Contraception: Challenging Cases and the Future

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Disclosures

- Research support-NICHD, Yale University
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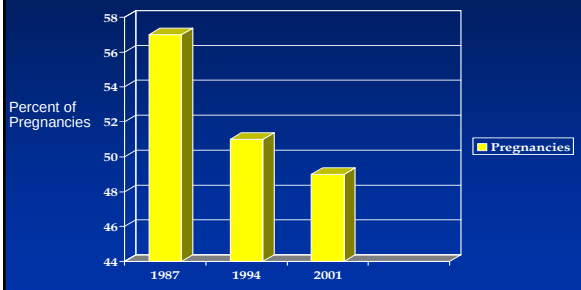
Topics

- Brief overview
- Case scenarios
  - VTE
  - Breast cancer
  - Obesity
  - Headache
- International importance of contraception

Unintended Pregnancies United States, 1987-2001



National Survey of Family Growth data, 1987-2001

A continuing high rate of unintended pregnancy-why?

- Poor women 4xs more likely to experience unintended pregnancy and 3Xs more likely to undergo an abortion
- About 11% of women at risk for unintended pregnancy were not using contraception; rate is 3% in U.K. and France
- Among women at risk for unintended pregnancy, only 2% use an IUD; 6% of at risk women use IUDs in the U.K. and 20% in France

TrussellJ, WynnLL: Contraception 2008; 77: 1-5

A continuing high rate of unintended pregnancy-strategies?

- Access and cost, e.g. co-pays, still a major barrier. For example, health systems that reduce or eliminate co-pays, e.g. Kaiser, see increased utilization
- Reducing side effects and better counseling
- Overcoming resistance to long-acting methods such as the IUD, DMPA, implants.
- Increasing availability of emergency contraception

TrussellJ, WynnLL: Contraception 2008; 77: 1-5

Everyday Risks in Perspective

Activity	Risk of Death
Risk per Year:	
Auto accident	1 in 5000
Fire	1 in 50,000
Riding bicycle	1 in 130,000
Airplane crash	1 in 250,000
Pregnancy	1 in 8700
Pregnancy Prevention:	
OC use, non-smoker	1 in 1,667,000
OC use, smoker	1 in 57,900
Tubal sterilization	1 in 66,700
Surgical abortion	1 in 142,900

TrussellJ, JordanB. *Contraception* 2006;73:437-439

VTE Risk and Contraception: Frequent Scenarios

- When should we screen for inherited thombophilias?
- What methods are appropriate for women on anticoagulants especially if for VTE treatment?
- Can DMPA and other progestin-only agents be used for women with a history of VTE?

Inherited Thombophilias

- Factor V Leiden mutation accounts for 40-50% of thombophilias with deficiencies in AT III, protein C, protein S and others accounting for the rest
- Factor V Leiden mutation seen in about 5% of Caucasian women, 2.2 % of Hispanic women, and 1.2% of African-American women

Case-Control Study of DVT Risk in OC Users Carrying Factor V Leiden Mutation

	RR (95% CI)	Incidence per 10,000 Woman-Years
Controls	1.0 (ref)	0.8
OCs only	3.8 (2.4-6.0)	3.0
V Leiden only	7.9 (3.2-19.4)	5.7
V Leiden and OCs	32.7 (7.8-154)	28.5

Vandenbroucke et al. *Lancet*. 1994;344:1453.

Routine Screening for Thrombogenic Mutations

- Screen 1 million potential combined hormonal contraception users for thrombogenic mutations
- Between 30,000 and 60,000 women would screen positive for a thrombogenic mutation
- Of these, only about 30 to 60 women will experience a VTE event – would need to screen 400,000 women to prevent 1 death

Bottom-line: routine screening is neither cost-effective nor clinically indicated but can be considered with idiopathic VTE especially in young, first degree relatives

MohllageeAP et al. *Contraception* 2006; 73:166-178

Anticoagulant Therapy for VTE and Contraception

- Extremely limited literature mostly examining effects of contraception on managing anticoagulant complications
- DMPA effective in preventing recurrent hemorrhagic cysts; LNG-IUD useful in treating menorrhagia
- WHO supports use of all but estrogen-containing contraceptives for women on anticoagulants for VTE

CulwellKR, CurtisKM; *Contraception* 2009; 80: 337-345
Medical Eligibility Criteria for Contraceptive Use; World Health Organization, Fourth Edition, 2009

Prior VTE and Contraception

- Use of combination hormonal contraception contraindicated in vast majority of women
- Two case-control studies of progestin-only contraceptives did not demonstrate increased risk of VTE but had limited numbers of cases and controls
- Both WHO and ACOG support use of progestin-only contraceptives for women with prior history of VTE

WHO Collaborative Study of Cardiovascular Disease and Steroid Hormones; Contracpetion 1998; 57: 315-324
HeinemannLA et al. *Eur J Contracept Reprod Health Care* 1999; 4: 67-73
Medical Eligibility Criteria for Contraceptive Use; World Health Organization, Fourth Edition, 2009
ACOG Practice Bulletin; Use of Hormonal Contraception in Women with Coexisting Medical Conditions; No. 73; June 2006

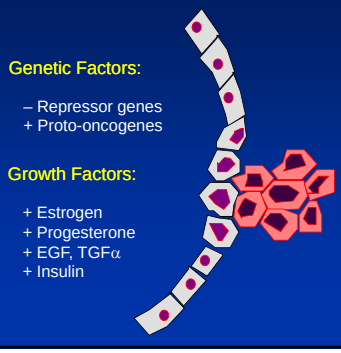
VTE Risk and Contraception: Frequent Scenarios

- When should we screen for inherited thombophilias? Idiopathic if young;1^0 degree relatives
- What methods are appropriate for women on anticoagulants especially if for VTE treatment? All but estrogen-containing products
- Can DMPA and other progestin-only agents be used for women with a history of VTE? Yes

Breast Cancer Risk and Contraception: Common Scenarios

- Does use of hormonal contraception increase the risk of breast cancer?
- Does family history of breast cancer in conjunction with use of hormonal contraception increase the risk of breast cancer?
- Can women carrying the BRCA gene safely use hormonal contraception?

Factors in the Early Development of Breast Cancer



Genetic Factors:

– Repressor genes
+ Proto-oncogenes

Growth Factors:

+ Estrogen
+ Progesterone
+ EGF, TGFα
+ Insulin

Tissue Factors:

Basement Membranes:

Immune Shielding

Angiogenesis

OCs and Breast Cancer Women's Care Case-Control Study

- **4,575 cases (invasive breast cancer) and 4,682 controls (population) were interviewed**
- **Women aged 35-64; data collected from 1994-1998**
- **Results**
  - 77% of case subjects and 79% of controls had used oral contraceptives
  - Risk in women who had *ever* used any oral contraceptive versus those who had *never* used an oral contraceptive was 0.9 (95% CI 0.8 to1.0)

Among women 35 to 64 yrs, current or former OC use not associated with increased breast cancer risk

Marchbanks PA, et. Al. Oral Contraceptives and the risk of breast cancer. *NEJM*. 2002;26;346; 2025-2032.

Oral Contraceptives and Breast Cancer Women's CARE Case-Control Study Summary

- No increase in risk for longer periods of use or higher doses of estrogen
- Initiation of oral contraceptive use at a young age *not* associated with increased risk
- Family history of breast cancer *not* associated with increased risk

Marchbanks PA, et. Al. Oral Contraceptives and the risk of breast cancer. *NEJM*. 2002;26;346; 2025-2032.

Other Issues Regarding Hormonal Contraception and Breast Cancer

- Available data indicates that breast cancer risk is not elevated in users of the 'mini-pill' or users of DMPA
- For women whose breast cancer has been treated, WHO does not recommend use of any form of hormonal contraception

Collaborative Group on Hormonal Factors in Breast Cancer, *Contraception* 1996; 54; 1s-106s
StromBL et al. *Contraception* 2004;69: 353-360
Medical Eligibility Criteria for Contraceptive Use; World Health Organization, Fourth Edition, 2009

BRCA Mutations and Breast Cancer Risk in Oral Contraceptive Users

- Two case-control studies suggest slight increase in risk with a duration effect though sample sizes small
- Cohort study showed no increase in risk with BRCA1 or BRCA2 carriers

UrsinG et al. *Cancer Res* 1997; 57:3678-3680
NarodSA et al. *J Natl Cancer Inst* 2002; 94; 1773-1779
MilneRL et al. *Cancer Epidemiol Biomarkers Prev* 2005; 14; 350-356

Breast Cancer Risk and Contraception: Common Scenarios

- Does use of hormonal contraception increase the risk of breast cancer? No
- Does family history of breast cancer in conjunction with use of hormonal contraception increase the risk of breast cancer? No
- Can women carrying the BRCA gene safely use hormonal contraception? Probably

Obesity and Contraception: Frequent Scenarios

- Does obesity affect effectiveness of oral contraceptives?
- Are the risks higher for obese women who use oral contraceptives?
- Does bariatric surgery affect efficacy of oral contraceptives?

Weight and BMI Studies of Combination Hormonal Contraception-I

- Transdermal patch
  - Zieman 2002-cohort; 6% pregnancy rate (5/83) among women >90 kg
- Oral contraceptives:
  - Holt 2002-retrospective cohort; pregnancy risk about 60% higher in women ≥70.5 kg; among 35 ug EE OC users, risk of pregnancy about 4.5 Xs higher
  - Holt 2005-case control; increased pregnancy risk with BMI >27.3 or weight >75 kg 60% and 70% respectively
  - NSFG 2002-retrospective cohort; pregnancy risk about 60% higher with BMI ≥30 but disappears after adjustment for age, race/ethnicity, and parity

ZiemanM et *al:Fertil Steril* 2002;77;s13; HoltVL et *al:Obstet Gynecol* 2002:99:820
HoltVL et *al:Obstet Gynecol* 2005;105:46; HuberLRB, TothJL: *Am J Epidemiol* 2007;166:1306

BMI and Oral Contraceptive Efficacy

Treatment + BMI Group (kg/m3)	No. women	No. pregnancies	RR (95% CL)
25 ug EE + triphasic NGM			
< 25	1147	12	
≥ 25	524	8	1.4 (0.6,3.4)
20 ug EE + 1 mg NETA			
< 25	787	9	
≥ 25	352	10	2.5 (1.0,6.1)
Overall			
< 25	1934	21	
≥ 25	876	18	1.8 (0.9,3.5)

BurkmanRT et al: *Contraception* 2009; 79: 424-427

Obesity and VTE Risk

- Dutch case-control study found that oral contraceptive users with BMI >25 compared to those ≤25 had 10X increased risk of VTE
- British case control study found increased VTE risk with BMI >25; if ≥ 35, risk 3X greater than normal weight users
- WHO has no restrictions to any form of contraception while ACOG suggests more consideration should be given to progestin-only forms and IUDs

AbdollahiM et al. *Thromb Haemost* 2003; 89: 493-498
NightingaleAL et al. *Eur J Contracept Reprod Health Care* 2000; 5; 265-274
Medical Eligibility Criteria for Contraceptive Use; World Health Organization, Fourth Edition, 2009
ACOG Practice Bulletin; Use of Hormonal Contraception in Women with Coexisting Medical Conditions; No. 73; June 2006

Bariatric Surgery and Oral Contraceptive Efficacy

- Issue has not been adequately studied
- One study demonstrated 2 out of 9 oral contraceptive users became pregnant after bileopancreatic diversion
- Another study of 7 morbidly obese women after jejunoileal bypass had decreased levels of oral contraceptive steroids compared to controls

Clinical Guideline; *Contraception* 2009; 80: 583-590
GerritsEG et al. *Obes Surg* 2003; 13: 378-382
VictorA et al. *Gastroenterol Clinics North Am* 1987; 16: 483-489

Obesity and Contraception: Frequent Scenarios

- Does obesity affect effectiveness of oral contraceptives? Possibly-more data needed
- Are the risks higher for obese women who use oral contraceptives? Increased VTE risk-consider progestin-only methods
- Does bariatric surgery affect efficacy of oral contraceptives? Possibly-very limited data

Headaches and Contraception: Frequent Scenarios

- Can women with migraine headaches use combination hormonal methods?
- Can women with severe headaches that are non-migrainous use combination hormonal methods?
- How does one manage women with migraines during the hormone-free interval?

Risk Factors for Stroke Among Women with Migraine Headaches

- Aura: 95% are visual (flickering light, spots, zig-zag lines; pins and needles; dysphasic speech). Precede headache and usually resolve within 1 hour afterwards
- Smoking: RR of stroke in one study of 34 among migraineurs, who smoked, and used OCs compared to non-smoking, non-migraineurs
- Age over 35: For 40 year olds with migraines on OCs rate of stroke 80/100,000; 20 year olds with migraines and on OCs rate was 8/100,000

HarrisM, KaneshiroB. *Contraception* 2009; 80: 417-421

Headaches and Combination Hormonal Contraceptives: Recommendations

- ACOG would recommend considering alternatives for all migraineurs but certainly for those with risk factors-no issues with other headaches. Can try continuous approach for women with headaches during hormone-free period
- WHO would not initiate for migraineurs over 35 or with aura-no issues for women with other headaches

Medical Eligibility Criteria for Contraceptive Use; World Health Organization, Fourth Edition, 2009
ACOG Practice Bulletin; Use of Hormonal Contraception in Women with Coexisting Medical Conditions; No. 73; June 2006

Headaches and Contraception: Frequent Scenarios

- Can women with migraine headaches use combination hormonal methods? If no aura and not over age 35
- Can women with severe headaches that are non-migrainous use combination hormonal methods? Possibly but discontinue if severity persists or worsens
- How does one manage women with migraines during the hormone-free interval? Consider continuous method BUT doesn't always work

Continued availability of safe and effective forms of contraception has a significant public health, economic, and even political impact worldwide.

Worldwide Daily "Table of Accounts"

- 1,000,000 conceptions
- 350,000 live births
  - >1/2 unplanned
  - 15% premature, little chance of survival
  - 10% die within 1 year
  - 5% with congenital anomaly
  - 3% mentally retarded
- 500,000 spontaneous abortions or stillbirths
- 150,000 induced abortions
- 1600 maternal deaths
- 75,000 mothers with complications or serious illness due to pregnancy

FathallaM: IHPIEGO Meeting, Miami: 1980

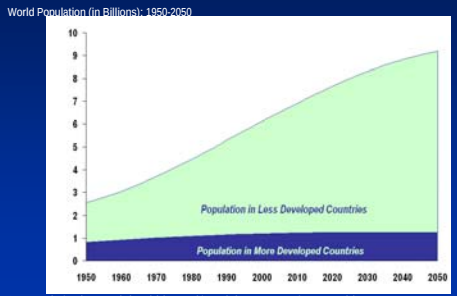
Human Reproduction- Worldwide

- 1/2 of conceptions unsuccessful
- 1/2 of conceptions successful but:
  - 1/3 not wanted, end in induced abortion
  - 1/3 not wanted or unplanned, carried to term
  - only 1/6 planned or wanted and result in a child

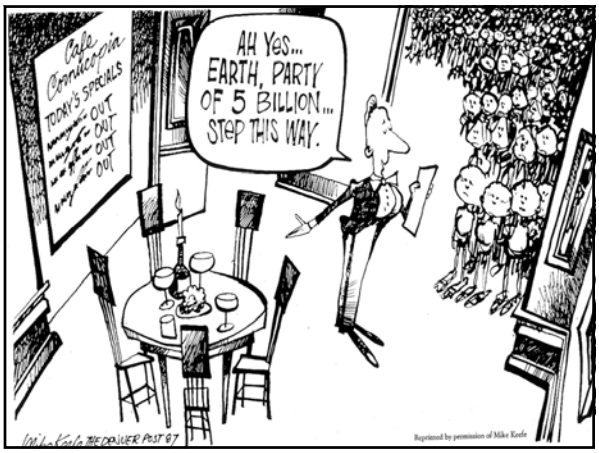
Human Reproduction- Worldwide

Despite a high degree of reproductive wastage, for the decade ending 2015, an estimated 750 million people will be added to the world's population or over 200,000 per day - more than the population of Worcester on a daily basis

Global Population Growth Is Driven by Developing Countries.



Source: United Nations Population Division, *World Population Prospects: The 2006 Revision.*



Global Population and the Environment

- Only 1% of the world's water is fresh
- Five major rivers including the Nile, Yellow and Colorado no longer reach the ocean; 70 more rivers are likely to achieve the same status soon
- Many major aquifers are running dry due to inadequate assessment of the ability to replace the water removed
- Pacific salmon fishing was stopped in 2008 on the West Coast due to excess water usage issues affecting spawning for the Sacramento and Columbia River systems.

United Nations Division for Sustainable Development 2007

Global Population and the Environment

- 1.1 billion of the world's population (about 17%) consume unclean water
- 90-95% of all sewage and 70% of industrial wastes are dumped untreated into surface waters
- By 2030, the polar ice cap will only be present in winter

Sierra Club, 2007; University of Colorado 2007

With loss of the polar icecap, polar bears may eventually only exist in zoos

Over past 50 years, have decreased the planet's forest cover by 50% and increased carbon dioxide emissions by over 30%

Across the world, 1.5 billion people are cutting firewood faster than the trees can grow back.

National Audubon Society, Sierra Club 2007

For each $7 spent on basic family planning during the next four decades, global carbon dioxide emissions would be reduced by 1 ton.

Editorial: *Lancet* 2009; 374: 949

Need to Raise the Status of Women in Developing Countries

Over next 10 years, 100 million girls will marry before their 18th birthday. This represent 1/3 of adolescent girls in developing countries (excluding China).

WHO Statistics, 2007

Americans make up 5% of the world's population but consume 1/3 of its resources and produce 1/3 of its pollution. We also are adding 2 million people to the world's population annually.

National Audubon Society

China's One Child Policy after 25 Years

- Despite policy, population still increasing at 10 million per year (equal to population of Belgium)
- Overall living standards improved with 200 million people no longer in poverty-1 million Chinese enter middle-class monthly
- Clearly a violation of the human right to reproductive choice but less controversial in China due to urban crowding, child care issues with two working parents, and costs of child care

HeskethT, LuL, XingZW. *NEJM* 2005;353:1171-1176
HeskethT, XingZW. *NEJM* 2006;354: 877 (letter)

Some Final Thoughts

- The U,S. approach of a “benevolent hegemony” is at best ineffective
- “A tree never grows to the sky”-German Proverb
- The Parable of the Boiled Frog
- Will autonomy be as dominant in our future ethical framework?