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“The Evil Among Us” or “The Buck Stops There”



Whenever I think about the almost incredible blindness to current ethical principles of my predecessors, I always wonder: What actions of today will later generations judge evil? Our government authorities are not a whole lot better. In *Bad Blood*, a three-decade study of the natural course of untreated syphilis that was sponsored and overseen by the US Public Health Service is described. While there was some bad publicity when this was first exposed in the 1970s, the tone was muted, partly presumably because the affected population was poor, rural, voiceless and black and partly because the project had extended over so many years that it was unclear where to focus the blame. There was more than enough to go around, of course, although I don't know whether any responsible parties actually were disciplined. It was a case of, “The buck stops there.”

So I was not too surprised to come across a recent newspaper article on the evils of our own military in the guise of the SHAD program. SHAD stands for “shipboard hazard and defense,” a program run by our armed forces to determine optimal approaches to combat germ and chemical warfare attacks on our sailors and soldiers in the late 1960s. Unfortunately, performing these tests exposed American servicemen to chemical and germ attack, without their consent and even without their knowledge. Some servicemen were exposed more than once. The effect of the exposures is ostensibly now under review to determine whether harm came to these unfortunate soldiers who had no reason then to distrust their bosses in the US Government.

While it's difficult to know how things looked 35 years ago, it's also hard to understand how certain ethical considerations could change. How could any civil authority run an experiment that puts a trusting colleague or ward at risk without telling him? I guess it would have been

difficult to get informed consent. “Would you mind if we test some nerve gas on you? It will help us prepare for a possible war in the future. We don't think it will cause any harm.” I wouldn't expect a gung ho response.

The US military, of course, has a dubious record in this area, from experiments with hallucinogens to deliberate radiation exposures on unsuspecting “volunteers” in the name of improving defense. I wonder not only how these sorts of projects were approved but also what kinds of people thought them up and carried them out. As best I can tell, and I'm not an investigative reporter, no heads rolled. The secrets eked out slowly over the decades. No celestial trumpets, no mea culpas. Just, “we'll look into this if we can locate the records.” There's not much ballyhoo because no one knows who was exposed. How many similar or worse projects remain unknown?

My point is not that the American government has initiated harmful testing of its own citizens and that some of these “studies” are difficult to describe without using adjectives like “evil,” “sadistic” and “cruel.” These are sad facts. Rather, it is a focused question. How could a physician not only sanction, but also participate in an observational study of a devastating disorder such as syphilis that is treatable? I doubt that these very same physicians would have hesitated for a second if offered money to be an expert witness for a patient who suffered the consequences of tertiary syphilis when the treating physician decided, “Aw, what the hell, I haven't seen tertiary syphilis in a while, let's just see what happens.” To the patient he might say, “I don't think this is really worth the aggravation of intravenous penicillin. Some patients die from penicillin allergies.” This dual standard may not be because the subjects were poor and black. The SHAD experiment was performed on servicemen, who probably

were of mixed races, although it would certainly be of interest to check this out. The dual standard most likely represented the dichotomy between a “research project” and general, ordinary medical practice. “Interesting science” versus bad medicine. As an aside, it is rare, for the two to not be mutually exclusive. There were no scientific breakthroughs in the Nazi “medical studies” on concentration camp victims. Good clinical trials require some measure of clinical equipoise; that is, a legitimate unsureness of best medical practice and then, of course, one needs “the best medical practice.” “Torture” versus negligence or bad medical practice is not of compelling clinical interest.

In the syphilis “experiment,” *Bad Blood* mentions only one physician's name I recognized, a prominent ophthalmologist, and did not mention any publications in medical journals. So I am unsure if the observations of this study were ever published, or even made. Assuming that some observations were, in fact, made, the question I pose is: how did the designers and authorities involved agree to do this? Would they have participated in overt torture? Would these doctors (and others) have agreed to actually inflict pain and suffering on others, versus simply allowing it to happen? Is there much difference between passive evil and active evil?

I've never understood how easy it has always been for people to torture each other, whether for political or religious reasons, but it has happened everywhere and in every century. Probably most of us do not understand this either. Although it is probably rare, still too many of us, even in the medical profession, tolerate harmful practices. We must all be vigilant and remember that no group has a corner on evil. It lurks among us.

— Joseph H. Friedman, MD

The Hidden Vulnerable Among Us



It is Labor Day weekend in the year 2002 and a family in Cranston is enjoying a backyard picnic unaware that their grandfather, age 79, will shortly complain of an unremitting headache, lose his customary appetite, feel feverish and take to his bed. Within a day he will become comatose; and tests will later confirm that he is a victim of West Nile encephalitis. The remaining family members are unaffected.

It is August in the year 1921 and a wealthy New York family is vacationing on the Canadian island of Campobello. A fire begins in the neighboring forest and all able-bodied persons rush to fight the flames threatening the many vacation cottages. The father of the family, a vigorous and athletic man of 39, participates actively in subduing the blaze. He returns to his cottage, exhausted but pleased that the fire had finally been extinguished. Within 24 hours, however, he complains of increasing weakness and painful cramps in his legs; and within another day he finds that he can no longer walk. A flaccid paralysis of both legs persists and physicians identify the affliction as acute poliomyelitis. No other members of the family are affected.

It is April, a Monday morning, in the year 1849 and a London family prepares to face a new day. The father leaves at daybreak to work in the stables of a wealthy mansion in the suburbs and the mother feeds the children before they go off to the local parish school. The father's labors keep him at his place of employment all week. When he returns to his home the following Saturday night he finds his wife and four children mortally ill with intractable diarrhea. By Sunday night he is the sole survivor in his family, the others having died of cholera.

It is autumn in the fateful year 1347. A terrible scourge called the Black Death has overtaken the Italian peninsula and is ravaging the prosperous port of Genoa. Thousands die of the disease, later to be identified as the bubonic plague. The contagion decimates the Genese population. Only an isolated monastery in the eastern hills seems to escape the mortal devastation.

Contagion, whether it be smallpox, cholera, tuberculosis, typhus or any one of a thousand other afflictions, has been an integral part of the human experience ever since people clustered together in rude villages. And only gradually has mankind begun to understand the origins, mechanics of spread and subtle nature of communicable disease; and with such knowledge mankind has devised ways of interrupting the spread of these infectious diseases.

The questions asked have always been the same: Why did grandpa come down with the disease but no one else in the family? Why were my wife and children taken while I was spared? And with widespread plagues, what had we as a community done, or not done, to deserve this terrible scourge? What human sin, what transgression, has provoked the divine authorities to punish us?

In some primitive cultures the rite of human sacrifice was regularly employed to stay the advance of a plague. Still later, an animal called a scapegoat was substituted in the hopes that the gods would be appeased.

The Black Death of the 14th Century, a bacterial disease of rats carried to humans by the rat's fleas, was most intense in the hovels of the poor with thatched roofs harboring colonies of black rats. Stone monasteries set on remote hillsides, with little

contact with the secular communities, tended to be spared the invasion of rats and hence the diseases carried by these rodents.

When cholera spread through the cities of the West in the 19th Century, it was commonplace to blame the victims for their fatal illness. Sermons blamed moral laxity, intemperance [alcoholism] and religious indifference for the fatal outbreaks. In Providence, for example, most of the cases of cholera were confined to the waterfront district, home to recent immigrants from Ireland, saloons and brothels. And thus the epidemic was viewed by those who escaped the scourge as evidence of divine displeasure directed against those whose faith differed from the faith of the majority or those who drank heavily. One sermon declared: "I firmly believe that if there had been no intemperance in the world, this pestilence [cholera] would not have been in the world. It was designed to teach and explain this great doctrine of a providence to the generation of the thoughtless, the negligent, and skeptical. The Cholera, I am convinced, will prevent more suffering than it will occasion."

By 1860 cholera had been shown to be a banal bacterial infection of the digestive system caused by sewage contamination of drinking water. Those living near the waterfront, whether they were saints or sinners, frequently drank contaminated water. And the London father who worked in a remote stable drank uncontaminated wellwater at the estate housing his place of employment.

Before an effective vaccine had been developed to make poliomyelitis a nightmare of the past, the causative virus was widespread and most children, particularly in poorer homes, were infected before age 6. But only rarely did the virus then spread to their spinal cord and only when the child's [or adult's] body was placed under extreme physical stress coinciding with the presence of the virus in the body. Physical exertion converted a benign viral infection into a paralytic disease. Thus, the curious paradox that polio victims were often the healthiest and most vigorous in the community.

And finally, why did grandpa take ill while the remaining family was spared? West Nile virus is transmitted to humans by the bite of an infected mosquito. Thus grandpa may have been the sole bite victim because he napped in the shade or he failed to use insect repellent. Or, perhaps, his genes made him more vulnerable. Recent studies in Paris have demonstrated that there are certain genes which facilitate the spread of this virus to the brain. It is likely, therefore, that many members of that Cranston family were also infected by the West Nile virus during that fateful picnic but that only the genetically vulnerable, such as grandpa, developed the serious manifestations of the viral infection, the others having only an inapparent infection.

Vulnerability to communicable disease is increasingly understood as a complex amalgamation of socioeconomic, ecological, nutritional, endocrinologic and genetic factors. The additional element of pure chance, of course, can never be totally eliminated. Moral turpitude, on the other hand, is rarely a measureable risk factor.

– Stanley M. Aronson, MD, MPH

Obstetricians & Gynecologists – Women’s Health Care Physicians

Patrick J. Sweeney, MD, MPH, PhD

Last year the American College of Obstetricians and Gynecologists (ACOG) celebrated its 50th anniversary as a specialty society. ACOG’s fellowship has increased from 12,400 members in 1975 to 40,800 in 2000. OB/GYN remains an attractive career choice for approximately 6% of graduating US medical students, offering a mix of medicine, surgery, primary care, and obstetrics. It is a particularly popular field among female medical students; for the academic year 2000-2001, 69.6% of all OB/GYN resident positions were filled by women. Hopefully male students will not be discouraged; a 2001 Gallup poll reported that just under half (47%) of women surveyed said they prefer a female OB/GYN, while 15% preferred a male, and 37% had no preference.¹ As one might expect, the results varied by age group with the younger women more likely to prefer a female provider.

Like most fields of medicine, Obstetrics and Gynecology has benefited greatly from the technical advances of the past few decades. Physicians practicing in the 1960s and 70s can recall the excitement that accompanied the introduction of the oral contraceptive and Rh immune globulin. The former empowered young women to safely and effectively control their reproductive futures. The latter eliminated Rh sensitization, allowing Rh-negative women the opportunity to conceive again without fear of a tragic intrauterine or newborn death. Yet, as significant as these events were, they are now taken for granted - overshadowed by increasingly sophisticated technical and scientific achievements.

Obstetrics and Gynecology has three formally recognized subspecialty areas. **Maternal-Fetal Medicine (MFM)** specialists provide care to the highest risk pregnant women. Prenatal genetic diagnosis (by chorionic villous sampling or amniocentesis), new screening tests for neural tube defects and trisomy 21, and advances in ultra-

sound imaging are just a few of the tools available to assist couples in having the healthiest possible babies. These advances in the management of high risk pregnancies, combined with the advances in neonatal care, have resulted in dramatic increases in the survival and subsequent normal development of infants born prematurely. Intrauterine transfusions and fetal surgery are also realities (see *Medicine & Health/Rhode Island*, May 2001 issue for more in depth discussions on the intrauterine diagnosis and management of several fetal conditions).

The subspecialty of **Reproductive Endocrinology and Infertility (REI)** has received a great deal of visibility and generated considerable controversy during the past decades. Beginning in 1978 with the birth of Louise Brown, the first “test tube baby,” reproductive specialists and medical ethicists have had to deal with increasingly sophisticated methods of **assisted reproductive technology (ART)** - e.g., **in vitro fertilization (IVF)**, **gamete intrafallopian transfer (GIFT)**, **zygote intrafallopian transfer (ZIFT)**, and **intracytoplasmic sperm injection (ICSI)**. Most recently the potential for human cloning has taken center stage in the reproductive technology arena; reproductive specialists, politicians, ethicists, and theologians are all concerned about the implications of cloning research.

Gynecologic Oncologists, like medical and surgical oncologists, are continually finding new ways to screen, diagnose, and treat pre-malignant and malignant disease. Research in the field of tumor markers holds the promise of

detecting cancers at very early, asymptomatic stages. Interdisciplinary strategies and new approaches such as sentinel node biopsy have resulted in integrated therapy and less radical surgery.

Urogynecology, which will likely achieve formal subspecialty status in the next few years, is finding new ways - both surgical and non-surgical - to treat women who suffer from the embarrassment and discomfort of incontinence. Urethral injections for sphincter deficiency can now be performed under local anesthesia, and preliminary reports indicate that a new surgical procedure using tension-free vaginal tape may be as effective as current retropubic approaches.

During the past decade, while the subspecialists have captured the technological limelight, general obstetricians and gynecologists have increasingly been called upon to serve as primary care physicians for women, a designation which approximately half of eligible OB/GYNs in Rhode Island have accepted. Data from the 1989 and 1990 National Ambulatory Medical Care Surveys revealed that obstetrician-gynecologists provided more office-based, general medical examinations to women 15 years and older than did general-family practitioners and internists combined.² By 1995 more than half of US women surveyed viewed their obstetrician-gynecologist as their primary care physician.³ It is noteworthy that these statistics pre-dated the increased time and emphasis placed on primary care by the OB/GYN residency programs; thus it is likely that

Table 1. Resources for Information on Hormone Replacement Therapy (HRT).

- The Women’s Health Initiative study report is available in the July 17, 2002, issue of JAMA, or on the JAMA website: jama.ama-assn.org/issues/v288n3/full/joc21036.html
- Women’s Health Initiative information, including statement from the study authors and fact sheets, are available at: www.nhlbi.nih.gov
- Additional information on the Women’s Health Initiative can be found at: www.whi.org.

the current level of primary care provided by OB/GYN physicians is considerably higher than these reports indicate.

Recognizing that the target audience for *Medicine & Health/Rhode Island* is the Rhode Island Medical Society's general membership, encompassing all fields and specialties, the manuscripts selected for this issue describe current approaches for four of the more common health issues facing women today. Dr. Kacmar's article succinctly describes new contraceptive options. After decades of very little innovation in the field of contraception - aside from altering hormone concentrations - several new delivery systems have recently been approved, including the patch and the intravaginal ring.

Perhaps one of the most frustrating diagnostic and therapeutic dilemmas facing both women and their physicians is **chronic pelvic pain (CPP)**. As many as 1 in 7 adult women may suffer from CPP, accounting for 10% of all outpatient gynecology visits. As Dr. Fox points out, many of these women will have endured their pain for months or years, and many will have been seen by one or more doctors for their problem. Dr. Fox's article presents a practical approach to the diagnosis and management of this common, yet frequently unrecognized condition.

The recognition of insulin resistance as a risk factor for coronary artery disease and type 2 diabetes mellitus has important public health implications. Recently a strong association between **polycystic ovarian syndrome (PCOS)** and insulin resistance has become apparent. Since PCOS affects approximately 5% of reproductive age women, primary care providers and others who provide care to women in this age group will find Dr. Plosker's article helpful and informative.

Dr. Frishman's article emphasizes the importance of preconceptional counseling. Women who are contemplating pregnancy should maximize their chances for a healthy outcome by seeking medical advice prior to conception. Aside from the obvious benefit - the ability to diagnose and treat

potentially harmful conditions - preconceptional counseling can identify inheritable and environmental factors, as well as personal behaviors such as diet, exercise, and the use of medications, which can have a profound effect on embryonic and early fetal development. Primary care providers should remind sexually active women of childbearing age that waiting to alter harmful behaviors like smoking and alcohol use until the pregnancy is confirmed (usually after a missed period and/or a positive pregnancy test) will not prevent very early embryonic exposure.

Finally, it is important to acknowledge the ongoing debate over the risks and benefits of **hormone replacement therapy (HRT)**. In the weeks following the National Institutes of Health's announcement that it was halting the arm of the **Women's Health Initiative (WHI)** study evaluating combined estrogen and progestin use in postmenopausal women, the offices of ACOG were flooded with calls from physicians, patients, and journalists. Women are understandably confused. An in-depth analysis of the WHI study is beyond the scope of this article. However, providers who counsel and treat postmenopausal women should read the report and avail themselves of additional resources (Table 1). Each patient should be evaluated individually, taking into account her family and personal health history, as well as her reason for taking HRT. Is she taking it to prevent heart disease, osteoporosis, or acute menopausal symptoms? For some women, HRT will continue to be appropriate, particularly for short term use. Others - e.g. those at risk for cardiovascular disease - may wish to consider the use of statin drugs and/or lifestyle changes (exercise and smoking cessation). Women who discontinue HRT should probably do so slowly over time, perhaps three to six months, to avoid sudden recurrence of symptoms.

The future of Obstetrics and Gynecology offers tremendous opportunities for both researchers and clinicians. Despite decades of research, some fundamental questions remain

unanswered, e.g. what initiates labor? The link between preterm labor and the mechanisms that underlie it will continue to be a major focus of research in the field. New HPV vaccines will likely reduce the incidence of early cervical cancer. As the Human Genome project nears completion and we discover a genetic basis for more and more diseases, the implications of genetic research will be particularly important to obstetricians, placing them in the forefront of preventive medicine. It has been said that gene technology will be the new scalpel. In addition to biochemical advances obtained through pharmaceutical research, the 21st century will undoubtedly witness the development of diagnostic equipment and surgical techniques beyond our current imagination. Obstetrician-gynecologists, as women's health care physicians, will continue to strive to see that the women they serve reap the benefits of this research and technology.

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New Contraception Options

Jennifer E. Kacmar, MD

Many contraceptive methods are available to patients today, yet unplanned pregnancy remains a significant problem in the United States. Of the 6 million pregnancies yearly in the United States, half are unintended. Roughly half of those end in abortion. Fifty-three percent of women with unintended pregnancies report using some form of contraception at the time of conception.¹

Several obstacles to appropriate use of contraceptives have been identified. Misuse and/or inconsistent use lead to ineffective results with barrier methods; and problems with irregular menses and breakthrough bleeding are common reasons for improper use or discontinuation of hormonal contraceptives. Additional factors include need for frequent use, myths and misperceptions about safety, and systemic side effects.²

Table 1 outlines current birth control options available to patients. Because a review of all options is beyond the scope of this article, the newest methods will be the focus of this review.

COMBINED HORMONAL CONTRACEPTION

Three of the newest available methods of contraception were developed from combination hormonal contraceptive pills - the monthly injection, the transdermal patch, and the intravaginal ring. Therefore, the mechanism of action and many of the risks and benefits are similar.

All combined hormonal methods of birth control contain an estrogenic and a progestagenic component. Estrogen acts primarily by suppression of follicle stimulating hormone (FSH) and luteinizing hormone (LH) to prevent ovulation. Progestins also suppress LH, preventing ovulation.

In addition, they cause alteration of the endometrium, inhibition of sperm capacitation, and thickening of the cervical mucus, impairing sperm transportation.

Combined hormonal oral contraceptives (OCs) are among the most extensively studied drugs in the world. They have been found to be safe, effective, and reversible, and can be used by most women through the reproductive years. Moreover, they confer many non-contraceptive benefits. These include menstrual cycle regulation, decreased dysmenorrhea, and improvement of anemia as well as reductions in risk for ovarian, endometrial, and colorectal cancers. Other benefits include prevention of bone loss, fibrocystic breast changes, pelvic inflammatory disease, and ectopic pregnancy. OCs have been used effectively for the treatment of acne, hirsutism, perimenopausal symptoms, and endometriosis.

OC use does carry some risk. The estrogen component of OCs may promote activation of the clotting system, increasing the risk of thromboembolic events, especially in higher risk women (e.g. smokers over 35 years of age or women with familial hypercoagulability disorders). Both estrogens and progestones may adversely affect blood pressure. In addition, older formulations had unfavorable effects on lipid profiles.²

Furthermore, with OCs, the systemic side effects, changes in bleeding patterns, and need for daily use contribute to inconsistent use or discontinuation. Despite a method-related failure rate of 0.1% with perfect use, typical use results in unintended pregnancy in up to 5% of women during the first year of use.² Twenty-five to 50% of OC users discontinue the method within the first year.²

The new methods of combined hormonal contraception were developed with these issues in mind. All three deliver combined hormonal contraception without oral ingestion, avoiding first pass metabolism and providing more consistent serum levels of hormone. Furthermore, each method was better tolerated and used with better compliance when compared to OCs.³ Each has unique features that may be more attractive to an individual patient; and, therefore, may result in less user-related failure. The following discussion describes each of the new methods, focusing on delivery method and dosing schedule, efficacy, side effects, and other distinctive characteristics.

MONTHLY INJECTION

The combined hormone monthly injectable contraceptive (Lunelle™) was introduced in early 2002. Lunelle™ contains 25mg of medroxyprogesterone acetate (MPA) and 5mg of estradiol

Table 1. Currently Available Contraceptive Methods

HORMONAL METHODS		BARRIER METHODS	INTRAUTERINE DEVICES (IUD)	SURGICAL STERILIZATION	OTHER
Combined	Progestin-only				
Oral contraceptive pills (OCs)	Oral contraceptive pills (OCs)	Condoms (male and female)	Copper-I	Fallopian tube ligation	Fertility awareness ("rhythm method")
Monthly injection	Quarterly injection	Diaphragm	Levonorgestrel Intrauterine System (LNG IUS)	Vasectomy	Abstinence
Transdermal patch	Implants	Cervical cap			
Intravaginal ring	Levonorgestrel Intrauterine System (LNG IUS)	Cervical sponge			
		Spermicides			

cypionate. The MPA suppresses ovulation for up to 42 days and the estrogen component acts to support the endometrium for approximately 16 days.⁴

The recommended dosing schedule is for intramuscular injection every 28 days, not to exceed 33 days between doses. The initial injection is generally given within 5 days of the onset of menses. Current recommendations require these injections be performed in a physician's office, but self-injectable devices are under consideration.

Studies of greater than 10,000 female years revealed a failure rate of 0.2% per 100 female years as well as a return to full fertility 2 to 4 months after the last injection.⁵

The bleeding profile among injection users was comparable to that of OCs, with slightly less breakthrough bleeding reported and a more regular bleeding pattern with regular use of the injection. In comparison to users of progestin-only injection contraception, Lunelle™ users reported fewer changes in bleeding pattern and were half as likely to report prolonged bleeding. A favorable effect on the lipid profile was also noted. However, in the United States, a trend toward weight gain of greater than 10 pounds per year of use was also noted. This weight gain was the leading cause of method-related discontinuation of the injection method in U.S. trials.⁵

TRANSDERMAL PATCH

The transdermal contraceptive patch (Ortho Evra™) offers a unique delivery system of combined hormonal birth control and has now been available since June 2002. Ortho Evra™ patches are applied weekly for 3 consecutive weeks to the abdomen, buttocks, upper outer arm, or upper torso (avoiding the breasts.) The fourth week is "patch-free," allowing menstruation to occur. Each patch delivers a daily dose of 150 mg of norelgestromin (the active metabolite of norgestimate) and 20 mg of ethinyl estradiol. The patch provides constant serum levels of hormone as compared to the peaks and troughs of OCs.⁶

The patch is extremely efficacious. In studies of over 22,000 cycles of use,

pregnancy occurred at a rate of 1 per 100 woman-years.⁷

Greater compliance was noted in transdermal patch users when compared to women using oral contraceptive pills. The patch offered good menstrual cycle control with breakthrough bleeding comparable to OCs. In addition, norelgestromin has been shown to have little androgenic effect, minimal alteration of the beneficial estrogen effect on lipids, and little or no effect on carbohydrate metabolism. The patch group was significantly more likely to report breast discomfort during the first two months of study (19% as compared to 6% in the OC group). However, only 1% of participants discontinued the patch as a result of this side effect. Application site reactions were also noted, but did not result in discontinuation of the method.^{6,7}

Weight gain was stable among patch users, with a mean change of <1 pound in up to 13 cycles of use.⁷ Excessive weight preceding use of the patch may adversely affect efficacy.^{6,7} Five of the 15 pregnancies that occurred were in study patients weighing more than 198 pounds; however, the number of patients in this category accounted for less than 3% of the study group.

Several studies of the patch were performed to determine adhesive quality. The transdermal system was evaluated in a variety of different climates and geographic locations without any significant difference in detachment noted. Patients were also studied in variable temperatures, humidity levels (including hot tubs and saunas), and during physical exertion. Overall, complete detachment occurred in 1.8% of users and partial detachment was reported in 2.9%.^(6,7) If detachment occurs, patients may reapply the same patch or a new patch within 12 - 24 hours without interruption of contraception. If greater than 24 hours passes, a back up form of birth control is recommended for one week.

INTRAVAGINAL RING

The intravaginal ring is another unique method of delivering combined hormonal contraception that became available in August 2002. NuvaRing™

is a flexible plastic ring that is inserted in the vagina by the patient between the first and fifth day of the menstrual cycle. The ring remains in place for three weeks, releasing a daily dose of 120 mg of etonogestrel and 15 mg of ethinyl estradiol. The patient removes the ring for a ring-free fourth week, allowing menstrual bleeding to occur.^{8,9} Like the patch, the ring offers sustained serum levels of hormone rather than peaks and troughs seen with oral contraceptives.

Early European studies of up to 2400 cycles reported no pregnancies with the ring system. Two larger studies of more than 12,000 cycles reported 1 - 2 pregnancies per 100 woman years.^{3,9} Ovulation resumes during the cycle immediately following discontinuation.⁹

Studies of the ring delivery system reveal good cycle control, with fewer bleeding days than a comparable OC. However, a multicenter trial found that menstrual irregularity as well as device-related events accounted for the majority of discontinuations.^{3,9} Expulsions, foreign body sensation, and/or coital problems were reported by 3% of users. Other adverse events reported frequently by ring users included vaginitis (13%), headache (12%), and leukorrhea (6%). The ring was noted to have good effect on lipid profiles, and only transient changes in the cervix and vagina noted on colposcopy.⁹

LEVONORGESTREL INTRAUTERINE SYSTEM

The levonorgestrel intrauterine system (LNG IUS, Mirena™) offers a completely different approach to contraception from the combined hormonal methods mentioned above. It combines the effectiveness of the IUD with the local benefits of a progestagenic component. The Mirena™ intrauterine device consists of a T-shaped polyethylene frame with a steroid reservoir at its stem which releases levonorgestrel at a rate of approximately 20 mg per day. With primarily local effects, the levonorgestrel causes thickening of the cervical mucus, inhibition of sperm capacitation, and alteration of the endometrium to prevent

pregnancy.^{10,11} In addition, inhibition of ovulation has been demonstrated in some women using the LNG IUS.¹⁰

Like other IUDs, Mirena™ is recommended for women who have had at least one child, are in a stable, mutually monogamous relationship, and have no history or risk factors for sexually transmitted infections. After evaluation for patient suitability, a certified medical practitioner can insert the LNG IUS at an office visit. The device is currently approved for up to 5 consecutive years of use. If continued reversible contraception is desired, a new LNG IUS can be inserted immediately following removal of the initial system.

The LNG IUS exhibits excellent efficacy with a 5-year cumulative pregnancy rate of approximately 0.7 per 100 women.³ Furthermore, about 80% of women desiring pregnancy conceived within 12 months of discontinuation of the LNG IUS.¹⁰

The progestogenic effects on the endometrium result in altered bleeding patterns, usually reflected by decreased menstrual flow. Up to 20% of women using the LNG IUS become amenorrheic within 12 months.¹⁰ Though not approved for treatment of menometrorrhagia in the United States, levonorgestrel releasing IUDs have been shown to be effective treatment for dysfunctional uterine bleeding, fibroids, dysmenorrhea, and endometrial hyperplasia.¹¹

Because the LNG IUS exerts primarily local effects, discontinuation due to systemic side effects is relatively uncommon. Reported systemic side effects, such as headache, mastalgia, nausea, and mood changes, have been found to peak approximately 3 months after insertion and then decrease with

continued use.¹¹ The rate of discontinuation due to hormonal side effects at 5 years was found to be 12 per 100 woman-years in one large study.¹¹ As with other IUDs, complete or partial expulsion can occur spontaneously in 2 - 10% of patients, and usually occurs within the first 3 months of use.^{10,11}

Although ectopic pregnancy is rare with the LNG IUS (an incidence of 0.2 per 1000 woman-years in one randomized study), progesterone IUD users are at increased risk when compared to users of other IUDs and to non-contraceptive users.¹¹ Any history of or risk factors for ectopic pregnancy are, therefore, considered relative contraindications to use of the LNG IUS. In addition, women who do become pregnant while using the LNG IUS require diagnostic testing to evaluate for ectopic pregnancy as early as possible.¹¹

CONCLUSION

A variety of new contraceptive methods are available. Each of these newer methods is safe, effective, and reversible, and all are associated with better tolerance and cycle control compared to OCs. Simplicity of use increases the likelihood of correct and consistent use and decreases the risk for method- and user-related failures. In addition, each method offers unique benefits, allowing contraceptive users and their physicians to tailor contraceptive choice to individual patient needs.

*Note: Use of brand names in this article is meant only to facilitate identification of products and does not imply endorsement.

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AUTHOR'S NOTE: Lunelle™ Monthly Contraceptive Injection is available from Pharmacia Corporation in two forms - vials or pre-filled syringes. On October 10, 2002, Pharmacia Corporation initiated a voluntary recall of pre-filled syringes due to a lack of assurance of full potency resulting in a possibly increased risk of contraceptive failure. Lunelle packaged in vials was not affected by this recall.



Chronic Pelvic Pain In Women

Sarah D. Fox, MD

Chronic pelvic pain (CPP) in women is a diagnostic and therapeutic dilemma which can be crippling for patients and frustrating for both patients and health care providers. CPP is defined as cyclic or non-cyclic, intermittent or constant pelvic pain of at least 2-6 months duration. Pain that is of acute onset, associated with fever or elevated white blood cell count, or associated with a mass, should not be categorized as chronic pelvic pain. A 1996 survey found that approximately 1 in 7 women, aged 18-50, experience CPP. No etiology of the pain was found in 61% of these patients. CPP accounts for 10% of all outpatient gynecology visits, and is responsible for 40% of all laparoscopies and 10-15% of hysterectomies. In the US, annual yearly costs of care for patients with CPP are estimated at \$880,000,000.¹ On a personal level, CPP impacts a patient's ability to work, care for herself and family, enjoy usual activities, and maintain a satisfying sex life. Patients can have multiple complaints and their visits can be time-consuming. CPP is a problem that requires patience, compassion and a systematic approach to management.

Most patients with CPP have lived with pain for months or years. They probably have seen more than one doctor for their problems. They are frustrated with the chronic and debilitating nature of the disease. Basic ground rules for treatment may help to circumvent some of the patients' frustration. Help the patient to set realistic goals. The goal of treatment should be pain reduction and restoration of normal activities, not always pain elimination. Ask the patient about her goals in treatment. She may only be looking for reassurance that she does not have a cancer or serious pathology. It may take multiple visits to establish a diagnosis, and multiple treatment regimens to obtain good results. It will take work on the part of the patient; there is no quick fix or magic pill. Reassure the patient that in some cases, no diagnosis is ever made, but that serious pathology can be eliminated and symptoms controlled. Encourage pa-

tients to find a single provider with whom they feel comfortable, and stick with him or her. Doctor-shopping delays diagnosis and leads to repetition of tests and procedures. To avoid frequent visits to the Emergency Department or lengthy phone calls, schedule frequent brief office visits. This allows the patient to address issues of importance to her and allows the provider to monitor progress while maintaining a normal schedule. Decide on a schedule with the patient (weekly or semi-weekly for 15-30 minutes) and stick to it. Do not allow the visit to run over. Do not allow a patient to pressure you to provide a diagnosis, or even treatment options at the end of the first visit.

Two basic neurological principles may help in the management of CPP. First, when a pain pathway becomes chronic, other signals transmitted along the same pathway, even a signal that should not be hurtful, can be interpreted as pain. This is similar to the phantom limb syndrome. Once established, these pathways can be difficult to break. This may help to explain why a diagnosis can be so difficult to make and why the pain can be so refractory to treatment. Second is the theory of hyperalgesic states.² Afferent nerves are stimulated by a painful stimulus. This signal is transmitted back to the dorsal horn, which then becomes hypersensitized. This can explain why women with pelvic pain may also describe vulvar pain or burning. The theory of hyperalgesia helps to explain the

complex array of presenting complaints in patients with CPP.

CPP most often is idiopathic. A major mistake in the management of CPP is to focus on diagnosis. Focusing on a diagnosis may be frustrating for both the patient and the provider, and may detract from efforts to manage pain and restore function. In those situations where a diagnosis can be made, it usually is related to one of five systems: gynecologic, bladder, bowel, musculoskeletal or neurological (Table 1). The three most common diagnoses are endometriosis, **irritable bowel syndrome (IBS)**, or **interstitial cystitis (IC)**.

Endometriosis has a prevalence of 10% in US women,³ and may be present in 40-50% of women with CPP.⁴ Endometriosis is a great imitator, and may present with a wide range of symptoms. Symptoms may be cyclic or continuous. Pain often worsens in the luteal phase of the menstrual cycle. Cyclic nature of the pain is suggestive of endometriosis, but not diagnostic, because all causes of CPP can worsen with menses. There may be involvement of adjacent organs giving irritative bowel or bladder symptoms as well as pain. Endometriosis is commonly associated with dyspareunia, particularly with deep penetration. On physical exam, there may be distinct tenderness over either adnexa or diffuse tenderness over the pelvis. Nodularity over the uterosacral ligaments is not common, but if present it is a good indicator of endometriosis.

Urological	Gastro-Intestinal	Gynecological	Neurological
Interstitial cystitis	Irritable bowel syndrome	Pelvic Inflammatory Disease	Ilio-inguinal and ilio-hypogastric nerve disorders
Renal lithiasis	Abdominal hernias	Endometriosis	Genito-femoral nerve disorders
Urethral syndrome	Ischemic bowel	Ovarian cyst	
	Chronic appendicitis	Pelvic adhesive disease	
	Diverticular disease	Pelvic congestion	
	Crohn's disease	Dysmenorrhea	

Table 1. Common Causes of Pelvic Pain

Irritable bowel syndrome may occur in up to 20% of the population.⁵ Patients will present with cramping abdominal pain, bloating and disturbed bowel habits, including more than 3 bowel movements per day or less than 3 bowel movements per week, alternating diarrhea and constipation, straining or fecal urgency, and mucus in the stool. Food and stress may worsen symptoms, and bowel movements may relieve them. Symptoms may worsen around menses, possibly due to prostaglandin effect on the bowel. Rome II Criteria (Table 2) may be helpful in making the diagnosis.

Interstitial cystitis occurs due to breaks in the glycosaminoglycan layer that protects the bladder mucosa. This allows the urine to contact the underlying tissue and causes pain and scarring. It is estimated that over 8 million people in the US are affected with IC.⁶ Patients have increased urinary frequency, urinating as frequently as every 5 minutes. Nighttime voids may continue at these intervals. They may also have pain that is worse with a full bladder and improves with voiding. IC tends to be an intermittent process, and can worsen with menses, potassium-rich foods, and stress. It is common for patients to describe vulvar pain and burning, as well as dyspareunia. Diagnosis is made in the office by instillation of a potassium solution into the bladder to reproduce symptoms, or by cystoscopy in the operating room. Although office cystoscopy is useful to rule out tumor or malignancy, it is not helpful in making the diagnosis of IC. The patient will be too uncomfortable to tolerate full distension, which is required to see the cystoscopic findings of IC.

Management of CPP should begin by ruling out known causes of pain, starting with serious causes such as a pelvic malignancy. Referrals for colonoscopy,

CPP most often is idiopathic.



cystoscopy, or surgical management of a pelvic mass should be used as needed. Once malignancy has been eliminated, careful history and physical exam and basic testing can be used to further explore causes of CPP. Basic diagnostic tools should include a history and physical exam, and a careful review of old records, to avoid duplication of tests. The history should include questions to elicit symptoms of endometriosis, such as cyclic pain worse with menses and dyspareunia; IBS, such as alternating diarrhea and constipation, mucus in the stool, and pain with change in stool consistency; and IC, such as urinary frequency, nocturia, and blood in the urine. If it seems likely that the patient has one of these diagnoses, referral to a specialist may be appropriate. Important diagnostic tests include a pregnancy test, cervical cultures for Gonorrhea and Chlamydia, urinalysis, and CBC to rule out infection. A pain diary is valuable. Stress to the patient the importance of the pain diary. Ask her to keep a notebook, take it with her wherever she goes, and record as much information as possible. She should include information about menses, quality and duration of pain, what she was doing when it started, and other symptoms including headache, bloating, bowel symptoms, back pain, and any information she feels may be relevant. Ideally the journal should cover a 2-3 month period. If she is unwilling or unable to keep a pain diary, encourage her to use a 10-point pain scale to rate her pain, where 1 is minimal and 10 is the worst she has ever experienced. This provides a useful quantitative measure of the

problem and its response to management.

The use of ultrasound as a diagnostic tool has been debated. Often, this will be a negative test. For many patients with mild pain, a normal ultrasound offers them reassurance, and this is all that they are looking for in consultation. If a pelvic mass is suspected, or if the patient is concerned about pelvic malignancy, ultrasound is a reasonable test. Laparoscopy is probably a less helpful tool for diagnosis. No diagnosis will be made in 40-60% of laparoscopies done for pelvic pain.⁷ While negative laparoscopy can be reassuring to patients concerned about cancer, endometriosis and other disease processes, in most cases of pain of uncertain etiology laparoscopy should not be part of the initial workup, and can be delayed while non-invasive treatments are tried. Patients with CPP are destined to have numerous surgical procedures, with little evidence that they improve the quality of life. It is in the patient's best interest to keep her surgeries to a minimum.

Treatment of women with CPP of unknown etiology should begin with general pain control principles. Most patients will have tried **non-steroidal anti-inflammatory drugs (NSAID)s**, but usually in a sporadic fashion. In order for NSAIDs to be effective, they need to be taken around the clock for at least 2 weeks, but ideally 1-2 months. NSAIDs taken sporadically encourage the patient to "pain monitor". The patient is much more aware of every twinge and actually experiences more total pain. Narcotics should be used minimally, for short periods of time, and as a last resort. It may be more helpful to refer the patient to an anesthesiologist for pain management before beginning long term narcotic treatment. Another option, particularly for cyclic pain, is to start a trial of hormonal therapy with a monophasic oral contraceptive. This needs to be used for at least 3 months. If oral contraceptives are not appropriate for or tolerated by the patient, IM medroxyprogesterone acetate (an off-label indication) or the new levonorgestrel releasing IUDs may be other medical options. An additional medical intervention is the use of **Gonadotropin releasing hormone (GnRH)** agonist treatment for 3-6 months, which puts patients into a pseudo-menopause.

ROME II CRITERIA	
In the past year, at least 12 weeks of abdominal discomfort/pain with 2 of 3 features:	
1)	pain relieved following defecation
2)	onset of pain associated with change in stool frequency
3)	onset of pain associated with change in stool appearance
Supported by abnormal stool form, abnormal stool passage, passage of mucus, bloating.	

Table 2. Rome II Criteria for Diagnosis of Irritable Bowel

If the pain improves, it is likely due to a gynecologic cause, such as endometriosis or adenomyosis.

Patients with chronic pelvic pain tend to reduce their activity and range of motion, which causes musculoskeletal spasm and worsens pain. Physical therapy is a very useful intervention, and can relieve pain in up to 80% of patients.⁸ A physical therapist with an interest in pelvic pain can provide good range of motion exercises, as well as some deep tissue techniques that will help to mobilize the patient. Patients should be encouraged to begin to return to normal activities, even if initially at a lower level. Behavioral modifications, including stress-controlling techniques such as massage therapy, yoga, and acupuncture may be helpful to some motivated patients.

In the 1960s, studies were published addressing the association of sexual abuse and psychiatric disorders to CPP.⁹ These led to the belief that CPP was a psychosomatic complaint found in depressed patients who had been sexually abused. Recent studies suggest that patients with chronic pain at any site are more likely to have a history of childhood traumatic life events. As for the finding of psychiatric diagnoses such as depression, there is no difference in women with CPP compared to people with other chronic pain syndromes. Abnormalities of scoring on standardized psychiatric profiles in patients with CPP return to normal when pain has been treated.¹⁰ Consequently, current thoughts are that the depression may be due to the pain, rather than the cause of the pain.¹¹ Patients should be questioned about a history of abuse or childhood trauma, and regardless of the answer, they should be involved in psychiatry, psychology or social services for counseling. If there is a history of traumatic events or

abuse, these issues can be addressed. If there is no history of such an event, counseling still provides important assistance in coping with chronic pain, including behavioral modifications and stress management techniques. If the patient is depressed, anti-depressants may be helpful for both the affective symptoms as well as the pain symptoms.

A multi-specialty approach to CPP appears to have the greatest success in treating patients.¹² If a multi-specialty clinic is available, make use of its resources. If it is not, involve a number of practitioners in treatment, including anesthesia for nerve blocks or medical management, physical therapy, and psychiatric services.

In conclusion, chronic pelvic pain can be both a diagnostic and treatment challenge. In treating patients with CPP, keep in mind the following points.

- Rule out malignancy – address the patient's concerns, and try to minimize interventions.
- If endometriosis, interstitial cystitis, or irritable bowel is suspected, treat accordingly.
- If pain is of uncertain etiology, begin a trial of NSAIDs, oral contraceptives, long acting progestones, or GnRH agonists. Try to minimize the use of narcotics.
- Use multi-specialty resources, including physical therapy, anesthesia, and counseling.
- Encourage relaxation techniques and alternative medicine options such as massage therapy and acupuncture.
- Use 10 point pain scale to get quantitative feedback on interventions.
- Do not feel pressured to come up with a diagnosis or treatment plan in the first visit. Make frequent appointments for the patient and keep to the allotted time slot.

- Help the patient to have realistic goals for treatment. Help her to mobilize and gradually return to normal activities.

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Polycystic Ovary Syndrome and Insulin Resistance

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Polycystic ovary syndrome (PCOS) affects 4% - 6% of reproductive-aged women.¹ Since the most recognizable clinical symptom is amenorrhea/oligomenorrhea, the condition has traditionally been managed by gynecologists and reproductive endocrinologists. More recently, a strong association between PCOS and **insulin resistance (IR)** has become apparent. Given the high prevalence of PCOS, and the important public health implications of IR as a risk factor for **coronary artery disease (CAD)** and type 2 diabetes mellitus, primary care providers, diabetologists, medical endocrinologists, cardiologists, and gynecologists should understand the endocrine and metabolic features of PCOS.

THE DEFINITION OF PCOS

The NICCHD has defined PCOS as a condition characterized by, in decreasing order of importance: (i) the presence of hyperandrogenism and/or hyperandrogenemia, (ii) oligo-ovulation, and (iii) exclusion of other causes of hyperandrogenism or oligo-ovulation. The presence of polycystic ovaries on ultrasound was noted as a possible inclusion criteria.²

CLINICAL AND ENDOCRINE PRESENTATION

In 1935 Irving Stein and Michael Levanthal described the classic phenotype of obesity, amenorrhea, hirsutism, and enlarged ovaries.³ Current understanding of PCOS suggests that perhaps only 60% - 70% present with the

classic Stein-Levanthal syndrome. For example, obesity is present in only 40% - 60% of PCOS patients, compared with an overall population prevalence 30% - 40%. Amenorrhea is present in just over 50% of women with PCOS. Fifteen to thirty percent of women with PCOS and documented anovulation will continue to report regular monthly bleeding. Sixty to ninety percent of patients have hirsutism. Ultrasonographic evidence of polycystic ovaries is present in 80% of anovulatory women, but 20% of ovulatory women and 14% of women on the birth control pill will have PCOS morphology on ultrasound.^{1,4}

Hirsutism is an androgen-mediated condition. **Testosterone (T)**, **androstenedione (A)**, and **dehydroepiandrosterone-sulfate (DHEA-S)** are elevated in PCOS. Total T, which includes T bound to **sex-hormone binding globulin (SHBG)** [and therefore biologically inactive] and free T [unbound and therefore biologically available] is increased in 70% of anovulatory women with hirsutism. DHEA-S, which in fact is derived from the adrenal gland and not the ovary, is elevated in 33% of women with PCOS. T and insulin both inhibit hepatic SHBG synthesis, resulting in a doubling of unbound bioavailable T from 1% in non-PCOS to 2% in PCOS women. The degree of androgen elevation in PCOS is mild, usually less than two times the upper limit of normal. The 30% of PCOS women with normal T levels will tend to have values towards the upper limits of normal, but may still have higher than normal free T resulting from low SHBG to account for their complaints of hirsutism and amenorrhea. A small percentage (< 5%) of women with apparent PCOS turn out to have non-classical, or adult onset, adrenal hyperplasia (adrenal P450c21 enzyme deficiency) as the cause of their hyperandrogenism. Twenty percent of women with hirsutism will have idiopathic hirsutism. Measuring T, DHEA-

S, and 17-OH-progesterone (the steroid substrate in the adrenal for P450c21 catalyzed glucocorticoid synthesis, and therefore increased in adrenal hyperplasia) is warranted in hirsute women. Androgen levels > 2X the upper limit of normal require further investigations to rule out adrenal or ovarian androgen-secreting tumors. A 17-OH-progesterone screening value greater than 200 ng/ml requires further evaluation for adult onset adrenal hyperplasia. Even in the presence of positive screening values, androgen-secreting tumors are exceedingly unlikely and adrenal hyperplasia is uncommon.⁵

Amenorrhea reflects anovulation and hence the high prevalence of infertility in PCOS, estimated at 55-75%.⁴ The anovulation is due to a combination of androgen-induced inhibitory actions in the ovary and to altered hypothalamic-pituitary-ovarian feedback.⁵ Progesterone production by the ovary is limited to the post-ovulatory phase of the menstrual cycle, and therefore is absent in PCOS. Since estrogen production in PCOS is not deficient, and there is a lack of progesterational protection conferred to the endometrium, prolonged endometrial exposure to unopposed estrogen triples the risk of endometrial carcinoma in PCOS.⁶ The risk of hemorrhagic dysfunctional uterine bleeding also increases.

Elevated androgens, obesity, and IR are associated with unfavorable cholesterol and triglyceride profiles, type 2 diabetes mellitus, hypertension, and CAD.

Polycystic ovaries are approximately 3X the volume of a non-PCOS reproductive age ovary. The ovarian capsule is pearly, white, smooth, and thickened. The ovary contains dense stromal tissue as well as increased numbers of small follicles < 10 mm in diameter. These are typically imaged on ultrasound as being just underneath the ovarian capsule, in an arrangement described as a "string of pearls". Cur-

"This article discusses the use of metformin, troglitazone, pioglitazone, rosiglitazone, spironolactone, finasteride, oral contraceptives, depo-provera, provera, and progestin-containing IUDs in the treatment of polycystic ovary syndrome. The author acknowledges that, although considered standard medical therapy, these medications are not approved by the FDA for use in this condition."

rent understanding is that the polycystic ovary morphology is a consequence of chronic exposure to elevated levels of androgens, rather than a cause of the hyperandrogenism. Patients often present with great apprehension about “cysts” on their ovaries. It is important to reassure patients of the descriptive rather than pathological nature of the term “polycystic.”

UNDERSTANDING THE CONCEPT OF INSULIN RESISTANCE

The most fundamental role of insulin is that of regulating cellular uptake of glucose. However, insulin has other critical roles in physiology, such as glycogen synthesis, lipid synthesis, protein synthesis, and growth and gene expression.⁷ By convention, the term IR refers to impaired insulin-mediated glucose disposal.¹ Individuals with IR require excessive amounts of insulin to maintain euglycemia. Since the “non-glucose uptake actions” of insulin are not impaired, the excessive insulin presence results in an exaggeration of the normal expected “non-glucose uptake” insulin-mediated responses. The exaggerated responses lead to the pathologic sequelae of IR.

INSULIN RESISTANCE AND PCOS – ENDOCRINE EFFECTS

Insulin has been shown to increase androgen levels in women with PCOS. Insulin decreases hepatic SHBG production, resulting in increased free T and free unopposed estrogen. Insulin inhibits hepatic **insulin-like growth factor binding protein – 1 (IGFBP-1)** production, resulting in increased free IGFs. IGF-II is highly prevalent in the human ovary, and stimulates androgen production. IGF-I may stimulate endometrial proliferation.⁵ These actions aggravate hirsutism, contribute to anovulation, and may contribute to endometrial hyperplasia.

INSULIN RESISTANCE AND PCOS – CARDIOVASCULAR IMPLICATIONS

There is a strong relationship between IR, type 2 diabetes mellitus, and CAD. IR is associated with central obesity, acanthosis nigricans,

hyperandrogenism, hirsutism, type 2 diabetes mellitus, hypertension, hypertriglyceridemia and/or low HDL-cholesterol, microalbuminuria, hyperuricemia, and increased plasminogen activator inhibitor – 1 levels. These are markers of or factors involved in the pathogenesis of CAD. Type 2 diabetes mellitus leads to blindness, renal disease, peripheral vascular disease, etc.

Fifty to seventy percent of PCOS women have IR, compared with an incidence of 10% - 25% overall.¹ Insulin resistance is mediated in lean PCOS women by intrinsic mechanisms, and in obese PCOS women by a combination of acquired (related to obesity) and intrinsic mechanisms.⁷ Between 7.5% - 10% of reproductive aged PCOS women have type 2 diabetes mellitus and approximately 35% have impaired glucose tolerance.⁸ The risk of type 2 diabetes mellitus is increased by 5X – 10X in women with PCOS compared with age and weight-matched non-PCOS women¹. Type 2 diabetes mellitus imparts a 2X – 3X increase in the likelihood of developing CAD regardless of age or sex,⁹ which may be significant given the young age of PCOS women. A long term retrospective cohort study of older PCOS women demonstrated an increased risk of mortality related to diabetes.¹⁰

Based on the presence of risk factors, it has been predicted that women

with PCOS should have a seven-fold increase in the risk of CAD.⁹ The best epidemiologic data looking at the issue of cardiovascular disease in women with PCOS comes from a retrospective cohort study of women in the U.K. with PCOS diagnosed prior to 1979 and followed until 1999. The study demonstrated a significantly increased risk of diabetes related mortality, non-fatal cerebrovascular accidents, and lipid abnormalities among PCOS-women compared with the study cohort. After correcting for body mass index, the risk of hypertension disappeared. Surprisingly, CAD, mortality from CAD, and mortality from all causes were not increased in the PCOS group.¹⁰ Acknowledging the limitations of data currently available, the risk of coronary disease in PCOS women with IR may not be as high as predicted. Nevertheless, given the known and theoretical risks, it is appropriate to consider women with PCOS at risk for diabetes and cardiovascular disease.

CLINICAL EVALUATION

Reproductive aged woman with hirsutism, acne, or alopecia should be evaluated, particularly if there is a history of menstrual irregularities. Physical examination should include weight, blood pressure, dermatologic assessment for hirsutism, acne, and acanthosis nigricans. A full gynecologic

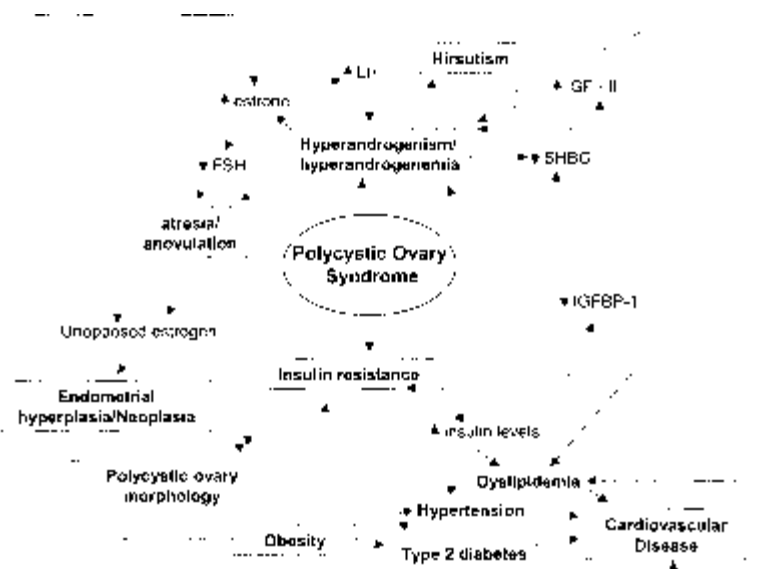


Figure 1 Representation of the self-perpetuating synergistic interactions between the metabolic and endocrine abnormalities that characterize PCOS.

examination should be undertaken. Endocrine evaluation should include T, DHEA-S, and 17-OH-P (in the follicular phase if ovulatory; random if anovulatory). With amenorrhea, other causes can be ruled out by evaluating FSH, estradiol, prolactin, and TSH. If there is a long history of unopposed estrogen, endometrial tissue sampling is appropriate.⁵ Metabolic evaluation should include a fasting glucose and fasting lipid profile.

Evaluating insulin levels as a means of determining IR is problematic and optional. The “gold standard” for determining IR is the hyperinsulinemic – euglycemic clamp technique. The subjects with IR are those who comprise the lowest quartile of the population being studied. This is a cumbersome technique, not suited for clinical practice.¹ Surrogate markers of IR suggested for clinical practice include a fasting glucose / insulin ratio < 4.5,¹¹ fasting insulin levels (10 – 14 mU/L = mild resistance; > 14 mU/L = severe resistance),¹² and/or a peak insulin level > 100 mU/L during an oral glucose tolerance test.¹² The reliability of surrogate markers in identifying an individual with IR is limited, and their ability to predict response to insulin sensitizing drugs has not been studied.¹³ An alternative is to assume from a practical standpoint that all women with PCOS are insulin resistant.¹³

HORMONAL TREATMENT

Hormonal treatment for PCOS must confer progestational protection to the endometrium. The choice of progestational treatment is tailored to the patient’s needs. If fertility is desired, ovulation inducing drugs are the treatment of choice. Ovulation allows an opportunity to conceive, and after ovulation the corpus luteum will secrete endogenous progesterone. If contraception is desired, then the oral contraceptive, depot medroxyprogesterone acetate, or the levonorgestrel intrauterine system are options since all of these contain progestins. If neither contraception nor fertility are issues, then cyclic medroxyprogesterone acetate, micronized progesterone, or even vagi-

nal progesterone are options in addition to the contraceptives discussed above.

While all of these options will protect the endometrium, the most comprehensive treatment is the oral contraceptive. It has a progestin to protect the endometrium. The estrogenic component increases hepatic SHBG production, which will bind free circulating androgens. By suppressing the hypothalamic-pituitary-ovarian axis, ovarian androgen secretion is suppressed. Regular withdrawal bleeding will occur. Acne will be improved in most instances, and there may be attenuation of hirsutism. Even with dyslipidemias and IR, the oral contraceptive is reasonable with careful monitoring since lowering androgens may actually improve the lipid profile and improve insulin sensitivity.

If hirsutism is a major concern, combination treatment with the birth control pill and agents such as spironolactone or finasteride that act at the hair follicle can be considered. The **Food and Drug Administration (FDA)** recently approved the topical agent eflornithine hydrochloride for hirsutism.

INSULIN SENSITIZING DRUGS

Insulin sensitizing drugs have become integrated into the treatment paradigm for infertile women with PCOS. Historically, the first line of treatment for PCOS-associated anovulation has been **clomiphene citrate (CC)**. The success of CC is limited because nearly 40% of amenorrheic PCOS women do not ovulate in response to CC.¹⁴ Previously, the only option for CC failures was triage to treatment with exogenous gonadotropins. Gonadotropin treatment assures ovulation but carries the risks of **ovarian hyperstimulation syndrome (OHSS)** and high order multiple gestation. Multiple gestation rates as high as 40% and rates of triplets or greater of 5% have been reported.⁵ Insulin sensitizing drugs spontaneously improve ovulation rates in anovulatory women with PCOS, and improve sensitivity of PCOS women to ovulation induction with CC.¹³ The presumed mechanism

of action is to improve insulin-driven glucose disposal. Insulin levels decline. This results in a drop in androgen levels, and an improved intra-ovarian environment favoring ovulation. Thus, women with PCOS who fail CC are now provided with a trial of combination therapy with insulin sensitizing drugs and CC concurrently before being triaged to more risky gonadotropin therapy.

Optimal use of insulin sensitizing drugs has not been determined in women with PCOS. A common strategy is to attempt ovulation induction using increasing doses of CC up to 150 mg. If the 150 mg dose fails, then an insulin-sensitizing drug is started and CC is retried initially at the 50 mg dose. If CC fails to achieve ovulation in combination with an insulin sensitizing drug at the 200-250 mg dose, then gonadotropins are used. An alternate strategy is to initiate the insulin sensitizing agent, observe for improvement in ovulation frequency, and add CC only if spontaneous ovulation does not occur after several weeks. The use of insulin sensitizing drugs in the management of metabolic and endocrine sequelae of PCOS other than infertility remains to be determined.

The greatest experience to date is with metformin. Metformin inhibits hepatic gluconeogenesis, allowing insulin levels to decrease. A secondary mechanism of action is modest improvement in glucose disposal (i.e. improved insulin sensitivity). Metformin often results in a small amount of weight loss, and there is debate about whether improved insulin sensitivity is a result of metformin treatment or a result of weight loss. Some, but not all, studies have found that metformin reduces androgen levels.¹⁵ To avoid GI side effects, metformin can be initiated at a dose of 500 mg po with dinner for four days, then 500 mg bid with breakfast and dinner for four days, then 500 mg qAM and 1000 mg qhs for four days, then 1000 mg po bid with meals. Nausea or diarrhea are usually transient.

Troglitazone was the only thiazolidenedione studied in PCOS.

Thiazolidenediones improve insulin action in the liver, skeletal muscle, and adipose tissue. Their major impact is by promoting glucose disposal in muscle. Troglitazone increased ovulation rates, improved hirsutism, ameliorated hyperandrogenemia, and improved insulin sensitivity.¹⁵ Troglitazone has been removed from the market because of rare reports of hepatic failure. The currently available thiazolidenediones piaglitazone and rosiglitazone have not been evaluated for PCOS.

CONCLUSION

PCOS is a heterogenous, self-perpetuating disorder characterized by hyperandrogenism, ovulatory dysfunction, and IR. (Figure 1) IR contributes to the endocrine and ovulatory abnormalities of PCOS, and treatment with insulin sensitizing drugs is an evolving but already integral part of therapy for anovulatory infertility in PCOS patients. The likelihood of an insulin resistant PCOS patient developing type 2 diabetes mellitus is increased markedly. PCOS patients should be evaluated for type 2 diabetes mellitus. The combination of hyperandrogenemia, obesity, and IR theoretically increases the risk of hypertension, stroke, and heart disease in PCOS patients, but epidemiologic data to date have failed to document as severe a risk as previously predicted. The clinician should continue to be concerned and vigilant regarding these risks, however, since the quality and extent of the data preclude definitive conclusions about the risks of IR in PCOS.



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NOTE: In the section "Insulin Sensitizing Drugs" we state, "The currently available thiazolidenediones piaglitazone and rosiglitazone have not been evaluated for PCOS." Since the submission of the manuscript for publication, preliminary reports have described a lowering of free testosterone in oligo-ovulatory or anovulatory insulin resistant PCOS women,¹⁶ ovulation in previous anovulatory PCOS women,^{16,17} and improved sensitivity to clomiphene in previously clomiphene-resistant PCOS women¹⁷ after initiation of treatment with rosiglitazone.

Preconceptional Counseling and Care: A Unique Window of Opportunity

Gary Frishman, MD

Preconceptional care refers to the prospective planning for a pregnancy *prior to* conception. This preventive care is one of the more cost-effective and beneficial interventions available to modern medicine and can dramatically improve the chances for a successful pregnancy. Although, by definition, preconceptional care takes place prior to conceiving, each year half of the six million pregnancies occurring in the United States are unintended.¹ In addition, the Centers for Disease Control and Prevention (CDC) reports that women with unintended pregnancies often delay seeking prenatal care, highlighting the difficulty in achieving the goals outlined in this paper.¹

A clinician should view each visit of a sexually active woman of reproductive age as an opportunity for counseling and encouraging preventive care. By incorporating preconceptional counseling into the preexisting health care model, overall costs should decrease. If not readily available, a system should be in place for referrals to genetic counselors, obstetrician/gynecologists, or other providers as indicated based on a patient's history and needs.

There are several windows of opportunity for counseling where providing information about preconceptional care should be the rule rather than exception: women inquiring about birth control, patients with a negative pregnancy test, and women who have recently delivered a baby. It is critical for a woman to have a plan in place prior to becoming pregnant since critical fetal development occurs 17 to 56 days after conception, when many women do not realize they are pregnant.² It is also important to counsel a woman who is on birth control as to the failure rate of whatever form of contraception she is using as well as the availability of post coital contraception (e.g. the morning after pill) should she wish to consider this. Depending on the patient's life style and the contraception used, consideration might be given to switching to a more reliable form. For example, the contraceptive patch might be more attractive for a younger patient who forgets to take the pill, or an IUD could be considered for a woman of advanced reproductive age who has completed childbearing and is in a monogamous relationship.

A woman's age should be taken into account during any counseling. *Adolescent* pregnancies are more likely to result in low birth weight infants along with prematurity and other adverse outcomes.³ *Older women* are at greater risk for chromosomal anomalies and miscarriages. Furthermore, the risk of a fetal death during pregnancy may be twice as high in a woman of advanced reproductive age as that in an adolescent woman, even after taking into account preexisting medical conditions.⁴ Providing access to care and planning for a pregnancy may improve the chance for a healthy adolescent pregnancy (or prevent an unintended one) whereas information about genetic counseling and intervention along with management of medical problems are among the mainstays of treatment of the older patient (independent of folic acid supplementation and lifestyle changes).

HISTORY AND EVALUATION

Medical history

A thorough medical history should include a history of asthma, thrombophilias, autoimmune conditions such as lupus, high blood pressure or cardiovascular disease, **phenylketonuria** (PKU), renal disease, cancer, and any other significant medical problems. All medical conditions should be properly managed both before and during pregnancy. For example, in women with type 2 diabetes mellitus, the risk of an associated congenital malformation can be significantly reduced by tight blood glucose control during organogenesis.⁵

Any medication that the patient is taking should be evaluated for safety in pregnancy. Any potentially unsafe medication should be changed prior to conceiving (as opposed to after a positive pregnancy test). This will allow time for whatever trial and error period is required until the appropriate dose and regimen can be achieved as well as avoid inadvertent use in an early, unrecognized, pregnancy. A classic example of this is the treatment of seizure disorders where certain medications (e.g., lithium) carry a Category D designation. Medications can play a major role in potential iatrogenic birth defects given because organogenesis begins approximately

17 days after fertilization. In addition to the **Physician's Desk Reference** (PDR) there are free programs available for a physician's **Personal Digital Assistant** (PDA) (e.g., <http://www.epocrates.com>) that can be used to check the safety of any medication in pregnancy. It is unusual in the practice of medicine to have such a powerful and free resource that permits authoritative care. In addition, the clinician should ascertain the use of alternative or health food supplements. Many patients, considering this information unimportant to their medical history, do not volunteer it.

Reproductive History

Pertinent details of the reproductive history include a history of two or more miscarriages in the first trimester or one or more miscarriages in the second trimester. A history of known cervical or uterine anomalies should be ascertained. The details of any pregnancy with a premature delivery, baby that required neonatal intensive care, and/or was born with a birth defect or congenital anomaly should be obtained.

Family and Ethnic History

The patient's family history should be ascertained for both medical conditions and ethnic background. In addition to a family history of congenital anomalies and mental retardation, questions should be asked concerning medical conditions that might adversely affect a pregnancy, such as familial conditions which pregnancy might unmask or exacerbate (such as diabetes) as well as previously asymptomatic conditions which can present during a gestation. With the increasing knowledge surrounding thrombophilias and the associated risk of adverse outcomes in both early and late pregnancy, consideration should be given to asking about a family history of any thromboembolic events or clotting disorders.

The father of the child should have his history obtained to ascertain any inheritable conditions that he might transmit to the pregnancy. Alcohol and tobacco have been shown to adversely affect sperm morphology and, furthermore, any substance or drug use is likely to be reflected in the safety of the household and an increased likelihood of exposure to the pregnant partner.

Although screening is well established

for the more common conditions such as sickle cell anemia for couples of African American descent and Tay Sachs for those of Ashkenazi Jewish descent, there are an increasing number of inheritable conditions to consider. A number of organizations (Centers for Disease Control, American College of Obstetricians and Gynecologists) recommend that the determination of cystic fibrosis carrier status be offered to all caucasian couples considering pregnancy. If the patient is positive on a screening test, her partner may then be tested and the couple counseled prior to conceiving. Although these inheritable conditions cannot be treated, obtaining the diagnosis before becoming pregnant may influence a couple's attitude towards pregnancy and will allow for an orderly counseling period, eliminating the panic that ensues when the diagnosis of an inheritable condition is made when a woman is already pregnant.

Preimplantation Genetic Diagnosis (PGD) is an additional technique available at some centers around the country including Women & Infants' Division of Reproductive Medicine. In PGD, the eggs or embryos are tested for certain genetic or chromosomal abnormalities prior to being transferred to the uterus. Women with recurrent miscarriages, those of advanced reproductive age and couples with identified genetic or chromosomal abnormalities can benefit by testing their embryos prior to their transfer to the woman's uterus. The aim of this technique is to achieve a higher implantation and pregnancy rate with a reduction in pregnancy loss, optimizing the chance for the birth of a child without the affected condition.

Substance abuse

Recreational drug and alcohol intake should be ascertained. Fetal alcohol syndrome is one of the most frequent recognizable causes of mental retardation in the United States.⁶ In addition to legal substances, women should be asked about their use of illicit substances, primarily cocaine, heroin, and marijuana. Many studies have reported increased rates of pregnancy-related complications and adverse perinatal outcomes for women who have abused substances during pregnancy compared with women who have not. Substance abuse complicated by addiction requires a structured program of counseling and treatment to alter one's addictive behaviors. Although self-reporting of illegal substance abuse is often inaccurate, pregnant women and women who are contemplating pregnancy are often motivated to be more honest by a desire to have a healthy baby. Reports

of illicit substance abuse during pregnancy range from 0.4% to 27%.⁷ A 1989 statewide study by the Rhode Island Department of Health reported that 7.5% of pregnant women admitted in labor, tested positive for an illicit substance.⁸ Since the toxicology screens identified use only within the previous 48 hours, the sporadic "recreational" users, or those who may have used drugs during the early developmental stages of pregnancy, escaped detection.

All women considering pregnancy should have documented immunity to rubella (German measles), confirmed via serologic tests because a history of rubella is not adequate.



Up to 30% of pregnant women may smoke. Tobacco intake may decrease the chance of becoming pregnant as well as increase the duration required to become pregnant.⁹ Tobacco use may also lead to a decrease in mean birth weight and an increase in the risk of preterm delivery. Up to 10% of perinatal mortality may be attributable to smoking.¹⁰ Excessive caffeine intake is associated with an increased risk of miscarriage.¹¹

Sexually Transmitted Diseases

AIDS in pregnant women bears special attention since prophylactic treatment with antiretroviral drugs has been shown to reduce the risk of vertical transmission from mother to baby by two-thirds.¹² Although AIDS no longer denotes a certain mortality, if a woman knows her diagnosis, she may wish to alter her plans for conceiving. Consideration should be given to performing cervical cultures for gonorrhea and chlamydia as well as assessing for hepatitis, syphilis, and other conditions as appropriate.

Vaccines

Patients should be asked about previous vaccination or risk factors for hepatitis B. This vaccine is safe to administer during pregnancy so that if a woman at risk is already pregnant the vaccine should still be given if appropriate.

All women considering pregnancy should have documented immunity to rubella (German measles), confirmed via se-

rologic tests because a history of rubella is not adequate. Although vaccination during pregnancy is likely to be safe, based on the fact that the vaccine is a live attenuated virus, it is recommended that the patient abstain from becoming pregnant for one month following vaccination. One Australian study found fewer than 60% of women were aware of the effect of rubella infection on pregnancy and roughly 15% had not been vaccinated.¹³ Although systems are largely in place to perform postpartum vaccination for rubella, vaccination should ideally be done prior to conception.

Vaccinating a woman of childbearing age for varicella zoster is more controversial. Although many adults have immunity to the virus, chicken pox is associated with significantly more morbidity in a pregnant woman than in a non-pregnant one. In addition, although fewer than 5% of all cases of Varicella Zoster occur among adults 20 years or older, 55% of all varicella-rated deaths are in this age group. In contrast to rubella, a history of prior chicken pox is sufficient. However, in the absence of this history, consideration should be given to antibody testing (IgG alone should suffice) with subsequent vaccination if appropriate. The patient should not conceive for one month after the second of this two-series vaccination. This recommendation is different from the package insert (which recommends a three month delay). The CDC has a site concerning vaccines in general (<http://www.cdc.gov/nip/home-hcp.htm>).

Routine Health Care

Patients should obtain all of their routine and preventive health care prior to becoming pregnant to minimize the risk of diagnosing (and having to work up and, possibly, treat) a newly discovered condition during a pregnancy as well worrying about the safety of any routine tests during pregnancy. In addition to a pap smear, dental status should be checked and a mammogram, if appropriate, should be obtained.

Contraception

When discussing preconceptional counseling, it is important to establish that the patient, indeed, wishes to conceive and to review options for contraception. This should be done both from the perspective of permitting all of the appropriate tests and interventions to be performed prior to conceiving as well as to allow the patient control over the timing of when she chooses to become pregnant.

Dietary History

It is important to obtain an adequate

dietary history, including a history (past or present) of anorexia, bulimia and other eating disorders. General dietary habits and vitamin intake (including excessive use) should be ascertained. Each year, approximately 4000 pregnancies are affected by neural tube defects in the United States. Folic acid supplementation has been shown to decrease this risk. Although more than ten years have passed since the United States Public Health Service recommended that all women who are planning to become pregnant consume 0.4 mg of folic acid daily, a recent study found that only approximately 50% of infertile women presenting to a Reproductive Medicine Center in Providence, Rhode Island, were taking a supplement at the time of their first visit.¹⁴

Home Environment and Domestic Violence

A history should include questions regarding exposure to lead, mercury, and chemicals. One major concern about pets is exposure to *Toxoplasma gondii*. In its severe form, this teratogen can cause congenital anomalies and fetal growth retardation. However, there is no current recommendation for routine universal screening for *Toxoplasma gondii*. Women with cats that go outdoors should avoid changing the cat litter, and all pregnant women should avoid eating or preparing rare or uncooked meat. A caution: even a woman who does not change the cat litter box is not fully protected, because the *Toxoplasma gondii* spores can become aerosolized.

The safety of the home should be assessed for domestic violence. The incidence of domestic violence against pregnant women has ranged in the literature from 4 to 8%.¹⁵ It is important to ascertain this information in a safe, private atmosphere and, where appropriate, to offer resources and develop a safety plan. That plan is particularly important during pregnancy when the patient is less mobile. Since rape may occur in cases of domestic violence, including married couples, effective contraception that is intercourse-independent should be instituted if desired. A chart review of the documentation of preconceptional screening in a women's health center found that many areas, such as domestic violence and nutrition dietary supplementation, had been discussed with the patient 10% or less of the time.¹⁶

Exercise and Pregnancy

Exercise in pregnancy is generally considered safe, but any exercise regimen should not be done on an intermittent or sporadic

basis because this is more likely to result in injury. As the joints become more mobile in pregnancy (secondary to the hormone relaxin), along with changes in a woman's center of gravity, the pregnant woman may be more accident prone than during her non-pregnant state. In addition, attempting to achieve one's maximal heart rate should be avoided: the appropriate goal is approximately 60% of the maximum heart rate. Data suggest that increases in core body temperature in pregnant women may increase the risk of neural tube defects.¹⁷ Although exercise can increase core body temperature, hot tub exposure carries the highest risk.¹⁸ An easy rule of thumb for the more casual exerciser is to not break a sweat. This will minimize the risk of overexertion and injury but still allow stretching, walking, swimming and other common exercise regimens. Pregnant women with specific medical problems should consult with their doctors before initiating an exercise program.

Seat Belts

The importance of seat belts cannot be overstated. Even though seat belts protect both the pregnant mother and her fetus, many pregnant women do not wear seat belts. Motor vehicles crashes are the most significant contributor to fetal death due to trauma, with two-thirds of all trauma during pregnancy resulting from motor vehicle accidents. The current recommendation is for a seat belt to be used with both a lap belt and shoulder harness in place.¹⁹

It is exceptionally rare that a health care practitioner can affect the lives of two patients with inexpensive and noninvasive interventions. Preconceptional counseling for a woman prior to her becoming pregnant is indeed a unique window of opportunity that should not be missed.

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CME Background Information

This CME activity is sponsored by Brown Medical School.

TARGET AUDIENCE: This enduring material is designed for physicians licensed in Rhode Island.

CME OBJECTIVES: At the conclusion of this course, participants should be able to

- * identify new contraceptive options
- * identify diagnostic signs and treatment options for chronic pelvic pain in women
- * describe polycystic ovarian syndrome and insulin resistance
- * identify the benefits of preconceptional counseling and care

NEEDS ASSESSMENT: The field of obstetrics/gynecology has advanced in the past decade. This issue will inform Rhode Island physicians of those advances.

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Hospital Private Practice Resident Intern Other

KEEP A COPY FOR YOUR FILES.

Keep a copy of the answers for your files. Compare them with the correct answers, which will be made available upon request, and receipt of submission requirements.

EVALUATION

Please evaluate the effectiveness of the CME activity on a scale of 1 to 5 (1 being poor; 5 being excellent) by circling your choice.

- | | | | | | |
|--|---|---|---|---|---|
| 1. Overall quality of this CME activity | 1 | 2 | 3 | 4 | 5 |
| 2. Content | 1 | 2 | 3 | 4 | 5 |
| 3. Format | 1 | 2 | 3 | 4 | 5 |
| 4. Faculty | 1 | 2 | 3 | 4 | 5 |
| 5. Achievement of educational objectives | | | | | |
| * Identify new contraceptive options | 1 | 2 | 3 | 4 | 5 |
| * Identify diagnostic signs and treatment options for chronic pelvic pain in women | 1 | 2 | 3 | 4 | 5 |
| * Describe polycystic ovarian syndrome and insulin resistance | 1 | 2 | 3 | 4 | 5 |
| * Identify the benefits of preconceptional counseling and care | 1 | 2 | 3 | 4 | 5 |

Please comment on the impact that this CME activity might have on your practice of medicine.

Additional comments and/or suggested topics for future CME activities.

Obstetrics & Gynecology CME Questions: *Circle One Response for Each Question.*

1. Of the 6 million pregnancies yearly in the U.S., approximately what percent are unintended?
 - a. 10%
 - b. 25%
 - c. 33%
 - d. 50%
 - e. 67%
2. Combined hormonal oral contraceptives have many non-contraceptive benefits, including all of the following except:
 - a. menstrual regularity
 - b. decreased risk of thromboembolism
 - c. decreased dysmenorrhea
 - d. reduced risk of ovarian cancer
 - e. improvement of anemia
3. The transdermal contraceptive patch contains:
 - a. estrogen only
 - b. progesterone only
 - c. estrogen and progesterone
4. The most common reason for discontinuing the intravaginal contraceptive ring was:
 - a. expulsion
 - b. menstrual irregularity
 - c. foreign body sensation
 - d. coital problems
 - e. Pap smear abnormalities
5. The levonorgestrel intrauterine system (Mirena™) provides contraception for a maximum of:
 - a. 1 year
 - b. 3 years
 - c. 5 years
 - d. 7 years
 - e. 10 years
6. Which of the following is a characteristic of chronic pelvic pain?
 - a. acute onset
 - b. fever
 - c. elevated WBC count
 - d. 4-month duration
 - e. pelvic mass
7. According to a 1996 survey, no etiology of the chronic pelvic pain was found in approximately what percent of patients?
 - a. 20%
 - b. 30%
 - c. 40%
 - d. 50%
 - e. 60%
8. When a specific cause for chronic pelvic pain can be identified, it is least likely to be associated with which of the following systems?
 - a. gynecologic
 - b. endocrine
 - c. urologic
 - d. gastro-intestinal
 - e. neurologic
9. Insulin resistance is associated with all of the following except:
 - a. central obesity
 - b. acanthosis nigricans
 - c. alopecia
 - d. hypertension
 - e. diabetes mellitus
10. What percent of anovulatory women have ultrasonic evidence of polycystic ovaries?
 - a. 20%
 - b. 40%
 - c. 60%
 - d. 80%
11. Up to what percent of perinatal mortality may be attributed to smoking?
 - a. 3%
 - b. 5%
 - c. 7%
 - d. 10%
 - e. 12%
12. Which of the following vaccines are contraindicated during pregnancy?
 - a. hepatitis B
 - b. influenza
 - c. rubella
 - d. all of the above
13. The most significant contributor to fetal death due to trauma is:
 - a. motor vehicle accidents
 - b. domestic violence
 - c. homicide
 - d. household accidents

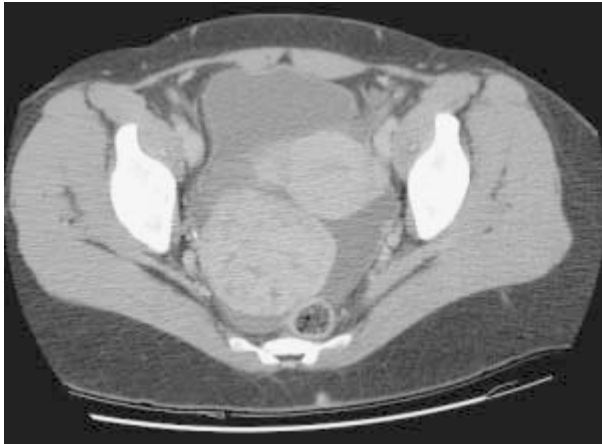


Figure 1.



Figure 2.

A Torsed Uterine Fibroid Presenting as a Radiologic Challenge

A 33 year old G2P2 non-pregnant woman presented to the ER with the sudden onset of severe lower abdominal and pelvic pain. Nausea, low-grade temps, and a sensation of pelvic pressure with urination accompanied the pain. She had a benign medical, surgical, gynecologic, and social history. Physical examination was significant for a low-grade temp, moderate abdominal pain, and a palpable, markedly tender, pelvic mass posterior to the uterus.

A CT scan demonstrated a 7.5-cm heterogeneous right adnexal mass of probable ovarian origin. (Figure 1) An ultrasound showed a 10-cm right adnexal mass separate from the ovary, the ovaries appearing normal (Figure 2). The dispute was settled at the time of surgery where a single large 10-cm fibroid was found which had torsed around its 2-cm base (Figure 3). After surgery the patient had a complete recovery with resolution of her symptoms.



Figure 3.

— BRYAN WATABE, MD, MAHESH JAYARAMAN, MD,
AND DONALD RAMOS, MD

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CMS National Surgical Infection Prevention Project: Quality Indicator Rate for Rhode Island 2001

Dede Ordin, MD, MPH

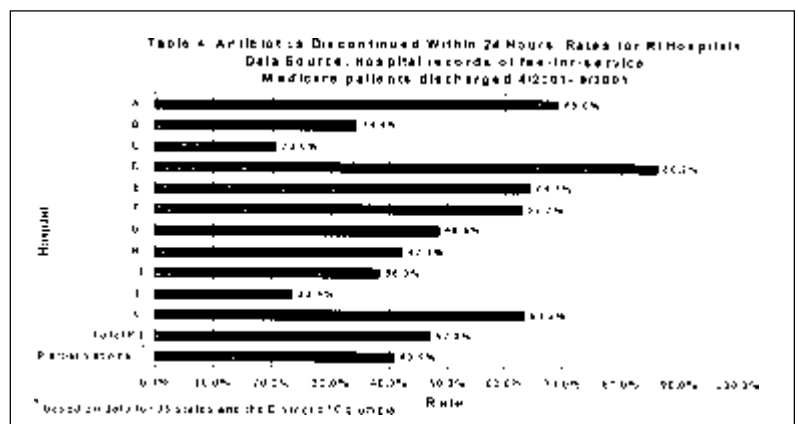
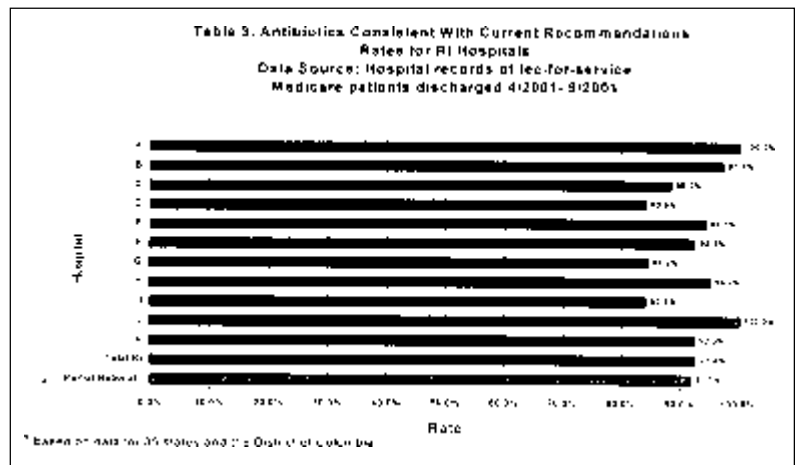
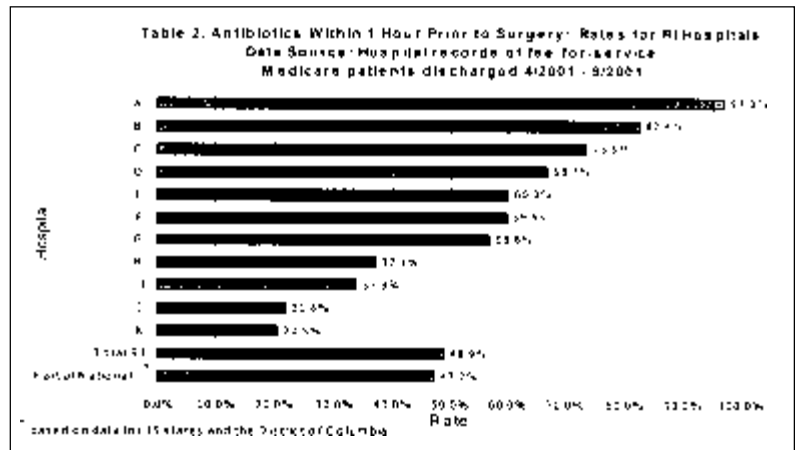
In the October 2002 issue of *Medicine & Health/Rhode Island*, we introduced the new Centers for Medicare and Medicaid Services (CMS) National Surgical Infection Prevention Project. Table 1 provides a brief review of these measures, which were developed by CMS and the Centers for Disease Control and Prevention (CDC) in collaboration with a national expert panel. The complete measure specifications and names of the organizations represented on the expert panel are available at www.surgicalinfectionprevention.org.

Tables 2-4 present the preliminary results of the measures for the state of Rhode Island. The data for these measures were abstracted by CMS from the charts of 671 randomly-selected Medicare patients discharged from Rhode Island hospitals from March 1 through September 30, 2001 with a procedure code for selected types of surgery. These include coronary artery bypass graft (CABG), other types of cardiac surgery, colon surgery, hip and knee arthro-

Table 1. CMS/CDC Quality Indicators Surgical Infection Prevention Project

- Proportion of patients who receive antibiotics within 1 hour before surgical incision
- Proportion of patients who receive prophylactic antibiotics consistent with current recommendations
- Proportion of patients whose prophylactic antibiotics were discontinued within 24 hours of surgery end time

For detailed measure specifications, including the list of surgical procedures eligible for the measures, see www.surgicalinfectionprevention.org



plasty, abdominal and vaginal hysterectomy, and selected vascular procedures such as aneurysm repair, thromboendarterectomy and arterial bypass. The hospital results are displayed in random order to preserve the confidentiality of the provider-level data.

Many hospitals, both nationally and in Rhode Island, are initiating quality improvement efforts to improve their performance on these quality indicators. RIQP will be working in voluntary partnership with all hospitals in the State to facilitate these efforts.

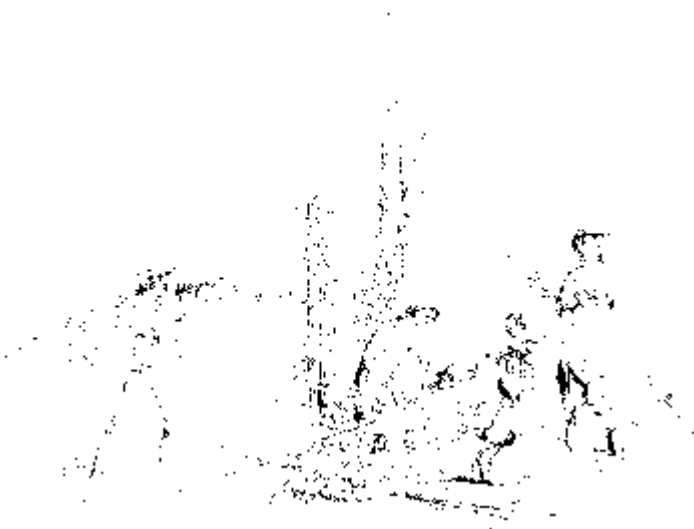
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7S0W-RI-SIP-03-01

The analyses upon which this publication is based were performed under Contract Number 500-02-RI02, entitled Utilization and Quality Control Peer Review Organization (now called Quality Improvement Organization) for the State of Rhode Island, sponsored by the Centers for Medicare & Medicaid Services, Department of Health and Human Services. The content of this publication does not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products, or organizations imply endorsement by the U.S. Government.

The author assumes full responsibility for the accuracy and completeness of the ideas presented. This article is a direct result of the Health Care Quality Improvement Program initiated by the Centers for Medicare & Medicaid Services, which has encouraged identification of quality improvement projects derived from analysis of patterns of care, and therefore required no special funding on the part of this Contractor. Ideas and contributions to the author concerning experience in engaging with issues presented are welcomed.

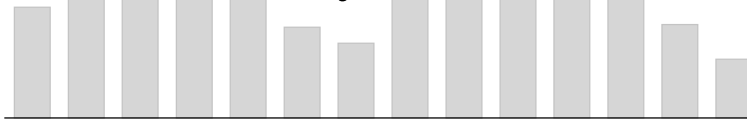


Grants Available from The Rhode Island Foundation for Polio Patients

The Rhode Island Foundation serves as the Trustee for the Rhode Island Medical Society End Polio Fund, established in 1966 from surplus donations collected by the Rhode Island Medical Society in a statewide poliomyelitis immunization campaign in 1963. Grants from this fund provide for the continuing care and support of financially needy polio victims residing in Rhode Island. Since 1966, the Foundation has disbursed the income generated from this fund to organizations within the state of Rhode Island charged with the supervision and care of those previously stricken by polio.

The Rhode Island Foundation seeks your help in identifying agencies serving individuals who are post-polio patients and have documented financial need. The Rhode Island Foundation will award two to three grants annually from the Fund, ranging from \$5,000 to \$10,000. For more information and to request an application, contact Libby Monahan by phone: (401) 274-4564, or e-mail: libbym@rifoundation.org. Deadline for submission of applications is March 1, 2003.

Health by Numbers



Rhode Island Department of Health
Patricia A. Nolan, MD, MPH, Director of Health

Edited by Jay S. Buechner, PhD

Infant Mortality in Rhode Island: A Time Trend Analysis

Samara I. Viner-Brown, MS, Hanna Kim, PhD, and William H. Hollinshead, MD, MPH

The infant mortality rate is often seen as a global measure of child health. The rate of infant mortality in Rhode Island and the United States as a whole has decreased four-fold over the past 35 years. However, the rate of improvement in both areas has slowed over the past fifteen years, nearly leveling off in the past five.^{1,2} In order to better understand the reasons for the recent lack of improvements in infant mortality rates, it is important to consider age of death, birth weight, and other contributing factors, including prematurity and multiple gestation births.

Methodology

Birth and death certificate data from Vital Records were analyzed for Rhode Island residents for the years 1987-2001. Rhode Island resident infant deaths (aged less than 365 days) were identified and linked to the corresponding birth records. **Infant mortality rates (IMR)** were computed as deaths per 1,000 live births. Rhode Island data for 1999-2001 are provisional. Infant mortality data for the United States was obtained from published sources.³

Prematurity data for both Rhode Island and the United States were obtained from the **National Center for Health Statistics (NCHS)** and the March of Dimes for the period 1990-1999.⁴ These data were used because Rhode Island's methodology for determining prematurity (i.e., gestational age recorded by physician) differs from that used by the NCHS (i.e., calculate gestational age using date of last menstrual period and infant's date of birth). To ensure comparability, the NCHS data as cited by the March of Dimes were used.

The **Perinatal Periods of Risk (PPOR)** approach developed by Dr. Brian McCarthy and the World Health Organization was modified for this analysis.⁵ The PPOR can be used by communities to monitor and investigate infant mortality and to identify gaps, target resources, and mobilize communities to action. The PPOR groups infant deaths by birth weight and age of death. By determining the "periods of risk" and the proportion of deaths attributable within each, risk factors can then be associated with each period.

Although standard PPOR studies include fetal deaths with gestational ages greater than 24 weeks, fetal deaths were not included in this analysis due to small

numbers and the large proportion with unknown gestational age or birth weight. Additionally, PPOR excludes deaths among infants with birth weights less than 500 grams. This analysis, however, includes all infant deaths. Data for three five-year periods, 1987-1991, 1992-1996 and 1997-2001, were analyzed.

Using PPOR guidelines, infant deaths were grouped by age of death (early neonatal, <7 days; late neonatal, 7-27 days; and postneonatal, 28-364 days) and birth weight (<1,000 grams, 1,000-1,499 grams, 1,500-2,499 grams, and 2,500 grams or greater). When birth weights were unknown, gestational age was used as an estimate for the period 1989-2001; gestational ages were not available for 1987 and 1988. Based on birth weight and age of death, infant deaths were grouped into three PPOR categories: maternal health, infant care and newborn care. (Table 1)

The PPOR model assigns all very low birth weight deaths to "maternal health", other neonatal deaths to "newborn care", and late deaths to "infant care". These categories can then be used to focus attention on contributing factors (e.g., maternal health: preconceptional health, perinatal care, and health behaviors; newborn care: congenital anomalies, neonatal care, and pediatric surgery; and infant care: sleep position, breastfeeding, and injury prevention).

Results

Between 1965 and 1985, the IMR in Rhode Island dropped from 22.3 deaths per 1,000 live births to 8.2 (down 63%, or 4.9% per year on average). Similarly, during the same time period, the US rate decreased from 24.7 in 1965 to 10.6 (down 57%, or 4.1% per year). Over the past fifteen years, the IMR has fallen more slowly in both Rhode Island and the United States. Between 1986 and 2001, the IMR decreased by 30% in Rhode Island (2.4% per year) and 35% (2.8% per year) in the

Table 1. Perinatal Periods of Risk: Definitions and Infant Mortality Rates, Rhode Island, 1987-2001

Perinatal Period of Risk (PPOR)	PPOR Definitions		Infant Deaths and Rates/1,000								
	Birth Weight (grams)	Age of Death	1987-1991			1992-1996			1997-2001		
			#Deaths	Rate	%All	#Deaths	Rate	%All	#Deaths	Rate	%All
Maternal Health	<1,499	Early Neonatal	315	4.3	50%	231	2.4	52%	258	4.1	63%
		Late Neonatal									
Newborn Care	500-2,499	Early Neonatal	98	1.3	15%	74	1.1	17%	56	0.9	14%
		Late Neonatal									
Infant Care	>2,500	Post Neonatal	169	2.3	27%	113	1.7	27%	91	1.5	23%
		Late Neonatal									
All Deaths*	All	All	627	8.6	100%	434	5.4	100%	405	6.5	100%

* Note: Table does not include cases with missing data

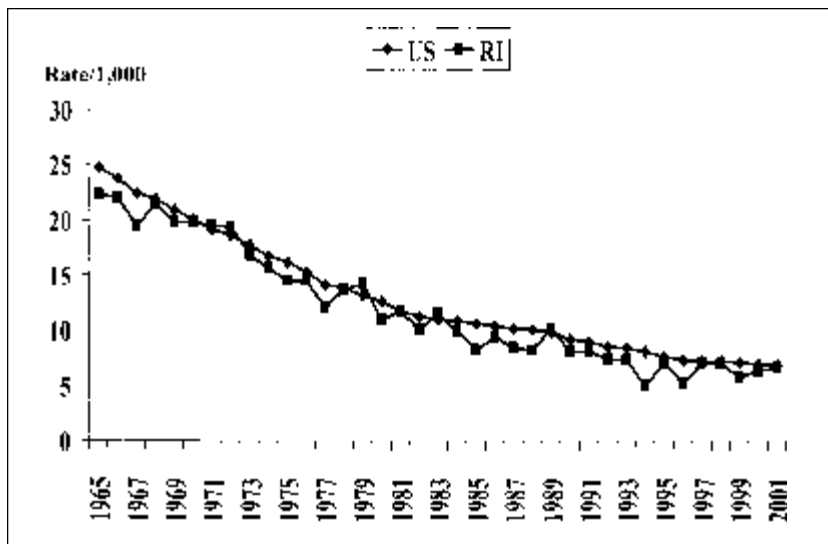


Figure 1. Infant Mortality Rates, United States and Rhode Island, 1965-2001.

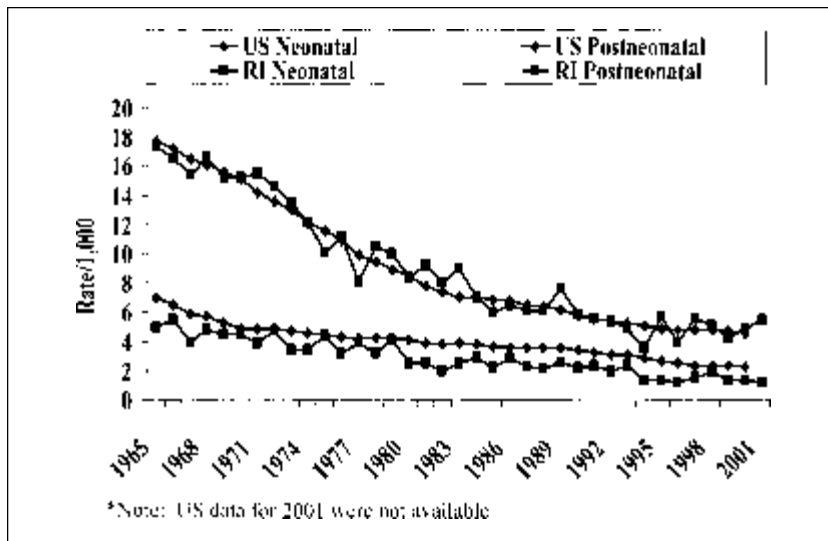


Figure 2. Neonatal and Postneonatal Mortality Rates, United States and Rhode Island, 1965-2001.

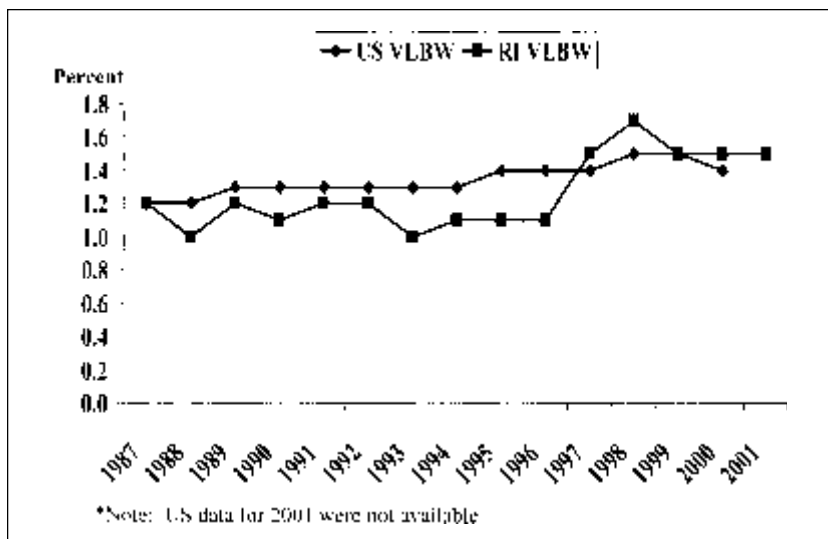


Figure 3. Very Low Birth Weight Births, United States and Rhode Island, 1987-2001.

United States. During the past five years, 1997-2001, decreases in infant mortality have been small, 7% in Rhode Island (1.4% per year), and 6% in the United States (1.2% per year). (Figure 1)

Declines in neonatal (occurring under 28 days of age) and postneonatal (occurring between 28 and 365 days of age) mortality rates in Rhode Island have also mirrored the national trend. However, during 1965-2000, Rhode Island experienced a slightly sharper drop in postneonatal mortality (72%) than the nation (67%). (Figure 2)

A comparison of three five-year periods shows that the average IMR fell from 8.6 in 1987-1991 to 6.4 in 1992-1996, but remained static at 6.5 for the 1997-2001 period. (Table 1) During these three periods, the proportion of infant mortality among those with birth weights less than 500 grams increased. During 1987-1991, 22% of the infant deaths were among those with birth weights <500 grams and by the 1997-2001 period, the proportion rose to 35%.

Based on the PPOR, the proportion of infant mortality in Rhode Island attributed to maternal health was significantly greater during 1997-2001 than both the 1987-1991 and 1992-1996 periods. (Table 1) During 1997-2001, 63% of the total infant mortality was attributable to maternal health compared with 50% and 53% for 1987-1991 and 1992-1996, respectively. The proportion of infant mortality that was attributable to newborn care and infant care was nearly the same for all three time periods, ranging from 14% to 17% for newborn care and 23% to 27% for infant care.

During the 1987-2001 period, the percentage of Rhode Island babies born at low birth weight (less than 2,500 grams) rose by 22%, from 6.0% to 7.3%. Similarly, the percentage of very low birth weight (less than 1,500 grams) babies rose by 25%, from 1.2% to 1.5%. (Figure 3) Although the number of Rhode Island babies born annually at extremely low birth weight (<500 grams) is small, the number has increased by 65%, from 20 in 1987 to 33 in 2001. At the national level, smaller increases were seen in low birth weight (10%) and very low birth weight (15%) births over the period 1987-2000.

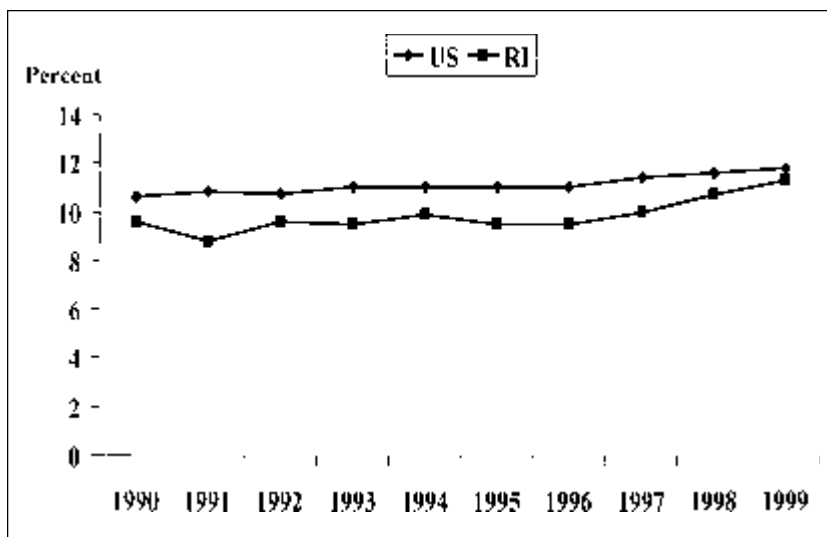


Figure 4. Premature Births, United States and Rhode Island, 1990-1999.

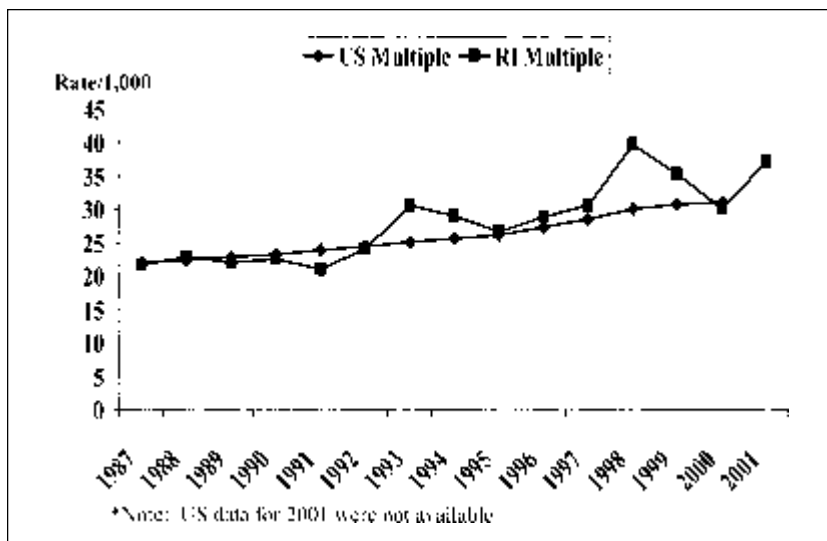


Figure 5. Multiple Births, United States and Rhode Island, 1987-2001.

The percentage of babies born prematurely (less than 37 weeks gestation) has also been rising steadily in both the United States and Rhode Island. Between 1990 and 1999, the percentage of premature births in the United States rose from 10.6% to 11.8%. (Figure 4) During the same period in Rhode Island, the rate of prematurity rose more sharply from 9.6% to 11.3%.

During the past fifteen years, the proportion of births that are multiple gestations (twins, triplets, and higher order births) has risen in the United States and Rhode Island. (Figure 5) Nationally, the rate of multiple births rose from 22.0 per 1,000 in 1987 to 31.1 in 2000, a 41% increase. In Rhode Island, the rise was significantly greater (71%), increasing from 21.8 in 1987 to 37.2 in 2001.

Discussion

The proportion of infant mortality in Rhode Island that is attributable to maternal health factors has increased in the past fifteen years. Factors contributing to this in-

crease include an increase in the number of very low birth weight (<1,500 grams) infants; an overall increase in prematurity; and an increase in multiple gestation births. The growth of multiple gestation births has also contributed to the increase in premature and low birth weight births.⁶

The lack of improvement in infant mortality has occurred while smoking rates among pregnant women have been declining and rates of early entry into prenatal care, including fertility treatment, may have been improving in the United States and Rhode Island. Addressing maternal health issues such as, preconceptional health, health behaviors (e.g., tobacco use, drug abuse, etc.), and perinatal care, including fertility treatment, may prevent deaths due to prematurity and very low birth weight. In addition, factors such as stress, poverty, and nutrition, along with other elements of primary prevention, must be addressed.

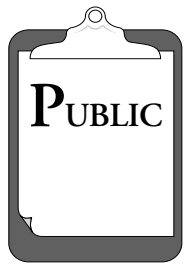
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Reptile-Associated Salmonellosis: A Preventable Pediatric Infection

Utpala Bandy MD, MPH, Helen McCarthy, PhD, Christopher Hannafin, DVM

EPIDEMIOLOGY

Salmonellosis, a major cause of diarrheal illness in the United States, causes an estimated 14 million illnesses and 600 deaths annually. There are 2,449 known *Salmonella* serotypes of which approximately 200 are detected in the United States in any given year.¹ Between 1987 and 1997, the rate of reported *Salmonella* infections (average of 40,169 reports per year) decreased from 19 to 13 per 100,000 persons. However, while some serotypes are reported to have decreased in frequency, serotypes associated with reptiles are showing an increase in frequency. The serotypes with the greatest average annual increase in the number of isolates reported from 1987 to 1997 are *Salmonella* Stanley, and *Salmonella* Marina; both serotypes are reptile-associated. Of the top 20 increasing *Salmonella* serotypes, seven, or 35%, are common to reptile-associated *Salmonella* serotypes (Stanley, Marina, Flint, Kintambo, Wassenar, Ealing, Carrau, and Abaetuba). Also, data from the National *Salmonella* Surveillance System, representing 441,863 *Salmonella* isolates from humans from 1987-1999, demonstrate that the rate of overall isolation of *Salmonella* is highest in the New England region; that overall, children have the highest *Salmonella* isolation rate; and that infants have a 4-13 fold higher rate of invasive disease than other age groups.²

In Rhode Island from 1997 to 2001

(Figure 1), the total number of cases of *Salmonella* infections (all ages) decreased from a high of 172 total cases in 1997 to 161 cases reported in 2001. The average number of *Salmonella* cases reported for this period in children younger than 5 years of age is 44, which represents an attack rate four to five times higher than for older children and adults. Of note is the fact that about a third of the cases (range 28.6 to 35.6%) in the under five age group had isolates known to be reptile-associated strains. Since cases are not interviewed, a history of a reptile in the home could not be confirmed. Of the isolates in children under five, there was an average of 2.8 invasive infections (bacteremias) per year (range 0-7). Whether the bacteremia isolates were reptile associated strains or

not is unknown as serotyping blood isolates for *Salmonella* bacteremia was not routinely performed until recently. It needs to be pointed out that the numbers reported here are underestimates and that the actual number of cases is probably significantly higher. Many cases of *Salmonella* illness are not reported, not every ill person seeks medical attention, and health-care providers may not always obtain a specimen for diagnosis.

An estimated 3% of American households own close to 7.3 million reptiles, and the number of reptiles imported into the U.S. has increased dramatically from 27,806 in 1986 to 798,405 in 1993.³ The majority of the imported reptiles are iguanas; snakes and turtles are also included in this category. Approximately 93,000 cases per year of *Salmonella* infections are estimated to be attributable to pet reptile contact.⁴ Reptile-associated *Salmonellosis* is not a new phenomenon. In the early 1970s, pet turtles were responsible for an estimated 280,000 cases of salmonellosis each year. The Centers for Disease Control and Prevention (CDC) estimated that in 1973 pet turtles accounted for 14% of the *Salmonella*-caused illnesses in the United States. In an attempt to control this number of *Salmonella* infections, a ban was enforced on all interstate shipment of pet turtles with shells of 4 inches or less in length. At that time, the

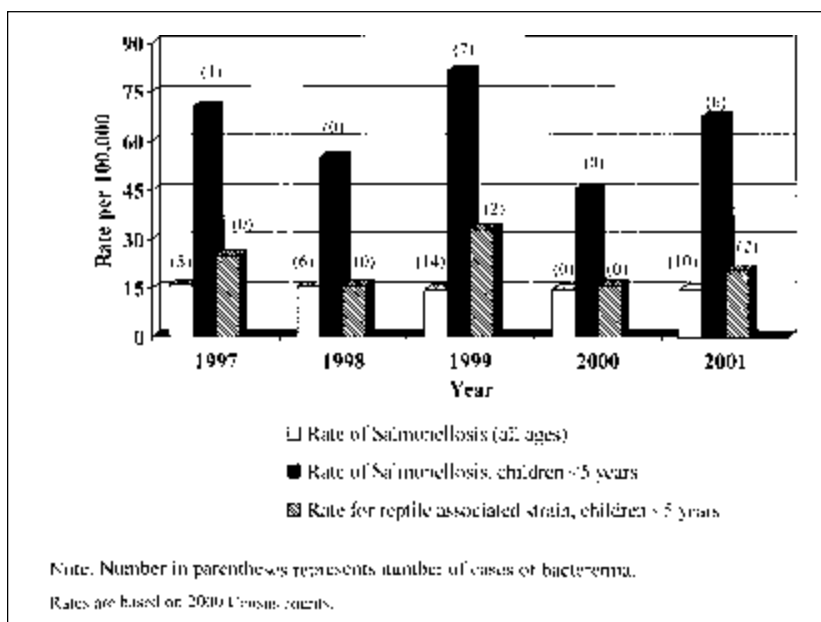


Figure 1.

U.S. Food and Drug Administration (FDA) reasoned that turtles larger than 4 inches did not pose as much of a threat for *Salmonella* infection because children would not likely fit them into their mouths. Since that time, studies have shown that direct contact is not necessary for transmission of *Salmonella* bacteria. Nevertheless, the ban on turtles proved to be very effective, because an estimated 100,000 fewer annual cases of turtle-associated salmonellosis occurred among children following the ban.⁵

TRANSMISSION

The principal habitat of *Salmonella* bacteria is the intestinal tract of humans and animals. *Salmonella* is endemic in reptiles; iguanas have long been known to harbor *Salmonella* bacteria. Because iguanas will not breed if closely confined, most of the pet iguanas sold in the U.S. have either been captured in the wild or have been bred in farming/ranching operations in Central America. Reptiles are infected from before birth, obtaining infection as live newborn or shelled embryos passing through the cloaca of the mother. Being captive bred, incubated and born, is no guarantee that any reptile is *Salmonella*-free; upon entry into the U.S. a large number of these animals (up to 90%) are already asymptomatic carriers of *Salmonella*. High rates of *Salmonella* in the feces of iguanas may be related to the eating of feces by hatchlings, a typical behavior for iguanas, and other vegetarian lizards, that establishes normal intestinal flora for hindgut fermentation. Reptiles can also become infected through contact with other reptiles. Infected reptiles periodically shed *Salmonella* bacteria in their feces. While treating animals with antibiotics may seem a logical first line of defense in preventing transmission, attempts to eliminate *Salmonella* in reptiles (as is true for humans as well) with antibiotics have been unsuccessful and can promote the selection of resistant strains.

Either direct or indirect contact with infected reptiles and their environment can cause human illness.^{4,7} The most common route for human infection is through oral ingestion. Individuals who handle a reptile, or who handle objects contaminated by a reptile, and then fail to wash their hands properly may ingest *Salmonella* bacteria. The exact means of transfer is not always evident and can be subtle. Direct contact with the animal is not necessary for transfer of *Salmonella*. Cases have occurred in children who did not have direct contact with the animal(s) but were infected after visiting another person who owned iguanas or after eating at a house of a person who owned an iguana.⁷ Identification of an uncommon *Salmonella* serotype in a person who has no other apparent exposure should trigger a more extensive investigation into a possible reptile linked exposure. In every case reported by the CDC, the diagnosed *Salmonella* infection was linked to direct or indirect contact with a pet reptile from which the same serotype was isolated. Therefore, a patient with *Salmonella* infection that cannot be traced to an identifiable source may have been exposed to *Salmonella* from a reptile.

CLINICAL ISSUES

The clinical manifestation of reptile-associated *Salmonellosis* is similar to that seen for other types of *Salmonella* infections. *Salmonellosis* manifests as acute enterocolitis, with sudden onset of headache, abdominal pain, diarrhea, nausea and sometimes vomiting. Dehydration, especially among infants may be severe. Bloodstream infections can be life threatening, especially in very young children, the elderly, or in persons with weakened immune systems. Infants younger than 1 year of age are at greatest risk for more severe forms including sepsis and meningitis. Symptoms may appear from 12 to 72 hours after exposure but usually occur within 18 to 36 hours after exposure. The disease is usually self-limiting and lasts from 4 to 10 days. *Salmonella* bacteria can remain in the stool for several days to several weeks after symptoms cease. During this time, infected persons can transmit the infection to others. *Salmonella* infections disproportionately affect infants and young children, especially bottle-fed infants. It is speculated that infant formula may allow for the multiplication of *Salmonella*. Persons who are immune-compromised or elderly, are also at a high risk for *salmonellosis*. Antibiotics given previously to a *Salmonella* infection may also play a role in the severity of the disease. Receiving antibiotics within 30 days before infection may be a risk factor for bacteremia. Antibiotics are suggested to increase susceptibility to *Salmonella* infection by altering colonic flora. Most people with *salmonellosis* will recover without antibiotic treatment. In severe cases, fluids may be needed to prevent dehydration. If *Salmonella* infection involves the blood or other non-intestinal tissues, antibiotic therapy is indicated. Food service workers, day care workers and health care workers should be excluded from work until diarrhea subsides.

PREVENTION

Public education through anticipatory guidance (including at prenatal visits) may be a more promising method of minimizing the risk of salmonellosis than prohibiting the sale of pet reptiles. To this end, a mailing with posters and patient information materials are sent to medical providers and school nurse-teachers. Physicians must be aware of the epidemiological features of *salmonellosis* and must recognize that reptiles carrying *Salmonella* may be the cause of *salmonellosis* and *Salmonella* sepsis. Veterinarians, pet shop owners and herpetological societies should provide educational materials and guidance about salmonellosis to reptile owners. Informing such owners about the correct methods for reptile food preparation, husbandry and handling can lead to cleaner environments and reduced propagation of the bacteria. Reptiles living in healthy environments are less likely to shed *Salmonella* bacteria. The staff in facilities that handle reptiles should follow recommended precautions for reducing the risk of transmission of *Salmonella* from reptiles to humans. Routine screening of reptiles by bacterial culture is unreliable due to the intermittent shedding of the bacteria and therefore discouraged. Prophylactic antibiotic treatment of asymptomatic animals is not recommended and

is not an effective method for prevention. Maintaining and separating reptiles and all the related food, bedding, water, waste and cleaning materials from contact with areas or materials used for humans will significantly reduce the potential for transmission.

RECOMMENDATIONS FOR PREVENTING TRANSMISSION OF *SALMONELLA* FROM REPTILES TO HUMANS

- Pet store owners, veterinarians, and pediatricians should provide information to owners and potential purchasers of reptiles about the risk for acquiring salmonellosis from reptiles.
- Persons should always wash their hands thoroughly with soap and water after handling reptiles or reptile cages.
- Persons at increased risk for infection or serious complications of salmonellosis (e.g., children aged less than 5 years and immunocompromised persons) should avoid contact with reptiles.
- Pet reptiles should be kept out of households where children aged less than 5 years or immunocompromised persons live.
- Families expecting a new child should remove the pet reptile from the home before the infant arrives.
- Pet reptiles should not be kept in child care centers.
- Pet reptiles should not be allowed to roam freely throughout the home or living area.
- Pet reptiles should be kept out of kitchens and other food-preparation areas to prevent contamination. Kitchen sinks should not be used to bathe reptiles or to wash their dishes, cages, or aquariums. If bathtubs are used for these purposes, they should be cleaned thoroughly and disinfected with bleach.

For additional information and access to resource materials visit: www.cdc.gov/healthypets/animals/reptiles.htm, or call the Office of Communicable Diseases at 401 222 2577.

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A Pelvic Vocabulary

This issue of *Medicine & Health/Rhode Island* is devoted to gynecological problems and hence it is appropriate to consider the etymological origins of the many anatomic words employed in describing the female genital tract.

Classical anatomists construed the pelvis as a large concavity and the word they chose was the Latin, *pelvis*, meaning a bowl or a laver. The vagina was given its name by the Italian anatomist Fallopio because it resembled the scabbard of a sword, the Latin name for which was *vagina*. The sense of a sheath or hollow extension is preserved in English words such as invagination. The Roman botanists also saw a resemblance between the elongated pod holding the vanilla seed and a sheath. They called the plant *vaginella* [with a diminutive suffix, meaning little sheath] which in Spanish became *vainilla* and in English, vanilla.

The word, uterus, is taken from the Greek word, *hoderos*, defining the womb and sometimes the abdomen. It is cognate with another Greek word, *estrus*, meaning

a frenzy or heat. The uterine cervix, the neck of the uterus, derives its name from the Latin word, *cervix*, meaning the neck [as, for example, in the phrase cervical vertebra]. An earlier Latin meaning of cervix defined that structure which binds the head to the body.

The uterine fundus is named for the Latin, *fundus*, meaning the bottom or the foundation; anatomically, it is that segment of a hollow structure furthest from its opening. The sense of bottomness appears in such words as foundation, fundamental, funds, and even profound. And a ship which sinks to the bottom is said to founder.

The uterine salpinx is named after the Greek word for trumpet since both are tubular with flaring ends.

The word, menopause, contains two roots. The *meno-* root is derived from a Greek word meaning month and appears in such similar words as menses, menstrual and month. An interval of six months, therefore, is called a semester; and three months, a trimester. The root *meno-* harkens back to the Greek word for moon. The crescent-

shaped interarticular cartilage that resembles a moon is therefore called a meniscus. Earlier calendric calculations were based upon the moon and hence many Latin words with the root, *mens-*, pertain to measurement [mensural, metric].

The *-pause* in the word menopause is derived directly from the Latin, *pausa*, and a similar Greek word meaning to stop, to cause to cease. The English word, pose, meaning to stay in place, stems also from the Latin, *pausa*.

The root *-parous* [as in words such as multiparous, nulliparous, viviparous and parity] is derived from the Latin, *parere*, meaning to bear, to bring forth; but is unrelated to the Latin root *pari-*, meaning equal, as in words such as parity and parimutuel. Thus the English word, parity, could mean either the degree to which a woman has borne children or the state of equality.

– Stanley M. Aronson, MD, MPH



Vital Statistics

Rhode Island Department of Health

Patricia A. Nolan, MD, MPH, Director of Health

Edited by Roberta A. Chevoya

Rhode Island Monthly Vital Statistics Report

Provisional Occurrence Data
from the
Division of Vital Records

Underlying Cause of Death	Reporting Period			
	January 2002	12 Months Ending with January 2002		
	Number (a)	Number (a)	Rates (b)	YPLL (c)
Diseases of the Heart	302	3,073	293.1	4,325.0
Malignant Neoplasms	200	2,397	228.7	7,637.5
Cerebrovascular Diseases	50	532	50.7	717.5
Injuries (Accident/Suicide/Homicide)	39	410	39.1	7,273.5**
COPD	48	504	48.1	540.0

Vital Events	Reporting Period		
	July 2002	12 Months Ending with July 2002	
	Number	Number	Rates
Live Births	1,255	13,558	12.9
Deaths	893	10,318	9.8
Infant Deaths	(15)	(114)	8.4
Neonatal deaths	(9)	(87)	6.4
Marriages	910	8,218	7.8*
Divorces	287	3,326	3.2
Induced Terminations	435	5,559	410.0#
Spontaneous Fetal Deaths	78	1,097	80.9
Under 20 weeks gestation	(73)	(1,026)	75.7
20+ weeks gestation	(5)	(71)	5.2

(a) Cause of death statistics were derived from the underlying cause of death reported by physicians on death certificates.

(b) Rates per 100,000 estimated population of 1,048,319

(c) Years of Potential Life Lost (YPLL)

Note: Totals represent vital events which occurred in Rhode Island for the reporting periods listed above. Monthly provisional totals should be analyzed with caution because the numbers may be small and subject to seasonal variation.

* Rates per 1,000 estimated population
** Excludes two deaths of unknown age.

Rates per 1,000 live births

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NINETY YEARS AGO

❁ [JANUARY, 1913] ❁

An Editorial on "Zoophilia" called the "modern sympathy for the laboratory mouse...a morbid sentiment cultivated by over-attention to fictitious tales of cruelty towards mice and guinea pigs... These hypersensitive people who rail at ... 'vivisectionists' may be brought to a saner view by learning that their mountain is only a mole hill, that the slight distress inflicted is insignificant compared to the immense amount of misery avoided..."

Halsey DeWolf, MD, in "Cyclical or Recurrent Vomiting," said that physicians had recognized vomiting as an entity as early as 1882, when Dr. Gee of London reported a series of cases. The cycles can happen in children from 2 to 12 years of age, and "periods of good health may vary from a few weeks to several months or even a year or more." The attacks themselves last from 2 days to a week or two. He differentiated cyclical vomiting from nervous vomiting (daily, often at or after meals), meningitis, and intestinal obstructions. For treatment, he recommended milk or malt sugar ("one teaspoon to desert spoonful every two hours.") A parent could try rectal feeding "though it is usually unsuccessful in young children."

Colonel L. Merrin Maus, Medical Corps, US Army, Governor's Island, New York, read "The Suppression of Vice Diseases Through Personal Prophylaxis and Meaningful Control of the Saloon and the Courtesan" to the Providence Medical Association, December 2, 1912. The Journal reprinted his talk. Briefly, Colonel Maus considered prostitution and alcoholism the "two great social evils of the day," and the "predominant causes of venereal disease and degeneracy in the human race." He recommended "total abstinence" as a requirement of public office (mayors, judges, aldermen, members of the police and fire departments, as well as other employees). As for prostitution, he urged "every state, community, town, village and district through the land" to enact laws "for the segregation of the demi-monde."

FIFTY YEARS AGO

❁ [JANUARY, 1953] ❁

John B. McCann, MD, and Paul P. Norman, MD, residents, had presented "Study of Prolonged Labor: An Analysis of 120 Cases Occurring in Primigravidae," at the Providence Lying-In Hospital Alumni Day. The Journal reprinted their talk. In two years, the clinic and private services had performed 13,655 deliveries (excluding miscarriages); 5,131 were primiparous labors. Defining "prolonged labor" as 30 hours or more, the authors found the key differentiating factor was the "high

incidence of serious complications ... in that group delivered by mid-forceps operations."

W.C. Hueper, MD, Chief, Carcinogenic Research Studies Section, Cancer Control Branch, NIH, had presented "Air Pollution and Cancer of the Lung" at the 5th Annual Cancer Conference for Physicians, under the auspices of the Rhode Island Medical Society. The Journal reprinted that talk. Dr. Hueper showed that cancer death rates were higher in industrialized than agricultural states.

An Editorial, "Report on the Health Needs of the Nation," analyzed the 282-page governmental report, objecting to recommendations for cooperative state-federal insurance programs: "...the commission allowed itself to be dominated by the thinking of those pressure groups in labor and social welfare that are still plugging for a comprehensive plan paid out of tax funds...the same socialistic propaganda."

Another Editorial, "A Doctor in the House," congratulated Dr. William Reid, an obstetrician newly elected to the Rhode Island House of Representatives from East Providence.

TWENTY FIVE YEARS AGO

❁ [JANUARY, 1978] ❁

Arjun K. Singh, MD, FRCS(C), George N. Cooper, Jr., MD, Robert Corwin, MD, Lester L. Vargas, MD, and Karl E. Karlson, MD, PhD, contributed "A Central Aorto-Pulmonary Artery Shunt for Cyanotic Neonates," a procedure for infants in need of an increase in pulmonary flow.

Robert L. Berger, MD, Duncan B. Dobnik, MD, and John R. McCormick, MD, from the Division of Cardiothoracic Surgery and Anesthesiology, the University Hospital and Boston University School of Medicine, presented "Surgical Management of Coronary Artery Disease," at Rhode Island Hospital. The Journal reprinted their talk, which argued that cardiac surgery would continue to have an important role in the management of substantial numbers of patients with CAD.

In "Some Group Practice Health Care Facilities in Rhode Island," Faiza Fowaz-Estrup, PhD, MD, predicted that more group practices would be starting in the state.

The FDA had required that estrogen package inserts warn: "Women taking estrogens have roughly 5 to 10 times as great a chance of getting endometrial cancer as women who take no estrogens." An Editorial, "FDA Complicates Estrogen Therapy," criticized that requirement: "It is appalling that the FDA insinuates itself in such arrogant fashion into the patient-physician relationship."

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