGNOSIS IN 1° TRIMESTER
- ADOPT PREVENTIVE PRECONCEPTIONAL STRATEGIES IN RISK POPULATION
- CONTINUE AUDIT & FOLLOW UP

"In every forest, every farm, every garden on the planet, what is under the ground creates what's above. That is why focusing on the ripe fruit is useless. Those already on the trees you can not change".

T. Harv Eker,2005

BIRTHCONGRESS.EU

Birth

Clinical Challenges in Labor and Delivery

CONGRESS PRESIDENTS

Roberto Romero (USA)
Gian Carlo Di Renzo (Italy)

VENICE

ITALY

POWERED BY MCA scientific events

14-17 November | 2018

PREIS SCHOOL

Permanent International and European School in Perinatal, Neonatal and Reproductive Medicine

GRAZIE

merci gracias thank you 谢谢

děkuji תודה tack どうも

tak

obrigado Баярлалаа

hvala kiitos

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danke kam спасибо

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