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CURRENT DEVELOPMENTS AND ISSUES: A SUMMARY

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IN VITRO FERTILIZATION

IVF patients are experimental subjects, World Health Organization official tells international IVF Congress, and IVF as a solution to infertility "makes no sense in any country"

"There has not been one single prospective, randomized controlled trial of the efficacy and safety of this particular procedure [IVF]", Dr. Marsden Wagner, Director of Maternal and Child Health, European Regional Office of the World Health Organization, told IVF practitioners gathered for the VI World Congress on In Vitro Fertilization and Alternate Assisted Reproduction in Jerusalem, Israel April 3. "Indeed, the published papers in this field can be characterized as 'show and tell'—that is, the reporting of non-evaluative description and uncontrolled comparisons of procedures, all done in" an effort to perfect the minutia of the process itself."

The position of the World Health Organization, he said, is that no new technology should be diffused or made an acceptable part of medical management before thorough, careful scientific evaluation. This, he added, has not been the case with IVF. Instead, he said, there has been "an uncontrolled proliferation of this technology."

One example, he said, was that Israel, with a population of 4.4 million people, has 18 IVF clinics.

"I think this can be seen only as totally inappropriate use of technology," he said.

The World Health Organization has developed a three-point program for the future use of IVF, he reported. The points are:

1. "IVF is clearly an experimental procedure by all criteria. It should not be included in the health *care* budget, but in the health *research* budget. It should be conducted as research. For example, [there should be] fully informed consent from all women as experimental subjects."
2. "There should be evaluation of the efficacy and risks of IVF, using experimental methods such as random controlled trials, and using population-based data—not clinical data based on voluntary submission of information. In other words, follow the Australian lead and do not authorize IVF clinics until they are prepared to report on their results."
3. "There should be full, honest information to the public and to the infertile women on the true success rates with regard to healthy babies."

Wagner critisized IVF clinics for defining success in various ways which made them appear to have a high rate when, in fact, they did not. Counting pregnancy as a success, he said, when only about one-third to one-half of pregnancies ever result in a live birth, was like saying: "Look, if I move the ball a little bit toward the goal, count it as a goal."

When success or efficacy is defined as live births per egg retrieval cycle, he said, the rate is 9.5.

"This is indeed a very low efficacy rate," he commented. "What it means is of

course that it's a 90% failure rate."

Commenting on the risks of IVF to the fetus and baby, he summarized available data on IVF pregnancies:

"One-third to one-half will die as fetuses. If they are bora alive, twice as many will die during the first month of life as is normal in any country. There is 27 times as much multiple birth among these babies. The perinatal morality rate is four times normal. The low-birth rate and preterm rate is also four times normal. Because the low-birth and preterm rates are so high, we must conclude that there is going to be considerable permanent handicap or disability in these children, secondary to the low birth weight and preterm birth."

While all of these parameters were bad for singleton IVF babies, Wagner added, they were much worse for babies born in multiple gestations. In an attempt to increase the number of IVF pregnancies, and thereby, the IVF success rate, he said, physicians have been transferring several eggs into the wombs of women, leading to more multiple births-triplets, quadruplets, etc—"with all their subsequent disasters."

To solve this problem, physicians tried a clinical approach: fetal reduction, that is, selectively killing fetuses in a multiple pregnancy. Wagner suggested an epidemiological solution to the problem.

"Why don't we redefine success as a healthy baby at one-month of age?," he asked. "If we did that, the contribution of multiple egg transfer to success rates would fall way, way down and I think would call for a reconsideration of that whole practice."

The cost of one IVF baby was high, Wagner said, citing an Australian governmental estimate of $40,000 Australian dollars. To that figure, he said, one should add all the extra medical costs involved in an IVF pregnancy.

"It has now been well established that there is increased hospitalization during pregnancy. There are increased obstetrical interventions at birth—cesarean section, etc. There is increased referal to neonatal intensive care. There are longer stays in neonatal intensive care . . . So it's probably reasonable to estimate that one IVF baby costs in excess of $50,000 U.S. dollars."

Wagner asked whether IVF was really a solution to infertility.

"Now the most optimistic scenario that could be generated from the data to date," he said, "is that, at great cost, about 8% of infertile couples in any country can be helped by IVF. In reality, it's probably closer to 5%. [This is] with considerable risk of not ending up with a healthy baby. So from the cost/benefit perspective, IVF as a solution to over-all infertility makes no sense in any country."

The money spent to produce one live birth of a baby at risk could probably prevent 100 women from ever becoming infertile in the first place, he said. The money could be used for programs on health education and surveillance and treatment of sexually transmitted disease.

The existence of present IVF services seriously drains money, resources, and physician and nurse talent away from pressing community health needs, including a more realistic and cost-effective program for management of infertility, he said.

The World Health Organization is bringing out a report which will expand on the points Dr. Wagner raised in his speech. It is available from WHO at this address: 2100 Copenhagen, Denmark.

Dr. Wagner's speech, delivered at the opening ceremonies of the World Congress on IVF, was coolly received by the IVF practitioners. In conversations following the speech, many practitioners, noting that Wagner had been invited to the Congress, characterized his critical comments as "rude." One Congress organizer compared Dr. Wagner to a dinner guest who eats the meal and then says that the food was terrible and he has to take a pill.

GENA COREA

Monash IVF group teams up with animal breeding company to produce animals with "high value characteristics"

The Monash IVF team in Melbourne, Australia has teamed up with International Breeding and Technology Services to produce a superior breed of goat, reports *The Southern Pensinula Gazette.* International Breeding and Technology is located in Rye, close to the Monash Medical Centre at Clayton.

The Monash IVF team, a world leader in IVF research, is using similar technology to breed goats. Ordinary feral goats are used as "surrogate mothers" to carry the embryos of pure bred Angoras.

On the farm at Rye, 800-1,000 feral goats will be implanted with Angora embryos, the *Gazette* reports.

This method of breeding goats has great export potential, according to David Worth, a consultant with Competitive Edge, the company marketing International Breeding and Technology Services.

Worth said: "They're endeavoring to produce goats with high value characteristics which therefore have a high market value . . . We see great opportunity in the sale of breeding stock internationally."

Between 30 and 40 people, generally businessmen-farmers, had invested in the program, Worth said. He added: "The investors lease the pregnant animals and the newborn are owned by them. When the animals are born, the lease ceases. The lease goes for six months, or however long the process takes."

"Monash is providing the technology for a financial return and a chance to use the research facilities," he said.

The chairman of International Breeding and Technology Services, Dr. Alan McLean, is a member of the ethics committee for the Monash IVF program. He owns the Rye Angora Stud and has been breeding goats commercially for 15 years.

Dr. Alan Trounson, director of the Centre for Early Human Development at Monash, heads the Monash group's operations at Rye.

"Dr. Trounson, an expert in nonsurgical transfer of ovaries, started working in animal IVF research back in the 1960s and moved into the controversial human IVF program with Professor Carl Wood in the late 70s," the *Gazette* reports.

The problem with Australia's goat industry, Trounson says, is its low quality and productivity.

"We want to boost the quality and productivity. Nonsurgical procedures means you repeatedly collect high quality animals."

The Southern Pensinula Gazette. February 17, 1988. Test tube kids bred at Rye.

Women worry about long-term effects of hormones used in IVF, Australian magazine reports

Many women are worried about the long-term effects of the superovulatory drugs used in IVF, Leta Keens reports in *The Australian Women's Weekly.*

"The doctors say there are no risks, that they've been used for years, but my point is that this particular cocktail of hormones has never been given before," Keens quotes one such woman as saying.

"The drugs do have the desired effect of raising the sucess rate of IVF, but they should be looked at in detail," comments IVF practitioner Dr. Alan Trounson. "There's no evidence that they're unsafe, but we should be concerned about everything we take and I would prefer to remove those drugs from the schedule if possible. Eventually, we hope to get back to collecting eggs in the normal ovulatory cycle."

Dr. Barbara Burton, president of the Infertility Federation of Australia and an unsuccessful IVF patient, argues that long-term follow up on IVF patients should be done. Questionnaires should be sent to the women 5,10, and 25 years after treatment.

"If they drop dead now, or suicide, no one knows about it," she comments. "No one has got statistics, either, on IVF children. Data is taken at birth, but there's no long-term follow up. When you're involved in infertility groups, you hear things casually on the grapevine; for

instance one baby developed a tumor when he was one year old. That sort of thing tends to make you worry; does it have anything to do with IVF?"

On another issue, John Taylor, scientific director of Integrated Fertility Services of Sydney, told Keens he believes that IVF and associated techniques are probably the only viable solutions to male infertility: "It's easy to control one egg over 28 days, but much more difficult to deal with sperm which are being produced at the rate of 100 million a day. Physiologically, the male reproductive system is much more difficult to understand than that of the female; it's also impossible to control."

LETA KEENS. June 1988. IVF: Is it worth it? *The Australian Women's Weekly:* 91–96.

IVF pregnancies more likely to result in ectopicpregnancy, spontaneous abortion, preterm delivery and perinatal death, A ustralians find

Ectopic pregnancy, spontaneous abortion, preterm delivery, and perinatal death were more common in IVF pregnancies than in pregnancies after natural conception, the National Perinatal Statistic Unit in Australia has reported. The Unit established a register of IVF pregnancies after being approached by the Fertility Society of Australia and the National Health and Medical Research Council. In *The Medical Journal of Australia,* the Unit reported data on 1,510 IVF pregnancies in 12 IVF centers in Australia and in one in New Zealand in the period 1979 to 1985.

The data were: Live births occurred in 57.5% of all pregnancies and in 69% of clinical pregnancies. The 902 viable pregnancies resulted in the birth of 1138 live-and-still-born infants.

There was a high incidence of ectopic pregnancies (5.2% of clinical pregnancies, about five times higher than national population figures) and spontaneous abortions (24.3% of intrauterine pregnancies). While ectopic pregnancy was slightly more common when tubal factors were the cause of infertility, other causes were also associated with a four-or five-fold increase in risk, the authors point out.

"Other contributing factors have yet to be determined, but one small study has indicated that the position of the catheter that transfers the embryos to the uterus may be important," they write.

The fact that some IVF teams have reported a low incidence of ectopic pregnancies supports the theory that differences in embryo transfer technique may be a factor, they state.

Of 902 viable pregnancies, 202 (22.4%) pregnancies resulted in multiple births. There were 700 children born after singleton births and 438 after multiple births.

Preterm delivery at fewer than 37 weeks' gestation occurred in 27% of viable pregnancies. While this outcome was to be expected in twin and triplet pregnancies, the authors comment, it was also common in singleton pregnancies (18.5%).

The high occurrence of preterm delivery may be explained by maternal characteristics and events in the later stages of pregnancy, the authors note, but other factors should also be considered, including the effects of repeated investigation of infertile women by dilation and curettage. Cervical incompetence, they note, may sometimes result from such procedures.

"Also, the possible role of treatment to induce ovulation should not be discounted," they add.

Ovarian hyperstimulation after the administration of clomiphene and pituitary gonadotrophins produces multiple corpora lutea and results in elevated serum levels of relaxin, they write. Preliminary studies of IVF pregnancies in the first trimester showed high serum levels of relaxin in both singleton and multiple pregnancies.

"Such endocrine disturbances could influence the subsequent outcome of the pregnancy," they observe.

Low birth weight (less than 2500 g) occurred in 34.8% of infants and 9.7% of infants had a very low birth weight (less than 1500 g).

The perinatal death rate was 47.5 deaths per 1000 births. In 1985, the perinatal death rate in Australia was 11.8 deaths per 1000 births. Still births accounted for about three-quarters of the IVF perinatal deaths. The other quarter were neonatal deaths.

Australia in general in 1985 had a stillbirth rate of 6.1 deaths per 1000 births and a neonatal death rate of 5.7 deaths per 1000 live births.

"The mode of delivery was caesarean section in 43.9% of in-vitro pregnancies—about three times higher than for the Australian population in the same period," the authors write.

The extent to which maternal characteristics or aspects of treatment by IVF contributed to the adverse outcomes of IVF has not been resolved, they state.

"Most embryos that are transferred to women after in-vitro fertilization fail to implant," they write, "and about one in six embryos that do implant never reach the stage of a clinical pregnancy. The reasons for these early reproductive failures are not known, but recent studies of chromosomal abnormalities in oocytes and preimplantation embryos should improve the understanding of the possible mechanisms in some cases."

That the quality of the embryo may be an important factor in these losses is suggested by the lack of any clear relationship between maternal age and preclinical abortion in their results, they note.

The authors point out that there are no population data from Australia and New Zealand on the prevalence of infertility and on the proportion of infertile couples who are likely to need IVF or GIFT. Such data are urgently needed from national health surveys, they argue, not just in regard to the provision of services "but also to encourage studies of the prevention of infertility."

The Australian In-Vitro Fertilization Collaborative Group (headed by Paul A. L.'Lan-caster). May 2, 1988. In-vitro fertilization pregnancies in Australia and New Zealand, 1979–1985. *The Medical Journal of Australia.* 148:429–436.

Australian IVF physicians say adverse IVF outcomes due to the women in the program, not to IVF; epidemiology research fellow disputes this contention

IVF practitioners responded to a report showing increased congenital malformations in children born of IVF by implicating—not IVF itself—but characteristics of the women in the programs. For example, they implicated the advanced age of some of the women or factors associated with infertility.

According to the report by the National Perinatal Statistics Unit, 37 (2.2%) of 1694 IVF pregnancies had a congenital malformation that was noted at birth, compared with 1.5 % of pregnancies for Australia nationally. Six children with neural-tube defects were born as a result of IVF, compared with an expected 1.2 children, and four children with transposition of the great vessels compared with an expected 0.6 children.

In an editorial in *The Medical Journal of Australia,* Fiona J. Stanley, Deputy Director and Principal Research Fellow at the NHMRC Research Unit in Epidemiology and Preventive Medicine at the University of Western Australia, challenged the contention of the IVF practitioners that the cause of the problem was the women in the program rather than anything associated with IVF.

"Advanced maternal age is not consistently associated with an increased rate of neural-tube defects or malformations other than Down's syndrome and other chromosomal abnormalities," she wrote.

She pointed out that infertility in most women in Australian IVF programs is due to tubal factors, according to the report by the Australian In-Vitro Fertilization Collaborative Group.

"Tubal infertility results from a variety of iatrogenic [doctor-caused] as well as infectious causes and is unlikely that situations that result in tubal infertility cause congenital malformations."

Other, less frequent causes of infertility may be associated with an increased risk, she noted.

"So, before it is assumed that this excess in congenital malformations is due to a higher maternal risk," she continues, "it is important to ascertain whether any of the in-vitro fertilization techniques and drugs that are used may be teratogenic."

She adds: "The effects of ovarian hyper-stimulation on the mother are not known, either during treatment or in the long term. These questions are important enough to warrant follow-up data collection on mothers as well as on the children of in-vitro fertilization."

Commenting on the Australian In-Vitro Fertilization Collaborative Group's report on IVF in the same issue of the medical journal (summarized above), Stanley notes that the cycles of treatment tabulated in the report were for those women who subsequently became pregnant. "Thus," she writes, "these data do not provide an accurate picture of all couples who were involved in in-vitro fertilization programmes and cannot be used to evaluate the programmes fully."

The information from the report allows an estimate to be made of the pregnancy rates after IVF. In 1986, more than-1,923 women began an IVF treatment cycle. (Because two IVF centers did not have data, the exact number is unknown.) Of the 4,507 treatment cycles reported, 689 (15.3%) resulted in pregnancy. Seventy-seven (11.2%) women experienced preclinical abortions. Thirty-six women (5.2%) had ectopic pregnancies, 159 (23.1%) women suffered spontaneous abortions, 15 (2.2%) women bore babies that were dead and 402 (58.3%) women bore live babies.

"Thus," Stanley writes, "the proportion of live births in 1986 was 8.9% per in-vitro fertilization treatment cycle . . . A higher proportion of these live births are of preterm single or multiple pregnancies and are at an increased risk of neonatal problems. Unless long-term follow-up is conducted of the children who are bora of in-vitro fertilization, their later handicap rates will go unrecognized."

These could well differ from those in infants who are born preterm to couples who have not undergone IVF, she observes.

The Federal Government paid an estimated $4.4 million for the pregnancies and live births that are described in the Australian IVF Collaborative Group's report, she notes, citing estimates by Dr. Ditta Bartels.

(In a subsequent letter to *The Medical Journal of Australia,* Bartels pointed out the typographical error in the foregoing. Stanley acknowledged the error in a reply to Bartels' letter. The correct figure for the amount the Australian government paid for IVF from 1980 to 1986 is $44 million and not $4.4 million. A report by the Commonwealth Department of Community Services and Health substantiates her costing estimates, Bartels writes in her letter. It provides a figure of $17 million for the costs to the government of IVF and GIFT for 1987 alone. When costs to the government for the IVF laboratory steps are figured in, the additional $2 million brings direct public expenditure to $19 million in 1987.)

Bartels, Stanley points out, suggests that her figures are underestimates because they exclude the hidden costs of the complications of pregnancy and additional neonatal intensive care for premature and multiple births, and do not include the private costs to parents and insurance companies. The costs of neonatal intensive care for the 107 very-low-birthweight babies reported in the Collaborative Group's article would be an extra $1.6 million (in 1983 Australian dollars), applying the rate of $14,983 for each baby calculated by previous researchers.

"Research into the causes of infertility and effects of in-vitro fertilization might reduce these costs in the future," Stanley

writes. "However, at present, while these large amounts of money are spent on in-vitro fertilization, study of the causes of infertility or its primary prevention in Australia virtually is neglected—a gross imbalance. There may be very important preventable factors, for example, the use of intrauterine contraceptive devices, pelvic inflammation, and venereal diseases such chlamydial infections."

FIONA J. STANLEY. May 2, 1988. In-vitro fertilization—a gift for the infertile or a cycle of despair? *The Medical Journal of Australia.* 148:425–426; DITTA BARTELS. July 18, 1988. High public costs of in-vitro fertilization programmes. *The Medical Journal of Australia.* 149:112.

No empirical evidence exists that IVF has a higher success rate than no treatment at all, Australian government report states

The Commonwealth of Australia is "most concerned about the absence of data which would allow a proper evaluation of IVF," the Australian Department of Community Services and Health stated in a 1988 report on IVF. IVF success rates are difficult to determine because there has been no comprehensive, centralized data collection which would make proper calculation of the success rate possible, states the report, *"Commonwealth Perspectives on IVF Funding: A Discussion Paper."*

"The situation is that as the first Australian IVF children approach their tenth birthday, there is as yet no centralised, comprehensive collection of data relating to the practice and outcome of IVF," the report observes. "This means that not only is it difficult under current arrangements to realistically determine the success of IVF as a treatment for infertility, but it would be extremely difficult to follow-up IVF children and patients to determine if there are any long-term consequences of this form of conception."

The best estimate now is that about 8.8% of treatment cycles will result in an ongoing pregnancy or the birth of a child, "but this may well overstate the case," the report notes. (The measure of input for this rate is treatment cycles commenced and the outcome measure is live birth and ongoing pregnancy.)

(In the United Kingdom in 1985, the reported ratio of live births to treatment cycles was 7.1% for new centres and 8.9% for established centres with an overall average of 8.5%.)

The report adds: "In the medical literature, IVF success rates have been calculated using all combinations of measures of input and authors frequently do not explicitly state the measures they have used. Overall, the whole question of success in relation to IVF is quite confused and obscure." (p. 6)

The 8.8% success rate figure, the report notes "does not sit well" next to the number of reported pregnancies published by the National Perinatal Statistics Unit (NPSU). If the success rate were really about 8.8%, it states, then we could expect 735 births to have resulted from the 8,360 treatment cycles begun in financial year 1986/87. But the NPSU reports only 402 live births for calendar year 1986.

"Even though the time periods are not directly comparable," the report notes, "the difference is such that it suggests either a lot of births are not reported to NPSU or the estimated success rate is too generous." (p. 8)

The Commonwealth of Australia study of IVF, conducted by the consultants Diagnosis Pty. Ltd., found that if the number of low birth weight babies were subtracted from the statistics, the success rate for an *unproble-matic* live birth was only 4.8%. The Commonwealth defined low-birth weight babies as problematic because they frequently require additional and intensive medical care (P. 10).

Further information from the report:

By the end of 1987, there were 18 IVF or GIFT (Gamete Intra-Fallopian Transfer) units in Australia: seven in New South Wales, three in Victoria, two each in Queensland, South Australia, and Western Australia, and one each in Tasmania and the ACT. Two other units are in process of formation.

The first IVF pregnancy in Australia occurred in 1979. Since then, 2,503 pregnancies, resulting in 1,851 live born infants have been reported. The number of women undergoing IVF is unknown. No central records are kept on this. But more than 5,000 women are estimated to have begun the IVF process in 1987 alone.

Pointing to the problem of inadequate data, the report observes that while attempts are made to provide reasonably accurate data about the outcome of pregnancies, there is no comparable data on how many women undergo IVF and how many treatment cycles they have.

The data base on IVF maintained by the National Perinatal Statistics Unit and the Fertility Society of Australia is at least a start towards complete collection of IVF data, the report notes, "but the Commonwealth is seriously concerned that this voluntary system has so far failed to provide comprehensive data on IVF and that no attempt has been made to establish long-term monitoring of IVF patients and children." (p. 7)

A recent study in Western Australia found that among women who discontinued IVF treatment for various reasons, 9% became pregnant with no further treatment and 29% adopted or fostered children. (Webb, Stanley F. and Moore, D. 1988. Increasing prevalence of multiple confinements in Western Australia and the impact of IVF. *Medical Journal of Australia.* In press.)

Among those who have been diagnosed as infertile, or have a long-standing fertility problem, there is a spontaneous pregnancy rate of about 25-30% (Collins, John A., et al. (1983). Treatment-independent pregnancy among infertile couples. *New England Journal of Medicine,* **309**(20) 1201–1206.)

"Therefore, some measures are needed to discourage couples from undertaking IVF and other expensive fertility treatments while there is still a good chance that pregnancy might be achieved spontaneously," states the Department of Community Services and Health report.

Among the problems the Commonwealth sees in the current IVF arrangements are:

1. It is "open to exploitation and overservicing. Because IVF is such a new procedure, there is not yet an agreed protocol for a standard IVF treatment cycle. Consequently, there is a large variation in the number of services provided to patients." The Health Insurance Commission has no way of knowing whether the units routinely providing more services are doing so because of a genuine belief that their protocol is best or because they are trying to maximise the Medicare rebate, either to finance research or to subsidise other parts of the procedure for which no benefits are payable (p. 31).

2. Inadequate data collection. No published data exists comparing IVF units.

3. Information available on the cost of IVF is "quite limited."

4. 'There are no incentives for providers not to treat patients for whom IVF may not be particularly successful."

5. Question about the success of IVF, the long-term safety of some drugs used in IVF and the high rate of congenital malformations and low birth weight infants among IVF children.

"The Commonwealth needs to assess the priority of funding IVF in relation to other demands on health funds. Is an expenditure of $17M a year on IVF justified when in the same year only $10.1M has been allocated for the National AIDS program, $23.9M for the National Campaign Against Drug Abuse and $32.9M for the National Community Health Program?" (p. 34)

In a discussion of the options for IVF funding, the Commonwealth report points out that the government could consider withdrawing Medicare benefits entirely since no conscious decision was ever made to fund IVF. ". . . The main problem from the Commonwealth's perspective is the questionable success of the treatment. There is no empirical evidence that overall IVF has a better rate of success than other infertility treatments or even

that it has a higher success rate than having no treatment at all." (p. 38)

The report continues: "IVF is expensive . . . At present there is very little public accountability for how these funds are spent."

At first glance, the report notes, the problem IVF appears to be solving is infertility, but actually, the problem is involuntary childlessness.

"IVF does not cure infertility. The couple is still infertile even after the completion of successful IVF treatment. Further, not all infertile couples wish to undertake IVF treatment or even have children at all. The Government needs to consider whether funding IVF is the best way to address the problem of involuntary childlessness or even whether this is an appropriate problem for Government concern. Perhaps funds would be better spent on a prevention program for infertility or a government-sponsored overseas adoption program? Perhaps more research is needed to examine the problem of infertility and assess to what extent infertility can be prevented. Perhaps more counseling programs are needed to help couples with fertility problems examine their options and needs? At present IVF is absorbing Commonwealth funds that might otherwise be made available for these other possible solutions." (p. 38)

The Diagnosis Summary Report on its study of IVF in Australia is an appendix to the Commonwealth report. It includes the following information:

1. Approximately half the IVF units in the Diagnosis study conducted research. "There was no indication that clinical research was separated from service capabilities in any of the units—in other words no patient was designated a research patient for whom no charge was raised." (p. 14)

Further: "The difficulty in the examination of the current IVF arrangements is to separate the service and the research from one another. The overall results of treatment cycle to live birth of less than 10% suggests that the process will remain experimental and subject to attempts to improve the current level of outcome. In providing any fee based on service, the Government and the medical profession, by way of the Australian Medical Association, have eschewed payment for research. They suggest that such funding should come from elsewhere . . ." (p. 28)

2. ". . . Male infertility is increasingly being treated by IVF, while essentially it is the woman who is undergoing the physiological stress of the procedure" (p. 40). One unit showed a four-fold increase in IVF for male infertility over a two-year period (p. 18). "Because the cause of most male infertility remains unknown, the number of patients who will be 'trailed' through IVF, in the hope that a successfull outcome will occur, may increase" (p. 33).

"In general, the worst prognosis for achieving either IVF or GIFT/PROST pregnancy is if male factor is the cause of the infertility. This must add a further cost increment in achieving a successful outcome as the success rate is considerably less than 8.8% when the reason for treatment is male factor infertility."

There has been some attempt to project IVF outcome on the number, morphology, and motility of the sperm but knowledge in this area is very limited. "IVF is useful for research in that it is the only method which can be used at present to establish reliably the fertilising capacity of the individual's sperm. There is a potential problem of IVF programs containing increasing numbers of such patients where the results are admitted as poor, and where the aim is to investigate
the fertilising capacity of the sperm. This is one area where the separation of research and service is extremely fine." (p. 40)

Few fertility treatments appear to benefit male factor infertility. The rationale for use of IVF and GIFT for male factor infertility "is the fact that the occasional pregnancy occurs and IVF provides positive evidence that fertilisation can occur." (p. 41)

3. "It is important to define the patient as the couple, not the female or the male, despite the fact that virtually all investigation and treatment involves the female only." (p. 30)

4. The most convenient way of assessing IVF success is to relate egg transfer to achieved pregnancy, but real success is the number of live births. "Even though confirmation of pregnancy has been considered the epitome of a successful outcome by some units, the fact that 'live birth' is the true measure of success is implicitly recognised by most units, where their noticeboards are covered with photographs of their IVF babies." (p. 35)

5. "It may be postulated that the relative lack of [IVF] success is placing pressure on the promotion of the experimental aspects of the procedure, which inevitably involves experimentation on the embryo by those who promote scientific method as the basis for progress." (p. 36)

6. When considering the chances for increased IVF success, a recent report in the *New England Journal of Medicine* is salutary. Nearly 50% of the eggs of an admittedly small group of infertile women undergoing clomiphene stimulation had abnormal karyotypes. The incidence of chromosome aberrations explains the low pregnancy rate after IVF. (Wramsby H., Fredga K., & Liedholm, P. (1987). Chromosome analysis of human ooctes recovered from preovulatory follicles in stimulated cycles. *New England Journal of Medicine,* **316** 121–124.)

7. Dr. Robert Jansen has commented on the high incidence of monozygote twins following IVF. He has warned of manipulation of the embryo and the culture medium which has an effect "that pushes through the filter of spontaneous abortion, as identical twinning, and may perhaps carry with it, sooner or later, the hazard of conjoined (Siamese) twins." (Jansen, (1984). *A practical ethical framework for in vitro fertilization and related reproductive technologies.* Presented at 3rd World Congress on IVF and ET, Helsinki, p. 8-9.)

8. Jansen and Davis McCaughey have is sued a warning against unbridled optimism concerning IVF as an infertility treatment: ". . . there is a danger that progress in other causes of human infertility (in addition to fallopian tube occlusion) may be hindered by the uncritical use of IVF and ET (embryo transfer). For example, IVF and ET have been used to treat unexplained inferility, endometriosis, immunological infertility and oligospermia—doubtless justifiable in individual cases, but, if funded too widely, likely to hinder development of more precise and specific methods of treatment that may turnout to have advantages over IVF an ET." (Jansen & McCaughey (1983). *Ethics in Medical Research, Appendix 111*:34.)

9. "The results of transfer of thawed embryos have been poor; and for donor eggs very few success have been reported. This area is clearly experimental, and at the present stage the costs of all treatment cycles involving frozen embryos or eggs should be metfrom research funding or by the patients themselves." (p. 44)

Commonwealth of Australia, Department of Community Services and Health. April 1988. *Commonwealth Perspectives on IVF Funding: A Discussion Paper.*

Risks of selective abortion in multiple gestation unknown, physician reports

Pregnancy reduction (reducing fetal number by transamniotic gestational sac punture) has been successful in a small number of women but "we have a long way to go before we can assess what the risk really is," Dr. James D. Goldberg told the annual convention of the National Medical Association in Los Angeles, California, USA.

The data so far suggest that pregnancy reduction offers some protection against morbidity and mortality for the remaining fetuses who progress to term, compared with infants born after multiple gestation, said Goldberg of the University of California, San Francisco, School of Medicine.

But, he added, the procedure also carries a relatively high rate of premature delivery and the psychological implications for parents who choose it have not been determined.

At Goldberg's institution, pregnancy reduction has been performed close to 20 times with just under one-third of the pregnancies resulting in preterm births.

One of the unknowns in pregnancy reduction is when transamniotic gestational sac puncture should be performed. Dr. Goldberg advises waiting until about the 12th week of pregnancy.

"The only failures in his study occurred with punctures performed during the second trimester in monochorionic gestations," *Ob. Gyn News* reported, "an indication that the technique probably cannot be recommended for reducing the number of monozygotic siblings, Dr. Goldberg said."

Ob. Gyn News. 1988. Evaluating risks of selective abortion in multiple gestation 23(19):3.

Criminologists may soon be discussing "white-coat" or "laboratory" crime, university lecturer in criminal justice writes

"The possibility now exists in Victoria that medical scientists and other hospital personnel may be convicted of criminal offences relating to in-vitro fertilisation and be sentenced to prison for up to four years," writes Christopher Corns, lecturer in criminal justice at La Trobe University in Australia. "Accordingly, criminologists, the medical profession, the Government, and the community may soon be discussing a new type of crime, which could be described as 'white-coat' or 'laboratory' crime."

Corns points to the Infertility (Medical Procedures) Act 1984 which came into effect in the Australian state of Victoria July 1, 1988. Under that act, certain activities are defined as crime. These include the cloning of animal gametes for a maximum penalty of four years in jail or a $10,000 fine; any "prohibited procedure"—four years' jail or $10,000; unlawful use of donated semen or ova—one year's jail or $2,500; receiving or making reward for surrogacy—two years' jail or $5,000.

"Any person who engages in this type of conduct and is convicted must, by definition, be defined in law as a 'criminal,'" Corns observes.

It is unlikely, he writes, that a Victorian court would impose jail sentence in any of the cases.

Australia recognizes two basic categories of crime—"conventional," such as assaults and theft, and "unconventional" or "white collar" crime like embezzlement. A third category may need to be created to cover offenders under the Infertility (Medical Procedures) Act, Corns writes.

He adds: "If the present rate of technological advancement continues through to the next century, it is likely that a whole range of scientific activity, medical and nonmedical, will become proscribed, criminal behavior thus creating, through legislative definitions, a potentially large, previously unrecognised group of criminals."

Jail sentences for such criminals, Corn argues, are neither necessary nor appropriate.

CHRISTOPHER CORNS. July 1, 1988. The birth of white-coat crime. *The Age.*

Infertile couples abused in IVF system, US offical says

Infertile couples, desperate for children, lacking information, and encouraged by enthusiastic doctors, are being abused in the IVF process, a senior US legal analyst, Alta Charo of the US Congress Office of Technology Assessment, said in Melbourne, Australia. Charo was in Australia to discuss her work in the U.S. on informed consent to IVF.

There is no conspiracy against patients, she said, adding: "But the end result may be the same in that nine out of 10 people walk out the door having undergone surgery, drug treatment, side effects, having lost time at work, having been on

an emotional roller-coaster, but not holding a baby."

Of 170 clinics in the U.S. about half have never been able to document a live birth as a result of an IVF procedure, she pointed out.

U.S. citizens spent $1 billion in 1987 for infertility treatment. An estimated 20% of infertility cases were caused by sexually transmitted diseases and could therefore probably have been prevented, she told reporter Sonya Voumard.

SONYA VOUMARD. June 2, 1988. Infertile couples abused in IVF system, says US official. *The Age.*

"Oocyte recovery" more properly called "oocyte capture" Yale IVF physicians argue

Decrying a " deterioration of the standard descriptive terminology" by their fellow IVF practitioners, two Yale University physicians in the United States have called for correct application of language. In an editorial in the *Journal of In Vitro Fertilization and Embryo Transfer,* Samuel S. Thatcher and Alan H. DeCherney list some recurrent inconsistencies in terminology. These include:

Oocyte recovery. "If oocytes are recovered, it suggests that at one time they were lost and have been regained. *Oocyte capture* appears somewhat ruthless but probably literally correct. *Harvesting* has a nice fertile connotation and, again, is literally correct but implies that clinicians are farmers."

Ovarian hyper stimulation. "Hyperstimulation traditionally has been considered as an unwanted consequence of exogenous gonadotropin administration. The prefix 'hyper' denotes *over* or *excessive* stimulation. If hyperstimulation is the desired response, then the patient is not overly, but appropriately, stimulated. Perhaps *follicular augmentation* or *controlled ovarian stimulation* would better describe this therapy."

SAMUEL S. THATCHER and ALAN H. DE-CHERNEY. 1988. The in vitro manipulation of terminology. *Journal of In Vitro Fertilization and Embryo Transfer.* 5(4):179–180.

IVF will leave domain of infertility treatment to become "a tool of wider medical significance" Czech scientist writes

IVF use has expanded beyond its "classical" sphere of application—on women with defective fallopian tubes—to be used on male and female infertility of various etiologies, Jan Tesarik of the Centre for Reproductive Medicine, Purkyne University Medical Faculty in Brno, Czechoslovakia, writes.

"The actual progress in the fields 01 ovarian cycle monitoring, gamete and embryo culture, cryopreservation, and micromanipu-lation has also contributed to the overall enlargement of the application scale of IVF in human reproductive medicine," he continues. "With the use of this technological progress the first steps have been made in advancing programs of oocyte and embryo donation, and studies aimed at utilizing pre-implantation human embryos for early genetic diagnosis are now under way. In the latter application IVF will, for the first time, leave the domain of infertility treatment to become a tool of wider medical significance."

JAN TESARTK. 1988. Developmental control of human preimplantation embryos: a comparative approach. *Journal of In Vitro Fertilization andEmbryo Transfer.* 5(6):347–362.

IVF opens the door to assessing a man's fertilization potential

A group of scientists from the Jones Institute for Reproductive Medicine and the Portsmouth Naval Hospital in the United States and the University of the Orange Free State, and the University of Stellenbosch, Ty-gerberg Hospital in South Africa, are developing a test to determine sperm quality, the Hemizona Assay (HZA).

"The advent of IVF ushered in the first direct laboratory assessment of a man's fertilization potential," they write in an editorial in the *Journal of In Vitro Fertilization and Embryo Transfer.* "While the appropriate uses of GIFT or intrauterine insemination (IUI) in conjunction with controlled ovarian hyperstimulation have proven to be significant additions to the repertoire of infertility specialists, IVF/ET uniquely provides actual observations about the number of eggs fertilized and the number of early-cleaving embryos available at transfer for pregnancy."

IVF itself is unsuitable as a diagnostic tool because of the high cost and "high emotional burden," the scientists note. They decided to develop the hemizona assay as a measure of sperm quality and subsequently obtained measurements of sperm binding from a single egg.

"Thus, the limited supply of precious human oocytes having useful zonae is extended by HZA," they write. "Only one human oocyte is needed per test to achieve useful data."

The scientists increased the available supply of human eggs by an extended intercontinental network.

"This was done by storing the oocytes in a salt solution for shipment to Norfolk," they write. After desalting, they note, these eggs worked well in the hemizona assay.

To date, their clinical results, though limited to a few dozen patients, are "gratifying," they report. They have found the HZ A index to be accurate in predicting IVF outcome to the point of embryo transfer. A much larger and statistically valid data set must be collected before they can judge the usefulness of HZA for predicting the fertilizing potential of a given man, they caution. Expectations that the HZA is a litmus test for severe malefactor cases are premature, perhaps unlikely, they add.

The scientists begin their editorial with a tale of two male-factor patients, "Mr. Andro L. Ogy" and "Mr. Epi D. Idymis," whose sperm was tested in the hemizona assay. Mr. Ogly had a high HZA index, 71. "Because his wife had tubal endometriosis, it was agreed that they would proceed with in vitro fertilization and embryo transfer therapy." Mr. Idymis' score on the test was 13. "Since a few 'good' sperm were apparently present, as indicated by HZA," the scientists write, "this encouraged his physicians to consider gamete intrafallopian transfer (GIFT) treatmemt, because Mrs. Idymis was believed to be reproductive unimpaired."

GARY D. HODGEN, LANI J. BURKMAN, CHARLES C. CODDINGTON, DANIEL R. FRANKEN, SERGIO C. OEHNINGER, THINUS F. KRUGER, and ZEV ROSENWAKS. 1988. The hemizona assay (HZA): finding sperm that have the 'right stuff.' *Journal of In Vitro Fertilization and Embryo Transfer.* 5(6): 311-313.

Research needed on role of husbands and doctors in the decisions of women to stop or continue in IVF programs, psychologists say

Women who decided to withdraw from IVF programs "believed that significant others in their life thought that they should stop IVF . . .", Australian psychologists report. "Women continuing with IVF believed that their actions would be supported especially by other infertile women, their husbands, and their doctor in the IVF program . . . Both groups of women were generally unwilling to go along with the wishes of other people, the only exceptions, to some degree, were the wishes of their husbands and doctor."

The psychologists delineate a task for future research: "There is a need to examine the role of husbands and doctors in the IVF-related decisions of women . . ."

Women who decided not to continue in IVF programs were less optimistic about another IVF attempt making them mothers, making their marriages happier, or improving the quality of their lives than women who decided to go on, the psychologists' study of 254 women in Australia found. All the women had had at least one IVF attempt. Both "continuers"

and "discontinues," the researchers found, "judged another IVF attempt as likely to involve some stress, disappointment, and financial strain."

Of the 254 women, 72 women did not want to continue with IVF while 182 decided to go on. Twenty-five percent of this later group already had children.

"In summary," the researchers wrote of their results, "women continuing and stopping IVF were very positive about the value of being mothers and the need to have more purpose in life, and together they disliked being stressed or disappointed and the possibility of having a divorce or taking medication. Those not wanting to continue believed that IVF would not make them mothers or give them the benefits of their own child and would not improve the quality of their lives or make their marriages any happier."

VICTOR J. CALLAN, BELINDA KLOSKE, YOSHTHISA KASHIMA and JOHN F. HENNESSEY. 1988. Toward understanding women's decisions to continue or stop in vitro fertilization: the role of social, psychological and background factors. *Journal of In Vitro Fertilization and Embryo Transfer.* 5(6):363–369.

Israeli physicians suggest ovarian cyst aspiration during IVF

When cysts form in the ovaries of women who have been superovulated in IVF programs, physicians might puncture and aspirate those cysts under the control of a vaginal ultrasound transducer, Israeli IVF practitioners suggest. This would avoid cancellation of the IVF cycle.

Fifteen women were included in the practitioners' study–10 in the study group and five in the control group. The physicians punctured and aspirated the ovarian cyst of each of the 10 women in the first group at about day eight of the cycle. The cyst was aspirated by the vaginal route by means of a 14-gauge needle, ultrasonically guided.

"Aspiration of the cyst in women in the study group permitted continuation of the IVF cycle," the physicians wrote. The treatment cycle of all the women in the control group with an ovarian cyst was canceled due to possible early luteinization.

One rare effect of pharmacological preparations commonly used to induce ovulation in IVF programs, the physicians write, "is the cyst formation of the ovary in these disrupted and nonsynchronized cycles. Indeed, it is possible that in certain cases of IVF with superovulation under hMG or FSH therapy, ovarian cyst formation is a by-product of ovulation induction. Lopata et al. mention that some patients in their series developed follicle cysts following stimulation with hMG. These were commonly observed during the early stages of a treatment cycle which followed a cycle abandoned during the previous month."

DOV FELDBERG, JACK ASHKENAZI, DOV DICKER, ARYEH YESHAYA, ISSACHAR VOLIOVITCH, and JACK A. GOLDMAN. 1988. Ovarian cyst aspiration during in vitro fertilization/embryo transfer (IVF/ET) cycles. *Journal of In Vitro Fertilization and Embryo Transfer.* 5(6):372–375.

Body fluids, cells, and tissues made available by IVF and GIFT programs open up new vistas for research in human reproduction, Indian IVF practitioners write

The many issues remaining to be resolved with regard to IVF in the Indian context include defining criteria for patient selection and determining the quality of drugs and supplies, which are mostly imported, Bombay IVF practitioners write to the *Journal of In Vitro Fertilization and Embryo Transfer.* "These aspects are currently under study," they add, as is the opening of new vistas for research in human reproduction by studying body fluids, cells, and tissues made avialable by the IVF-ET and GIFT programs where these tissues are taken for routine evaluation."

Commenting on the need for IVF in India, the physicians write: "A large number of Indian women opt for tubal

sterilization as a terminal family planning method. Some of these women perceive a need to conceive again due to unforseen child loss. This need has necessitated the introduction of IVF-ET to restore fertility to the tubectomized women in whom microsurgical reanastomosis of the tubes is not possible or not successful in restoring fertility."

The physicians, from the Institute for Research in Reproduction, Jehangir, and the King Edward Memorial Hospital. Parel, both in Bombay, began collaborating on exploratory studies in IVF in 1982. They launched a full-fledged IVF program in August 1985. Since then, they have treated 121 women. Seven live births ensued.

They used three different protocols for ovarian stimulation. In the third protocol "the menstrual cycles were programmed by treating women with hormonal oral contraceptives and then subjecting them to ovarian stimulation."

The IVF practitioners also established a GIFT program. To date, 31 cycles have been treated (they do not mention how many women), four pregnancies have occurred and one baby was born January 6, 1988, "the first GIFT baby in India." Two pregnancies are on-going, they add, and one aborted.

T. C. ANAND KUMAR, C. P. PURI, K. GOPALKRISHNAN and I. N. HINDUJA. The in vitro fertilization and embryo transfer (IVF-ET) and Gamete Intrafallopian Transfer (GIFT) program at the Institute for Research in Reproduction (ICMR) and the King Edward Memorial Hospital, Parel, Bombay, India. *Journal of In Vitro Fertilization and Embryo Transfer* 5(6):376–377.

Adding fetal bovine uterine fibroblasts to IVF culture seems to help

Adding fetal bovine uterine fibroblasts to the culture medium for in vitro development of the embryo after fertilization seems to reduce the incidence of cellular fragmentation in embryos and increase implantation rates, a Ph. D. student said at the annual meeting of the American Fertility Society in Atlanta, Georgia, USA.

Results of a study of 100 fertilization/embryo transfers in 76 women showed that the implantation rate was twice as high among women whose embryos were cultured with fetal bovine uterine fibroblasts than among those whose embryos were cultured in the standard medium, said Klaus E. Wiemer, Ph.D candidate in reproductive physiology at Louisiana State University.

The student's work received the American Fertility Society's grand prize award for 1988.

Ob. Gyn News. 1988. Altering culture medium doubles IVF implantation. 23(24):3.

GIFT

Mobile Oocyte Incubation Unit developed for GIFT in Taiwan

An IVF team in Taiwan has developed a compact laboratory that can be placed in the operating room in an effort to improve its success rate for gamete intrafallopian transfer (GIFT). The laboratory is called a Mobile Oocyte Incubation Unit.

"In the 1970s and early 1980s," physicians from the Ob/Gyn department of the National Defense Medical Center in Taiwan wrote, "in vitro fertilization and embryo transfer (IVF/ET) offered a unique methodology for overcoming intractable infertility. In spite of the great efforts made to enhance the efficiency of its performance, the rate of success has not satisfactorily increased."

In the early stages of their own IVF program, from April 1984 to March 1986, they write, they achieved a very poor pregnancy rate. Because of this low rate, they began concentrating their efforts on GIFT in April 1986. But their GIFT success rates were also unsatisfactory—a 23.8% pregnancy rate among the first 21 women selected.

The unsatisfactory rate might be attributed to the distance between the embryo laboratory and the operating room, they theorized. So they developed

the Mobile Oocyte Incubation Unit that could be placed in the operating room beside the operating table. After the unit was used, the pregnancy rate for the following 19 women increased to 42.1%.

MIN-TSIR SHIH, MU-HSIEN YU, TANG-YUAN CHU, DAVID SUN, CHIA-KOON LEE, and CHTEN-TTEN HSU. 1988. A Mobile Oocyte Incubation Unit (MOIU): A device for improvement of the Gamete Intrafallopian Transfer (GIFT) program. *Journal of In Vitro Fertilization and Embryo Transfer.* 5(4): 188–194.

SURROGACY

"Child-projects" defended by surrogacy broker

"In the past the child was a gift of God," writes a French surrogacy broker. "Nowadays, it must be pointed out, it is the fruit of a project of the couple."

The broker, gynecologist Sacha Geller, operated a surrogacy outfit in Marseille until the government ordered it closed.

"The child of the surrogate does not belong to her any more than the child resulting from artificial insemination belongs to the donor, for the genetic contribution is exactly the same in both cases," Geller writes in *Human Reproduction.* "The child belongs, we believe, to those who have conceived the project of having it: indeed without them this child would never have come to life."

When a child born of a surrogate arrangement is given up to the commissioning couple, this is not child abandonment, but child restitution, he argues. ". . . It is given back to its true parents."

Geller continues: "Besides, when she is paid, the surrogate does not sell a child, she is paid for her collaboration with the child-project conceived by the couple. Surrogacy is not child-selling, it is a form of what John Robertson has felicitously termed 'collaborative reproduction.' It may be said that the surrogate is placing her 'procreative force' at the couple's disposal, in the same way as a worker does for his employer with his 'working force,' and this undertaking can be perfectly accepted from both the ethical and the legal standpoint."

S. GELLER. 1986. The child and/or the embryo. To whom does it belong? *Human Reproduction.* 1(8):561–562.

Five people want custody of a child born under surrogacy arrangement after commissioning couple separates

Two married adults who commissioned a child through a surrogacy arrangement separated a year after the child's birth and are now engaged in a battle to adopt her. The mother, Norma Lee Stotsky of Pataskala, Ohio, also sought custody of the child for a time. She reluctantly gave up the quest both because she did not have the money to fight and because the fight was taking a strong toll on her family, her lawyer, Patricia Grimm, said.

Stotsky gave her day-old child to the couple, Beverly Seymour and Richard Reams, in January 1985 after receiving $10,000. The child, Tessa, is related to neither Seymour nor Reams. When Reams proved to be infertile, the couple used a sperm donor, Leslie Miner.

"What you've got here are a bunch of nice people who were all acting in good faith, a darling little 4-year-old girl, and a complete mess that I am praying she will never become cognizant of," said Ream's lawyer, Kim Halliburton.

Tessa's case has been in and out of the judicial system for more than two years, with more than a dozen lawyers involved, Tamar Lewin reports in *The New York Times.* In January, Probate Court Judge Richard Metcalf dismissed both Reams' and Seymour's petitions to adopt Tessa on the ground that they had failed to post bonds required by the court. Juvenile Court will now decide who gets custody of the child. In the meantime, a couple on the East Coast is also interested in adopting her, lawyers involved in the case told reporter Lewin. The Association for Surrogate Parenting Services, run by Kathryn Wyckoff, handled the business arrangements for Tessa's birth.

Complicating the case, Lewin reports, has been confusion over Tessa's birth certificate. It originally named Stotsky's husband as the father. Later it was changed to list Reams as the father.

TAMAR LEWIN. January 26, 1989. A custody case with extra tangles. *The New York Times.*

ARTIFICIAL INSEMINATION

Artificial insemination as successful at home, without professionals, as in climes

The success rates for artificial insemination were the same whether the procedure was performed by the partner at home or by professional staff in a clinic, a study of 52 women with primary infertility showed. It was a randomized, cross-over study performed by Dr. Hendrikus V. Hogerzeil and associates at the University of Amsterdam Medical Center.

An additional 86 women with primary infertility who were not part of the cross-over trial chose insemination either in the home or the clinic. Pregnancy rates in the two groups were the same. Seventy-two women with secondary infertility chose insemination either at home or in a clinic. Again, success rates in both groups were the same.

"These findings indicate that home insemination should be considered for all couples, according to the investigators, who note that this kind of involvement may increase the man's self-esteem and stimulate acceptance of the child."

Ob. Gyn News. 1988. Artificial insemination found as successful at home as in clinics. 23(21):24.

BIRTH REGULATION

Breastfeeding important as contraceptive

Breast feeding reduces a woman's fertility and thus functions as a contraceptive in many countries. This leads to better spacing of births and decreases infant mortality rates.

"Demographers have shown that the interval between successive births is a principal determinant of marital fertility and in populations without access to modern forms of contraception, this birth interval will be largely determined by the duration of breast feeding," *Nature* reports.

Changes in breast feeding practices create the need for artificial contraception so that births can be spaced optimally. A major change in breast feeding has occurred in many countries with the introduction of milk substitutes. It has also been shown that "breast feeding duration is generally shorter among young, affluent, urban, educated women than in their older, poorer, rural, less-educated counterparts," *Nature* states.

Breast feeding rates and breast feeding duration have declined but the use of artificial contraceptives has not increased at the same rate in many countries. This can lead to drastic changes in women's fertility rates as well as increases in infant mortality and maternal ill-health.

But the impact may be very different for different countries. This is dependent on womens' average life span, fertility rates, the percentage who breast feed so that their fertility is inhibited and the percentage who use artificial contraceptives.

When the percentage of women breast feeding is high such as in Senegal, then a reduction in breast feeding requires a large increase in contraceptive use to offset the increase in fertility. For countries where contraceptive use is high, a decrease in breast feeding does not require much increase in contraceptive use.

Child mortality can be reduced if the birth interval between first and second children is at least two years. A new pregnancy "cuts off the milk supply, leading to the abrupt weaning of the older child," *Nature* states. The disease called Kwashiorkor means literally "the disease of the displaced one" and is caused by malnutrition when the child loses its supply of protein when it is weaned too early.

Breast feeding also increases maternal health as it causes a prolonged period when no menstruation occurs. This in turn prevents anemia. *Nature* states, "the potential benefits of breast feeding for the health of the mother and the child are so enormous that protection of breast feeding should always be uppermost when formulating public health policies for developed or developing countries."

SHYAM THAPA, ROGER V. SHORT and MALCOLM POTTS. 1988. Breast feeding, birth spacing and their effects on child survival. *Nature* 335: 679–682.

Contraceptive vaccine against sperm

"It may be possible to immunize a woman against her partner's sperm," *New Scientist* reports.

By injecting female guinea pigs with a protein found on the outside of sperm, researchers made the females immune to sperm and they did not get pregnant when mated with males. The effects of the immunization wore off after 6–15 months. Six male guinea pigs were also immunized and allowed to mate but did not succeed in impregnating females.

A similar protein has not yet been found from human sperm but researchers are looking. John Aitken of the Medical Research Council's Reproductive Biology Unit in Edinburgh, Scotland states that, "in the next millenium, contraceptive vaccines will play an important role, especially in developing countries."

LYNDA BIRKE. 1988. Sperm protein holds key to contraceptive vaccine. *New Scientist* October 15: 30.

Abortion pill approval causes controversy in France

France has recently approved a drug that induces abortion, according to Peter Coles of *Nature.* The drug, known as RU-486 or Mifegyne, is produced by Roussel-Uclaf laboratories in France and has previously been approved only in China.

RU-486 works by blocking the effect of progesterone, the hormone that normally maintains a pregnancy. This causes the uterine lining to break down and the embryo is expelled by uterine contractions.

According to French regulations, the pill must be given together with prostaglandins (which increase contractions) since when given alone, it is only 80% effective. It can only be used during the first 49 days of pregnancy, when the progesterone levels are low enough for the drug to be effective and the woman must take the drug in the presence of a doctor.

There is a 3 % risk that the embryo will not be expelled after treatment. In these cases the woman is encouraged to undergo a conventional abortion since the effects of the drug on the fetus are unknown. Other risks with the drug are prolonged bleeding, incomplete expulsion of the embryo or the placenta with an increased risk of infection.

"French researchers are now looking at the effectiveness of RU-486 during the second cycle of ovulation as a means of birth control—its main function in China," states *Nature.* "The World Health Organisation has also asked that Roussel-Uclaf make the drug available at reduced cost to developing nations."

RU-486 is controversial in many countries and antiabortion groups have successfully stopped its use in the U.S., according to *New Scientist.* After having received approval to sell RU-486 in France, many staff members at Roussel Uclaf received threats from anti-abortion groups. This led the company to withdraw the drug from the French market.

But the French minister of health, Claude Evin, has forced the company to put the drug back on the market. "Evin invoked a law stating that French women have a legal right to abortion and another that compels companies to market a drug deemed to be in the public good," states *New Scientist.* If the company refuses, the ministry of health can seize the patent for RU-486 and give it to another drug company.

PETER COLES. 1988. French government approves abortion pill for commercial use. *Nature* 335: 486; 1988.

French government forces company to market abortion pill. *New Scientist* November 5: 24.

PRENATAL DIAGNOSIS

Fetus diagnosed prenatally as having cystic fibrosis found to be healthy at birth

A 17-year-old pregnant woman receiving care at John Radcliffe Hospital in Heading-ton, England was told, after amniocentesis and ultrasound scan, that she might be carrying a child with cystic fibrosis. After genetic counseling, she decided to have an abortion but later changed her mind. She gave birth to a live boy without cystic fibrosis who, at six months of age, is well.

Physicians at the hospital caution that this false-positive prenatal diagnosis of cystic fibrosis based on ultrasonographic and laboratory test results underscores the need to exercise great care when interpreting unusual ultrasound findings.

Ob. Gyn News. 1988. Potential for false positives in prenatal diagnosis of CF. 23(24):11.

EMBRYO EXPERIMENTATION

European Commission conference on embryo research

The first international bioethics conference on human embryos and research was held in Mainz, Federal Republic of Germany in November 1988. The conference was initiated by the European Commission to bring together scientists, lawyers, and theologians to discuss research guidelines for work with human embryos, according to *New Scientist.*

Anne McClaren, head of the Mammalian Development Unit of Britain's Medical Research Council, "stressed the importance of research into embryos, especially in the areas of hereditary diseases and in-vitro fertilization," *New Scientist* states.

Others at the meeting were in favor of strict legislation. Albin Eser, director of the Max Planck Institute for Foreign and International Criminal Law in Freiburg, FRG, stated that "the price of modern reproductive medicine was 'first and foremost, the victimization of those embryos that need to be "used up" for the development and investigation of in-vitro fertilization'" *New Scientist* reports.

The major dividing line during the conference was over the question of when an embryo becomes a person to be protected by the law. Some insisted on seeing the embryo as a person from conception, others such as McClaren stated that the embryo has "individuality" only after 14 days.

Mary Warnock, who chaired the British committee on human fertilisation, would like to see a European set of guidelines for licensing and monitoring embryo research and in-vitro fertilisation. She is worried that this may not come about since several countries have or are planning laws that would forbid human embryo research.

DON KIRK. 1988. Europe fumbles toward agreement on embryo research. *New Scientist* November 19: 20.

Current status of human embryo research in Europe

Very few European countries have passed laws regulating human embryo research but many are formulating legislation, according to *Science.* These include Britian, France, Denmark, Switzerland, Sweden, and Austria.

Most countries would allow research on embryos up to the 14 day limit. "In sharp contrast, however, [the Federal Republic of] Germany's Ministry of Justice is drafting a law that would make it a criminal offense-punishable in principle by up to 5 years in prison to engage in any research that could be considered harmful to a human embryo," states *Science.*

One major reason for this legislation is "a reawakening of national sensibilities over human experimentation carried out by Nazi doctors," *Science* continues.

Pediatrician and medical historian E. Seidler, from the University of Freiburg took part in a joint meeting held by the

government of FRG and the Commission of the European Economic Community. He said: "I come from a country in which there was, in the past, a long discussion on what type of life was worthy to live; that is why I am very anxious when I hear this type of issue raised."

Only Denmark has passed legislation which forbids research on human embryos. However, this measure is considered tentative while researchers and society are given a chance to think over the ethical issues.

Most countries agree that certain practices such as human cloning, genetic engineering in sex cells, and making chimeras using human and animal embryos should be made illegal. Major disagreement is over using unfertilized eggs to produce embryos for research and "whether research should be allowed at all on an embryo unless it is aimed at improving the chances that the embryo will turn into a healthy human being," *Science* reports.

DAVID DICKSON. 1988. Europe split on embryo research. *Science* 242: 1117–1118.

Virus plus oral contraceptives may cause cancer

Female sex hormones may interact with human papilloma virus to cause cervical cancer, according to *New Scientist.* This in turn may mean that women who take birth control pills (which contain hormones) and who have the virus (which causes genital warts) may have a higher risk of developing cervical cancer.

Studies indicate higher cervical cancer rates in women taking birth control pills and in women with papilloma virus infections. New studies suggest that "the two factors may interact," states *New Scientist.*

SHARON KINGMAN. 1988. Sex hormones turn virus into cancer agent. *New Scientist* November 5: 30.

FETAL TISSUE

Fetal tissue use found acceptable in U.S.

"A special panel convened to answer questions about research using human fetal tissue [in October] concluded that although 'it is of moral relevance' if the tissue is obtained from induced abortions, nevertheless 'the use of such tissue is acceptable public policy'" states *Nature.*

Previously, the Human Fetal Tissue Transplantation Research Advisory Panel had met without being able to draw conclusions.

"The panel took pains not to take a moral stand on the contentious issue of abortion, instead concluding that so long as abortion was legal, then cadaverous tissue obtained from aborted fetuses could legitimately be used for research," *Nature* reports.

JOSEPH PALCA. 1988. Use of fetal tissue deemed acceptable. *Nature* 335: 756.

Meeting on Parkinson's disease held in Sweden

Results of the first transplants of human fetal brain tissue into the brains of Parkinson's patients was presented at a meeting in Sweden in November, according to *Dagens Nyheter.* The two patients were middle-aged women who were treated at the University Hospital in Lund, Sweden.

Olle Lindvall of the department of neurology at the hospital in Lund stated that the two women showed "small but positive improvement." Researchers at the meeting speculated that transplantation of fetal tissue may also make possible the treatment of Alzhiemers disease, epilepsy, and damage to the spinal cord.

BENNY ANDERSSON. 1988. Operationer ökar hopp om bot. *Dagens Nyheter* (Stockholm) November 12: 16.

Frozen fetal tissue may lead to tissue banks

"Scientists at Yale University School of Medicine in Rochester, New York, [U.S.] have succeeded in implanting tissue from the brains of human fetuses into adult monkeys after they had frozen the fetal tissue for a long period," states *New*

Scientist. This could lead to the "possibility of building a 'bank' of tissue for transplants that could help to treat people with Parkinson's disease," *New Scientist* continues.

1988. Frozen grafts could lead to bank for brains. *New Scientist* November **19:** 28.

GENETIC ENGINEERING

Ice-minus bacteria evaluated

Stephen Lindow, a plant pathologist from the University of California at Berkeley (U.S.), caused an environmental controversy in 1988 when he planned to field test a genetically engineered bacteria. The bacteria was engineered to prevent frost from developing on plants that had been sprayed.

After the first experiments, he has reported that the "ice-minus" bacteria protected potato seedlings from frost and that the bacteria were not detected outside the 30 meter buffer zone around the test plot.

1988. Ice minus risk. *New Scientist* November 19: 19.

Field tests of manipulated bacteria end prematurely

"Biotechnica, a biotechnology company based in Cambridge, Massachusetts, has halted its field test of a strain of *Rhizobium meliloti* engineered to have enhanced nitrogen fixing capabilities because the microbe failed to increase the growth of alfalfa," *Nature* states. The test was carried out despite local protests in Pepin County, Wisconsin, where the test plot was located.

C.E. 1988. Field tests end. *Nature* 335: 582.

Industry prepares for environmental releases

"In the next year, the Wistar Institute of Philadelphia [Pennsylvania, U.S.] hopes to test outdoors a genetically engineered vaccine against rabies in South Carolina and Virginia," *Science* reports. "In preparation, it has added an unusual member to the project team that includes specialists in genetics, viruses, and molecular biology. It has hired top public relations firm Hill and Knowlton."

Wistar created a controversy in Argentina last year when researchers smuggled the vaccine into that country and tested it outdoors in cattle without the Argentinian government's knowledge. The experiment was stopped when the information became known.

Other biotechnology companies have been caught up in controversies about releasing genetically engineered organisms into the environment and they are now trying to repair the damage. For instance, Monsanto and Crop Genetics International are using public relations to improve their images, to inform the public about future tests and to try to build credibility.

By presenting information well in advance of actual tests, the companies are also removing the newsworthiness of the tests.

MARJORIE SUN. 1988. Preparing the ground for biotech tests. *Science* 242: 503-505.

NSF official resigns after scandal

"Amid ongoing Justice Department probes of allegations that he worked for a biotechnology company while serving in public office, David T. Kingsbury, assistant director for biological, behavioral, and social sciences at the National Science Foundation (NSF), has resigned," *Science* states. Kingsbury was chairman of the White House Biotechnology Science Coordinating Committee and had "a central role in shaping broad federal guidelines governing the conduct of recombinant DNA research and the commercialization of biotechnology products," *Science* continues.

There is no evidence that Kingsbury made any decisions that favored the biotechnology company, Porton, while he worked at NSF. The controversy Kingsbury has caused will lead to stricter overviews of employee's business connections before they are hired by NSF.

MARK CRAWFORD. 1988. Kingsbury resigns from NSF. *Science* 242: 28.

Genetically engineered plant to be field tested in Sweden

Rapeseed plants genetically engineered to produce more protein will probably be field tested in Sweden during the spring of 1989, according to *MiljöAktuellt.* The plant has been developed by the Swedish plant breeding company Hilleshog together with Plant Genetic Systems of Belgium.

Hilleshög has asked the Swedish Hybrid DNA Delegation (which previously regulated laboratory work with recombinant DNA) to review the company's own risk assessment of the test. At the current time there are no regulations or laws in Sweden that regulate these kinds of experiments. But Hilleshög has voluntarily submitted the test to the delegation for final approval.

The Swedish Environmental Protection Board has asked the Swedish government for directives for this type of experiment but no action has been taken so far.

KRISTINA FAXEN. 1988. Försök med genmodifierad raps på åker. *MiljöAktuellt* (Stockholm) November 10: 10.

Mini-bullets to implant new genes in plants

"A new method of inserting genes into plants will enable geneticists to transfer DNA into plants that were previously inaccessible to genetic engineering," *New Scientist* reports. "Using a 'shotgun' technique, researchers will be able to insert genetic material into the cells of plants without having to strip the cell wall."

The new genes are placed into plasmids, small rings of DNA which are then mixed with tiny particles of tungsten. The particles are then placed on a plastic bullet that is fired down a tube, against a plate perforated with small holes.

The tungsten particles continue through the holes and perforate the plant cells on the other side carrying the new genetic material into the cells. The particles are small enough that they do not destroy the plant cells.

STEPHEN DAY. 1988. Miniature bullet shatters traditional crop engineering. *New Scientist* October 29: 36.

News from the 26th International Genetics Congress

Over 4000 participants attended the 26th International Genetics Congress in Toronto, Canada, during August 20–27. One of the highlights of the congress was the presentation of research showing that "human genes can now be introduced into sheep in such a way that the protein products of the genes are made in the mammary glands and secreted into the animals' milk," *Science* reports.

The genes that have been tested in this manner are for a blood clotting factor (factor IX) and alpha-1-antitrypsin, an enzyme inhibitor. The levels of these substances produced in the milk were low.

The same technology of making transgenic animals is being used to try to engineer better domestic animals. Pigs have been engineered to have genes for human growth hormone in order to produce leaner meat, but these experiments have caused abnormalities in the animals.

"The females never go into estrous and are sterile, possibly because they are so lean that they do not produce hormones normally," *Science* states. "Animals of both sexes are lethargic, have muscle weakness, and are susceptible to developing arthritis and gastric ulcers, which often prove fatal."

JEAN L. MARX. 1988. Gene-watchers' feast served up in Toronto. *Science* 242: 32–33.

Status of animal patents in U.S. and Europe

The U.S. Patent Office approved the first patent of a genetically engineered animal (a mouse) in 1988. The U.S. Congress was asked to step in and evaluate this new development.

The U.S. House of Representatives "has passed legislation, H.R. 4970, reinforcing the Patent and Trademark

Office's April 1988 assertion that, under current law, genetically altered animals are patentable matter," states *Chemical and Engineering News.* The new law will give fanners some protection as on-the-farm reproduction of genetically engineered and patented animals will not be considered patent infringement.

The European Patent Office has not made a decision on animal patents as yet. But the "European Commission has decided to press for new patent laws so that biotechnologists in the European Economic Community can rely on the same protection as do their counterparts in the U.S. and Japan," *New Scientist* states. This would include patenting genetically engineered animals.

"The Japanese patent office is also about to grant patents on genetically engineered plants and animals," *New Scientist* reports.

1988. House approves genetic animal patent bill. *Chemical and Engineering News* September 19:18; STEVE CONNOR. 1988. Animals to be patented in Europe. *New Scientist* October 15: 26.

Patented mouse now on the market

Laboratories can now buy the "oncomouse" from Du Pont. The transgenic mouse contains human oncogenes, genes that cause cancer and is the first example of a genetically engineered animal that has been patented. The mice cost 50–100 US dollars a piece, 10 times more than a standard laboratory mouse.

ALUN ANDERSON. 1988. Oncomouse release. *Nature* 336: 300.

First gene therapy experiments approved but delayed after controversy

"The Recombinant DNA Advisory Committee (RAC) of the U.S. National Institutes of Health (NIH) has approved an experiment to introduce lymphocytes containing a bacterial gene into terminally ill cancer patients," *Nature* reports. The experiment was given approval on October 3 "despite the fact that an RAC subcommittee on human gene therapy had voted unanimously four days earlier to defer approval until it received additional details about the experiment," *Nature* states.

The bacterial gene would be used as a marker to track the lymphocytes in the body. At a previous meeting, the subcommittee requested more information on the mouse model used, proof that the gene inserted properly into the lymphocytes, and that the virus being used would not reproduce once inside the patients.

The subcommittee received a letter from the two researchers involved but it did not answer these questions. The subcommittee then recommended that RAC delay approval of the experiment. Four days later, the two researchers came to the RAC meeting with the missing information but refused to give the committee paper copies.

They withheld the data because they were afraid that presenting it in a written form would make the results public and this in turn could jeopardize publishing articles in *Science* and the *New England Journal of Medicine,* according to *Science.* However, the editors of both journals state that presenting data to a governmental body would not be a risk and that they would never have suggested withholding such data.

The entire controversy has led James Wyngaarden, director of NIH to delay approval of the experiment, according to a second *Nature* article. Wyngaarden wants the experimental protocol reevaluated in light of the questions raised by the RAC subcommittee.

JOSEPH PALCA. 1988. Gene transfer to humans approved in face of advice. *Nature* 335: 577; BARBARA J. CULLITON. 1988. NIH delays gene transfer experiment. *Science* 242: 856–857; JOSEPH PALCA. 1988. NIH delay first gene transfer. *Nature* 335: 754.

Researchers may soon be able to target genes

When new genes are introduced into another organism, researchers have only been able to cross their fingers and hope that they would insert somewhere in the chromosome. But they could not control

where the gene would insert.

Recent developments may mean that a gene can be targeted to insert exactly where researchers want it to, according to *Science.* Targeted gene transfer would improve the possibilities of curing genetic diseases with gene therapy.

The experiments that raise these possibilities were carried out by Mario Capecchi and Kirk Thomas of the University of Utah at Salt Lake City (U.S.). They managed to inactivate a defective mouse gene by targeting a new gene to insert in the middle of the defective gene. They could also target a healthy gene to this site, thus curing the defect.

JEAN L. MARX. 1988. Gene transfer is coming on target. *Science* 242: 191–192.

Is there a schizophrenia gene?

"Independent research teams hunting a genetic cause for schizophrenia each claim to have the answer," *New Scientist* states. "Their conclusions, which disagree, have fueled controversy among psychiatrists seeking to explain the disease."

Timothy Crow, head of psychiatry at the Clinical Research Centre at Northwick Park Hospital in Middlesex, England, states that his research supports a gene on the sex chromosomes. Hugh Gurling at the Middlesex Hospital in London claims that his group has found the schizophrenia gene on chromosome 5.

Both researchers studied different families. The controversy has increased since a third research group has tried to use Gurling's gene probe on 10 other families with a high incidence of schizophrenia. Their results show no link between schizophrenia and chromosome 5 in these families.

Crow and Gurling hold by their respective theories and each claim that the other is wrong.

CATHY READ and ROSALIND RAMSAY. 1988. Teams pinpoint schizophrenia gene. *New Scientist* November 12: 31.

Researcher claims that alcoholism is hereditary

A Swedish researcher claims that alcoholism has a strong hereditary link. Sören Sigvardsson, from the department of behavioral genetics at Umeå University, states that certain personality types are at high risk of becoming alcoholic. Men are especially susceptible.

Sigvardsson has studied personality development in children and states that it is possible to predict who will become alcoholic already at 11 years of age. Children classified as searching for excitement and new experiences and who do not respond to threats or punishment were considered to be at risk.

Sigvardsson states that personality type is dependent on genetic factors. He does admit that the social environment can play a role as well.

ANITA SJÖBLOM. 1988. Alkoholism går i arv. *Dagens Nyheter* (Stockholm) October 5.

Possible link between Down's syndrome and enzyme

"Researchers from the U.S. and Israel have introduced a human gene responsible for some symptoms of Down's syndrome into mice," states *New Scientist.* The gene caused the mice to age prematurely and there were indications of mental retardation.

The gene codes for an enzyme called superoxidase dismutase 1 (SOD1). The enzyme activates oxygen to create oxygen radicals which are highly reactive. Overproduction of SOD1 can thus cause an increase in reactive oxygen which can damage tissues, especially cell membranes.

This type of damage is seen in the brains of people with Down's. Similar damage was seen in the mice with the human SOD1 gene. The damage causes brain cells to become "leaky" which in turn impairs their ability to send nerve signals.

FRANCESCA ALLEN. 1988. Mouse model links ageing to Down's syndrome. *New Scientist* October 15: 32.

Blood test to detect Down's syndrome

"A simple test that measures the concentrations of three different proteins

in a pregnant woman's blood could detect more than 60% of the fetuses with Down's syndrome, according to Nicholas Wald of St. Bartholomew's Hospital in London and his colleagues," *New Scientist* reports. "The new screening method could reduce the number of children born with Down's in Britian each year from about 900 to about 350."

Amniocentesis is offered to women over 36 but this method only detects 30% of Down's cases. This new test will make it possible to screen all pregnant women. The substances measured are human chorionic gonadotrophin, oestriol, and alpha-fetoprotein.

"The new study suggests that the mother's age should no longer be taken as the prime indicator for screening," *New Scientist* states. "It is simply one of several variables that need to be used," state the researchers.

1988. Screening method will reduce Down's babies. *New Scientist* October 15: 32.

Gene for Alzheimer's still elusive

The gene for Alzhiemer's disease is not on chromosome 21 as was previously believed.

In both Alzhiemer's and Down's syndrome, nerve cells have similar abnormalities. This led many to speculate that the gene for Alzheimer's could lie on chromosome 21, the extra chromosome that people with Down's are born with.

However, in a study of 15 families with Alzheimer's, no link could be established with the disease and chromosome 21, according to *New Scientist.* Some researchers are doubtful that susceptibility to Alzheimer's disease is genetic.

In a related article in the same issue of *New Scientist,* researchers at St. George's Hospital in London have found that dementia in elderly patients is often misdiagnosed as Alzheimer's. This in turn means that many patients may be receiving improper care or may be incorrectly taking part in drug trials set up to test new treatments for Alzheimer's.

1988. Alzheimer's gene evades neurologists . . . *New Scientist* October 15: 33; 1988. . . . while doctors question diagnosis. *New Scientist* October 15: 33.

Continued search for cause of muscular dystrophy

The gene for muscular dystrophy is very large and researchers have developed a theory for how deletions of parts of the gene cause different forms of the disease. But it now seems that new results will force researchers to modify this model, according to *New Scientist.*

One mutation of the gene causes the most severe form, called Duchenne muscular dystrophy (DMD). Another mutation causes Becker muscular dystrophy (BMD) which is less severe.

A link has previously been found between the protein dystrophin and the gene that mutates to cause muscular dystrophy. Dystrophin was missing completely in DMD but small amounts were present in BMD. The theory was that the differences in these two forms of the disease were caused by different types of mutations.

However, a study of 29 patients in the U.S. has shown that the 13 patients with DMD and 13 patients with BMD had the same type of mutations in the gene.

CATHY READ. 1988. Flaw in muscular dystrophy theory. *New Scientist* November 19: 27.

Genetic screening of familial amyloidosis now possible

It is now possible to test for familial amyloidosis in Sweden using genetic probes. This opens up the possibility for testing possible carriers as well as for prenatal diagnosis.

The disease is characterized by accumulation of amyloid in organs and tissues. This in turn causes a range of neurological problems. The disease usually does not present itself until late in life, on the average between the ages of 50–70 and is twice as common among males as females.

GÖSTA HOLMGREN, ULF DRUGGE, ERIK LUNDGREN, OLA SANDGREN and LARS STEEN. 1988. DNA-teknik gör det möjligt spåra anlagsbärare med familjär amyloidos med polyneuropati. *Läkartidningen* 85: 3677–3679.

Anti-clotting heart drug having problems

Tissue plasminogen activator (TPA) was approved by the U.S. Food and Drug Administration for treating heart attack victims in 1988. The drug is produced by genetically engineered bacteria and is marketed by the biotechnology company, Genentech.

TPA sales are much lower than expected and have caused Genentech stock prices to decline, according to *Nature.* And now "questions have arisen over the ethics of the company's promotion and testing of the drug," *Nature* states.

"Seven class action lawsuits have been filed against Genentech, on behalf of stockholders claiming that the company withheld adverse information about TPA's promise while company insiders sold off 24 million US dollars in shares," *Nature* reports.

A congressional committee has also found that 15 researchers taking part in trials of the drug owned stock in Genentech. There is speculation that this may have biased the trials and eventual approval of TPA.

MARCIA BARINAGA. 1988. Problems with anti-clotting drug. *Nature* 335: 751.

Heart drug allowed in Great Britian

The anticlotting drug, tissue plasminogen activator (TPA), has now been approved for use in Great Britian, according to *New Scientist.*

Human TPA is produced by cells that have been genetically engineered to contain the TPA gene. It is unlikely that it will become a big seller however. The cost of the drug is prohibitive and most hospitals will not be able to afford it.

1988. Heart drug reaches Britain-at a price. *New Scientist* November 12: 23.

Human genome project starting up in US

"With the total budget for the genome project reaching 50 million US dollars for fiscal year 1989, both the National Institutes of Health and the Department of Energy are adding staff and securing outside advice," *Science* writes.

"At NIH, Elke Jordan has been named director of the new Office of Human Genome Research," *Science* states. She will be working with James Watson who has been appointed as associate director for human genome research.

The Department of Energy now has a steering committee and a budget of 18 million US dollars for its part of the genome project.

LESLIE ROBERTS. 1988. Genome project. *Science* 242: 1123.

Biologists encouraged to refuse military funding of biotech

"Department of Defense (DoD) officials have been building the U.S. research program in defensive biological warfare (BW)," *Bio/Technology* reports. "They claim such efforts are vital for national security, particularly because new biotechnology techniques pose novel threats. Critics, including some prominent biologists, counter that DoD's expanding programs are an unsettling threat to international relations, and that putting biotechnology to such use is wrong."

This has led the Committee for Responsible Genetics in Boston, Massachusetts (U.S.) to urge fellow scientists to sign a pledge protesting the militarization of such research. They urge their colleagues to refuse funding from the military and to refuse to participate in military research as well.

More than 500 scientists have signed the pledge, including a number of Nobel laureates. Many are sceptical of DoD's claims of defensive research.

"Recombinant DNA methods are so limitless and one could make any number of variables, so defense is literally impossible," states Nobel Laureate Christian Anfinsen of Johns Hopkins University.

JEFFREY L. FOX. 1988. Some biologists want DoD out of biotech. *Bio/Technology* 6: 1144.

Biotech evaluated by European Communities

The first two four-year biotechnology programs sponsored by the European Communities have been evaluated according to *Nature.* The projects did not attract the kind of industrial backing that was expected and the next program is recommended to sponsor just a few, large projects. These seem to have more potential for encouraging industrial participation.

PETER NEWMARK. 1988. Europe evaluates its four-year plans in biotechnology. *Nature* 335: 579.

Conflict over leadership in British biotechnology

"An argument between the heads of Britian's research councils over who should take charge of the country's effort in biotechnology is jeopardising cooperation between scientists on the ground," *New Scientist* reports. The controversy is distressing many scientists since there is considerable collaboration between the different councils.

The Medical Research Council (MRC) is attempting to take away control of biotechnology from the Science and Engineering Research Council. The Agricultural and Food Research Council would like to see this happen so that it could split the control between itself and the MRC.

STEVE CONNOR. 1988. Friction at the frontiers of British biotechnolgy. *New Scientist* October 22: 31.

Danish biotech industry wants gene tech law changed

The Danish biotechnology company Nor-disk Gentofte plans to build a new factory in Ireland. The factory will produce insulin using genetic engineering methods. The company is moving because they are dissatisfied with the restrictive law on genetic engineering and the environment in Denmark and the slow moving bureaucracy that it has created.

But the company has not been entirely candid. Ireland is offering a very large investment grant to the company as an incentive. Gentofte's move has come at the same time that the Danish government is discussing liberalizing its law on genetic engineering.

The changes would make it easier for companies to carry out small scale production and would remove the necessity of obtaining permission for scaling up production. However, all research with recombinant DNA would still require permission, and the prohibition on environmental release of genetically engineered organisms would stand.

STAFFAN DAHLLÖF. 1988. Lag om genteknik i stöpsleven. *Kemisk Tidskrift* (Stockholm) 13: 63.

German biotech lab to be built in U.S.

"The chemical and pharmaceutical giant BASF AG announced on 11 November that a genetic engineering laboratory and pilot plant originally planned for West Germany [Federal Republic of Germany] will now be built in Boston [Massachusetts, U.S.]," *Nature* reports.

Since September 1, 1988, new regulations requiring companies using genetic engineering to submit to public inspection have taken effect in FRG. BASF did not want to deal with environmentalists and was afraid of exposing itself to competitors. The company also decided that Boston provided a better intellectual climate for their research.

JOSEPH PALCA. 1988. Boston nets BASF. *Nature* 336: 300.