Policy Forum

Fertility Awareness: Jet-Age Rhythm Method?

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THE present crisis (*1*) in contraceptive R&D through the virtual withdrawal of large pharmaceutical companies—caused in part by enormous legal liability exposure, stringent, long-term toxicology, and exceptionally long lead times—suggests we take another look at one of the least efficacious methods, natural family planning (NFP).

At present, optimal NFP requires daily measurement of basal body temperature (often affected by extrinsic factors such as illness), coupled with examination of cervical mucus to estimate the onset of ovulation. Popularity and efficacy are low—primarily because of the required, lengthy abstinence from intravaginal coitus. Indeed, the level of acceptance of any birth control method, predicated solely on a determination of the "safe" period, is bound to be inversely proportional to the extent of required record keeping and to the number of days demanding abstinence from coitus. Thus, reliance on the "sympto-thermal" method of NFP requires an average (*2*) of 17 days of such abstinence. Measurement of certain biochemical changes, however, if done accurately and simply, could reduce this period by more than 50% and thus improve significantly NFP's poor image.

Since the ovum's fertile period is short (~1 day), precise knowledge of the passage of ovulation would provide assurance that unprotected coitus is now safe (the green light). Unfortunately, such assurance covers only the postovulatory (luteal) half of the menstrual cycle (Fig. 1). Prediction of ovulation by 3 to 4 days is needed before NFP can be extended to the preovulatory (follicular) phase. Such an extended advance warning (the red light) is required because sperm can remain viable in a woman's fertile mucus for approximately 3 days.

Hormonal changes over the course of a woman's menstrual cycle have been studied (*2*) extensively in blood and urine, and, to a lesser extent, also in saliva. Of these body fluids, saliva and urine are most suited for use in home testing. As shown in Fig. 1, a biochemically rational red light could be based on detecting the rise in the estrogen estradiol or in the pituitary luteinizing hormone (LH), which precedes the onset of ovulation. Since the estradiol rise is more gradual (48 to 168 hours, with median of 83 hours) as compared (*2*) to that of LH (24 to 56 hours, with median of 32 hours), detection of the increased production of estradiol (or its metabolites) offers considerably longer advanced warning of the onset of ovulation—a prerequisite for an effective red light. As seen in Fig. 1, the green light could be based on detecting the occurrence of two events in the postovulatory, luteal phase: the second increase in estradiol concentration or, even better, the major increase in progesterone (or its metabolites).

Recent advances in analytical biochemistry (*2*), partly based on monoclonal antibody techniques, now make it possible to measure accurately the rise of progesterone metabolites in a few drops of urine. These have already led to reliable signaling of the green light in the home through as few as one or two simple measurements per month. Equally facile detection of estradiol is more difficult (*2*), but it is only a question of time before an effective home-use method for estrogens will also be available. The ultimate approach, the use of two dipsticks (or other simple technique) for reliable measurement of estradiol and progesterone levels in saliva, is clearly feasible, provided a sufficient effort is dedicated to such a project. This method would require no toxicology, Food and Drug Administration (FDA) scrutiny should be much shorter than with drugs, legal exposure would be minimal, and most importantly, such a project is within the technical and financial resources of relatively small diagnostic companies.

What would it take to stimulate such efforts? A missing stimulus is the demonstration that convenient ovulation prediction and detection in the home represents a significant commercial opportunity with a potentially wide customer base. Until now, measurement of such hormonal changes has focused on women with infertility problems—a limited group, though a highly committed one. Indeed, most of the practical advances in the field have been accomplished through the high motivation and cooperation of fertility-

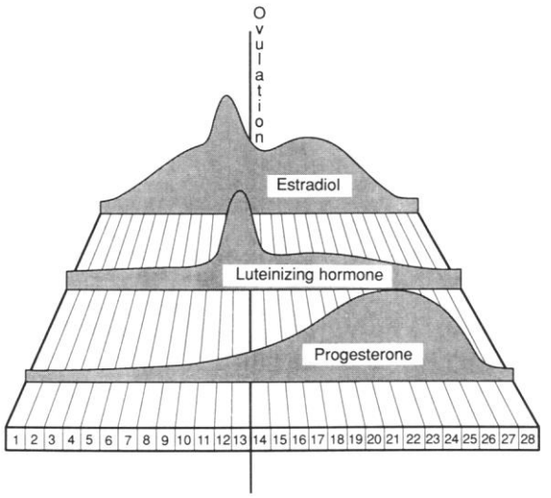

Fig. 1. Some hormonal changes during a menstrual cycle.

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impaired couples for whom neither cost nor convenience have been major disincentives.

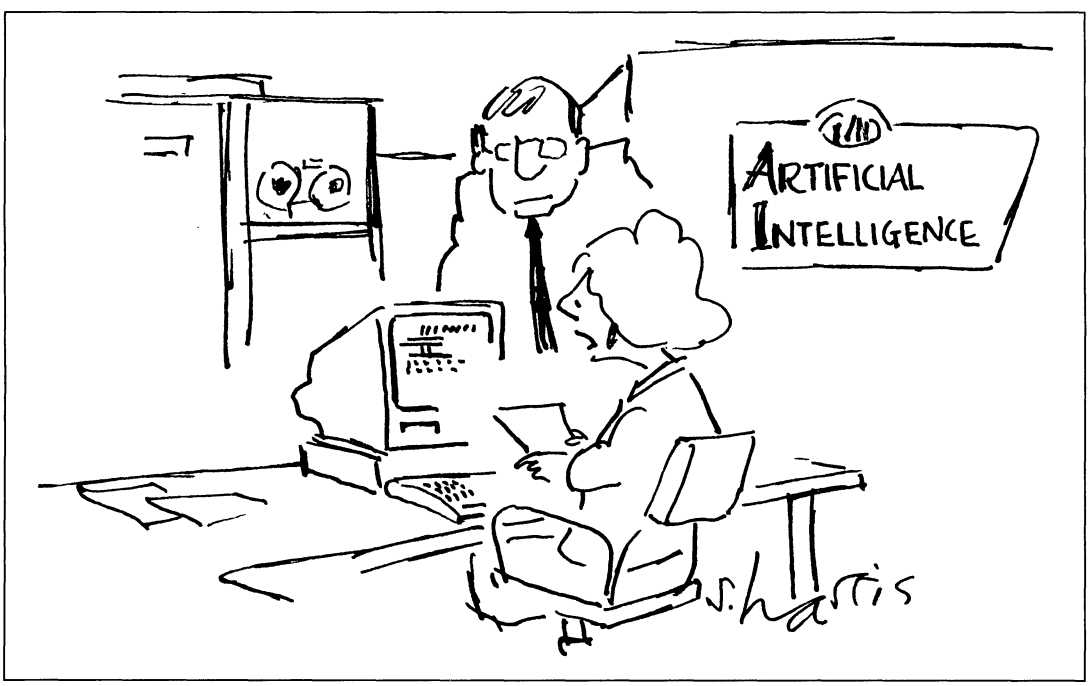
Dedicating serious scientific efforts in America to improving birth control for couples unwilling or unable to use "artificial" methods makes political and ethical sense. But there is a second and much more important consideration, beyond the realm of birth control, which could represent the needed profit incentive for significant, industrial R&D commitments to jet-age NFP. For female joggers and athletes, for flight attendants criss-crossing multiple time zones, and, especially, for professional women postponing childbearing until their late thirties, fertility awareness may turn into a rallying cry. The most expensive part of such R&D, in terms of money and time, will be the collection of epidemiological data (under standard home-use conditions) on women of diverse ages. The range of individual variability in the monthly onset of rising estradiol and progesterone levels must be determined over a significant period of time in a much larger population sample than is currently available (*2*). Only then can suitable parameters be set for the dipstick to serve as a reliable red and green NFP light based on two measurements during the follicular phase and one or two measurements during the luteal phases (Fig. 1) of a woman's menstrual cycle. Once such convenient assays for hormone levels have been developed and fertility awareness acquires a broad constituency (women interested in general health awareness, contraceptors depending on NFP, and fertility-impaired women), research is bound to escalate on the potential use of nonhormonal, biochemical indicators (*2*) of ovarian function.

Because so many American women pass through the educational system learning deplorably little about the menstrual cycle, college and university students may be the most suitable test group on which to conduct a major epidemiological study. (Even if uninformed, they are more likely to be able and willing to learn.) Such a recommendation is supported by a recent survey at Stanford University, in which the hypothetical availability of a biochemical ovulation predictor was posed to 240 female undergraduates (*3*). More than two-thirds of the respondents were prepared to purchase and use such a product for ovulation detection. This positive response rate was unaffected whether the woman menstruated regularly (66%) or irregularly (67%), or was sexually active (65%) or inactive (70%); it rose to 78% among women who did not keep track of their menstrual periods. Similar conclusions (62% interested in educational aspects of biochemical ovulation detection) were reached (*4*) from 156 respondents of such a questionnaire distributed among Mormon students attending two Utah universities.

Eventually, many a woman in our affluent society may conclude that the determination of when and whether she is ovulating should be a routine item of personal health information to which she is entitled as a matter of course. And why not use such a hormonal dipstick method for ovulation detection and prediction also as a routine teaching tool in high schools? Given the present political climate in America, emphasis on fertility awareness rather than birth control may be the best strategy. Yet who knows? It may even lead to a reduction in unwanted pregnancies.

REFERENCES AND NOTES

1. C. Djerassi, *Science* **245**, 356 (1989).
2. For leading references, see "Natural fertility regulation today," *Int. J. Gynaecol. Obstet.*, suppl. 1 (1989).
3. R. McCormick and L. A. Salsburg, research paper (1989) on educational aspects of ovulation detection in C. Djerassi's Human Biology course ("Feminist Perspectives on Birth Control").
4. S. Smith, research paper, "The receptivity of Mormon society to an ovulation detection test" (1989), at Stanford University (*3*).



"I gave it the traveling salesman problem. It said he should give up sales and go into banking."