35-40:

47.5:

Body and Mind BY MELVIN KONNER, M.D.

Childbearing and Age

REALIZED NOT LONG ago that a dozen or so of the women I know, most of them in their late 30's old friends, peers, colleagues - were spending more time than they'd like in infertility clinics. I found that this fact somehow added to my aches and pains, that it imposed on me a kind of gnawing unease, adding to my heightened sense of age, as I pass 40. The longing to create new life can be deep and abiding, and even to witness that desire denied is painful.

Perhaps my generation is feeling the pain more acutely than some; we thought we could do anything. All those marches and love beads, the greening, the optimistic songs. And our liberated women would keep on marching beside the men - into medicine, law, politics, business, up to the laboratory bench and onto the playing fields. Children? The folder was stamped "Postponed."

What caught up with us was something far more profound than the simple truth that the human body ages, that it becomes more difficult as one gets older to undertake all variety of physical feats, from running marathons to bearing babies. What was at work here is anthropologically significant: a form of preprogrammed aging, if you will, programming unique to

Only in humans, among our near relatives, does the end of female reproductive life precede the tidal wave of aging by many years. Evolutionary theory has it that the amount of energy put into begetting offspring is directly related to mortality; that is, life cycles seem genetically disposed to last about as long as it takes to reproduce. Thus, once monkeys and apes can no longer produce babies in the wild, they soon die. Not so for

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Age 12.7:

followed by a

Menarche begins

POST-INDUSTRIAL HUMANS

Can begin bearing

humans. Women come to an end of their reproductive capacity and they and their spouses live on for another 20, 30 or 40 years.

But consider the world in which we evolved - say the world of 50,000 years ago. Life expectancy at birth was around 30 years, with the average skewed by high mortality in infancy. If you look now at life expectancy after childhood, in hunter-gatherer tribes that still exist much as they did in the Stone Age the !Kung San, or Bushmen, of the Kalahari Desert in southern Africa, for instance - old age, as we understand it, is far from a sure thing. According to studies done by the anthropologists Nancy Howell and Richard Lee, the average life expectancy, if you've made it to 15, is 55.

But, interestingly, the average age at which a !Kung woman has her last child is about 39. The numbers may tell an evolutionary story: one that explains that humans are not so different from other animals after all. It's just that the human mother needs to stay around to care

her offspring, humans have an extraordinarily long childhood. There needs to be enough energy to enable an animal to complete its reproductive cycle - to perpetuate itself. The last child, born, say, when the mother was 39, needs care to grow to an age at which its own reproduction could begin, at 16 or so, to insure continuity of the lineage. The mother could then die at 55 with a certain, as it were, evolutionary peace of mind.

Such theories help explain why the human reproductive clock may have been designed to run out about when it does. They don't explain how the clockwork slows down. But new technology and research are beginning to provide that explanation.

A human female doesn't generate eggs after birth. My 9-month-old daughter has all she will ever have - more, in fact, because they are steadily lost from birth onward; fewer than half remain when fertile cycling begins. In the last century or two, improvements in nutrition and health in general are probably reUnlike humans, monkeys and apes die soon after losing their capacity to produce bables. Average ages are used, above, to illustrate that contrast among the species.

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Unique genetic programming works against the ability of women to bear children as they get older.

sponsible for increasing the reproductive span to nearly 40 years. Still, when you look through a laparoscope - a thin fiber-optic tube for spying on internal organs through a small hole in the skin - at an ovary that has been through hundreds of cycles, even in a superbly healthy American female, you see a scarred, battered organ. Every fertile cycle ordinarily entails the release of one egg from its surface; a part of that surface has had to swell with a spot of bloody fluid, then burst open to disgorge the egg.

Death

An analysis published last year in Science by Jane Menken and James Trussell of Princeton and Ulla Larsen of Lunds University in Sweden is among those that have confirmed declines in fertility with age: Childlessness rose from around 5 percent in a group whose members married between ages 20 to 24, to around 9 percent in the 25-to-29 age group. For those marrying in the early 30's it was over 15 percent, in the late 30's, more than 25 percent. marriages For beginning between 40 and 44, it was over 60 percent.

The scarring of the ovary, though dramatic, is only one mechanism of reproductive aging. Much of the process is hormonal. Fertile cycling is maintained by hormones produced by the ovary; these depend on pituitary hormones, which in turn require a releasing hormone from the hypothalamus, in the brain. Both the onset of reproductive capacity at puberty and its later phasing out are genetically timed by interac-

tion of these hormones. Then, too, there is the steady decline in the number of eggs - but not just from being released once a month, which would use up only 500 or so, over an average reproductive span, of the 400,000 estimated to be present at puberty. Finally, those eggs that do survive until about the age of 35 have a greater likelihood of having an extra chromosome in the nucleus a disastrous piece of luck that can result in a disorder such as Down's Syndrome. Evolution seems to have produced a system that screens out most such abnormalities, however, by discharging the defective embryo.

New research also implicates the womb itself. The uterus, it turns out, loses its hospitality. The environment it creates for implantation and for the maintenance of pregnancy begins to be less suitable. It, too, depends on hormones that help prepare the uterine lining and enable the embryo to function. As the hormones decline, the the hormones decline, the uterus ages, loses half its weight from age 30 to age 50, and begins to decline to decline. and begins to dry out. Collagen and elastin - two crucial proteins that make it durable and flexible, as they do skin connective tissue throughout the body - decline markedly.

HE NEW ART and science of making test-tube babies respects the aging uterus. Because what is being introduced is an already-fertilized egg, the issues of egg production and union with sperm are moot by the time of implantation. The question is: Will it take? R. G. Edwards of Cambridge University, who shepherded the first test-tube baby, in 1978, says: "All of our available evidence indicates that the uterus, and not the ovary or the embryos themselves, is the cause of the declining incidence of pregnancy in women over 40." Patrick Steptoe, another in-vitro fertilization pioneer, has made a similar point on spontaneous abortion after age 40. And Zena Stein of the New York Psychiatric Institute State published an analysis in The American Journal of Epidemiology showing that miscarriage rises sharply after age 35, not only because of an increase in fetal abnormalities with age but also be-cause of rejection by the uterus of an even larger number of normal fetuses.

At the same time, the administration of an experi-

mental birth-control drug called RU-486 prevents implantation by acting against the hormone progesterone. It also has the effect of terminating a pregnancy in which implantation has recently occurred. It is one of the ironies of modern medicine that we study with equal eagerness the means to prevent or terminate pregnancy and the means to promote or maintain it. Analysis of the receptivity of the uterus is crucial to both. Thus, science un-doubtedly will turn on itself, in trying to solve infertility, by experimenting to overcome the effects of RU-486.

Controversy continues about how to advise women. Certainly there is little risk in waiting until the early 30's to have a baby. In the late 30's, the risk of involuntary childlessness becomes substan-tial, and in the early 40's, great. Yet motherhood is possible for many women even until age 50. On Oct. 1, Pat Anthony, 48 years old, of Johannesburg, gave birth to her own grandchildren — triplets conceived in-vitro by her daughter and son-in-law thus proving the power of at least one 48-year-old womb as a surrogate for another half its age. And despite the generally unfavorable odds, there have been many successful in-vitro attempts for individual women in late 30's and early 40's.

Life holds risks, and the intelligent young woman can theoretically try to assess the loss she would feel if she ended up infertile, add in the likelihood of childlessness if she waits to a given age, and weigh the sum against the personal advantages of waiting

ing.

Of course, real life is not that simple. Careers have a logic of their own. And, because most women are not willing to try this alone, the right man must come along. There is the possibility of adoption, though this itself is not emotionally painless. It can result in as much parental satisfaction as comes to biological parents.

How to guess the future? The medical frontier is continuously moving forward. Artificial insemination, invitro, surrogacy — who knows what's next? Surely one can count on some future chemical magic that will enhance implantation and maintain pregnancy. Yet, neither that hope nor the consolation of evolutionary understanding can erase the discomfort that arises from an arbitrarily waning force of life.