MEDICAL PRACTICE

Clinical Topics

Donor insemination: report of a two-year study

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British Medical Journal, 1977, 1, 1327-1330

In the past few years the more liberal attitude to therapeutic abortion and the widespread use of the oral contraceptive pill have led to a decrease in the number of babies available for adoption. Donor artificial insemination (AID) has been practised in Britain for some years, mainly in the private sector. Owing to a change in the influence of legal, ethical, and theological considerations it is now an accepted method of treating the infertile couple when there is a history of azoospermia, severe oligospermia, rhesus incompatibility, or the presence of genetic disorders. We report a two-year study of AID as practised within the National Health Service.

Legal implications of donor insemination

As the law stands in England a child born as the result of AID is illegitimate, the husband's consent to artificial insemination being immaterial. This is because the child is not of the husband but of a man whose identity is unknown to all but the medical practitioner. The child should therefore be registered as of illegitimate birth, father unknown. The mother and her husband should then apply to adopt the child and because of regulations in the Adoption Act proceedings cannot be taken until at least four and a half months after the child's birth. As the child will obtain a short form of birth certificate he should be told that he has been adopted. Whether the child should be told that he is the result of AID is open to many

arguments. The AID child is usually not told about his origins but, of course, each couple must decide on this important issue themselves.

The new law relating to identification of the natural mother by a child for adoption may make one wary of future Acts regarding AID children that might be enforced.

Falsification of birth registers does take place. If, however, a false declaration is made serious consequences might result apart from the penalties that might be incurred under the Perjury Act.¹ The ambiguous position of the AID child with respect to the inheritance of property from either the sperm donor or from the mother's husband is still a major legal anomaly.

There is no legal requirement that the woman's husband should consent to AID. If he does not consent to treatment it does not constitute adultery by the wife. The Scottish Court of Session² upheld this decision, and, although there appears to be no case law in England, this decision probably would be accepted as good law. Adultery is sexual intercourse between two persons, at least one of whom is married to another person. Although sexual intercourse for this purpose must include some penetration of the woman by the penis, some religious teaching holds that insemination by donor semen would be adulterous.

Problems may also arise from using genetically unsound or infected spermatozoa, and there is the possibility of action for damage by the child against the medical practitioner for birth with some physical defect. This cannot be barred by any form of consent given by the mother.³

These potential difficulties require that the medical practitioner protects himself so far as possible. It is our practice for the wife and husband to sign a form of consent in the presence of an independent witness. This form is a slight modification of one recommended by the Medical Defence Union. It states: (1) that the couple authorise the artificial insemination of the wife by means of semen supplied by a donor, and (2) that the birth of such a child will not defeat the claims of any person to any titles, estates, interests, or funds. They acknowledge that the possible consequences of the procedure

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have been explained including the risk of transmission of disease.

The document for completion by the donor states that he is supplying semen for the purpose of artificially inseminating a woman whose name has not been disclosed to him. He acknowledges that it has been explained that the use of semen supplied might be held to be adultery and that he consents to supply semen on condition that his name is not disclosed and that the written consent of the woman and her husband is obtained. This is the document recommended by the Medical Defence Union. The consent form is verified in writing by his wife if the donor is married.

As the legal basis of AID is uncertain at present an early regularisation of the law with reference to AID is necessary and if the recommendations of the Peel Committee⁴ are accepted it would do much to further this end.

Evaluation of the couple for AID

Each couple referred for AID is interviewed, both members together, and the legal, psychological, and religious problems associated with the procedure are discussed in detail. Opportunities for adoption are reviewed. If there is any evidence of an abnormal mental state in either partner a psychiatric opinion is sought.

ASSESSMENT OF THE HUSBAND

Often the husband's fertility has been evaluated before referral. If this has been omitted or is incomplete investigation is started. Two 24-hour urine specimens are assayed for follicle-stimulating hormone (FSH),⁵ luteinising hormone,⁶ pregnanetriol,⁷ oxosteroids, oxogenic steroids,⁸ and oestrogen.⁹ At least two specimens of semen are analysed. Chromosome studies and testicular biopsy may be arranged if indicated. In cases of azoospermia a prolactin level is determined and a skull radiograph performed to show the pituitary fossa.

Patients in whom the FSH concentrations are raised and the semen analysis shows a count of less than 5×10^6 /ml are assumed to have testicular failure and no treatment is offered. Men with normal FSH concentrations and counts varying between $5-10^6$ /ml are offered treatment with mesterolone, 100 mg daily, for at least four months. When there is evidence of pituitary failure judged by low or absent levels of FSH and luteinising hormone a clomiphene stimulation test is performed; if this shows a response treatment with clomiphene citrate, 50 mg daily, on alternate weeks for four months is prescribed. Patients with either a block in the tubules judged by a normal testicular biopsy and azoospermia or a varicocele are referred for surgical opinion.

ASSESSMENT OF THE PATIENT

The patient is examined and fallopian tube patency tests, usually by hysterosalpingography, are performed. Insemination is undertaken when bilateral tubal patency is evident or when the uterus is normal and one of the tubes shows normal filling and spilling. Insemination is not attempted in the presence of bilateral tubal occlusion.

A baseline hormonal analysis is arranged. Twenty-four-hour urine samples are collected on cycle days 3, 7, 10, 11, 12, 13, 14, 15, 20, 22, and 26 in a regular 28-day cycle. Adjustments in the days of collection are made if the cycle is longer. These samples are assayed for FSH,⁵ luteinising hormone,⁶ oestrogen,⁹ and pregnanediol.¹⁰ Ovulation is judged to occur when there is mid-cycle peaking of luteinising hormone ($40-160$ IU/24 h) accompanied by a rise in oestrogen concentrations ($140-300$ nmol/24 h; $38.1-81.7$ μ g/24 h) and a subsequent rise in pregnanediol concentrations ($8-23$ μ mol/24 h; $2.4-7$ mg/24 h) on the 20th and 22nd day of the cycle.

Patients who are not ovulating according to these criteria are treated with clomiphene citrate starting on a dosage of 50 mg daily for five days from the fifth day of the cycle and increasing to 150 mg daily until a response is achieved. The response is judged by measuring urinary oestrogen from days 10-16 and urinary pregnanediol on day 20 and day 22. In those patients who produce a good oestrogen response to clomiphene but who show no evidence of corpus luteum function a single injection of human chorionic gonadotrophin, 5000 IU

intramuscularly, on day 13 often produces the desired rise in pregnanediol concentrations.

During the insemination cycles patients are often asked to keep basal body temperature charts. All patients collect two 24-hour urine samples for estimation of pregnanediol one week after ovulation was judged to have occurred.

After the initial assessments the couple are requested to consider the problems of AID at home and if they still wish to proceed a further appointment is made, giving them the chance to bring up any outstanding points. At this second interview the husband's general health is assessed in an attempt to rule out any condition that might compromise his capabilities as a father. The blood groups of both patients are determined, and their physical characteristics in terms of height, weight, stature, and colour of the eyes and hair are noted. The consent form for AID procedures is signed.

The donor

Most donors have been undergraduate or postgraduate students. A full medical history is taken and physical examination performed when indicated. The donors' family histories are reviewed in detail in an effort to limit the risks of genetic or familial disease. The general physical characteristic features in terms of height, stature, and colour of the hair and eyes are recorded. The blood group and rhesus factor are determined and screening tests for venereal disease and hepatitis performed.

The anonymity of the donor is maintained by using a code system, and a fee of £4 is paid for each specimen produced. This money comes from a departmental "research fund" set up for this purpose and administered by the local treasurer. Patients selected for AID are asked to contribute to the fund.

All accepted donors have a semen analysis with a minimum count of 40×10^6 /ml, a motility of at least 60%, and over 60% morphologically normal forms. The minimum count and motility is lower than that accepted by some other centres. Beck found that half the men examined qualified as potential donors using semen with a count of 52×10^6 /ml and 75% motility and normal forms.¹¹ Of our potential donors 29% have been rejected on grounds of family or psychiatric history or because their semen analysis did not fulfil the foregoing criteria.

Both fresh and frozen semen are used. Semen is produced in the department, and an aliquot is sent immediately for bacteriological studies. When semen is intended for storage in liquid nitrogen it is allowed to liquefy. On liquefaction 10% analar glycerol is added in drops with continuous agitation. The semen is placed in 0.5 ml straws labelled with the donor's code and the date, and the straws are suspended in liquid nitrogen vapour for seven minutes. After this the straws are plunged into liquid nitrogen and stored until used.¹² Owing to the rapid turnover the storage time rarely exceeds eight weeks.

The use of frozen semen allows a better matching to be attempted and enables multiple inseminations to be performed during one cycle. Freezing techniques result in a 30-40% decrease in the motility of spermatozoa after freezing and thawing processes. Ultrastructural changes occur in many spermatozoa after freezing.¹³ Despite the concern regarding chromosomal damage Sherman found abnormalities of the progeny in only 1% of births resulting from the use of frozen semen.¹⁴ Semen that is to be used fresh is kept in a water bath at 32°C until needed. The semen is divided into aliquots of 0.5 ml, which are placed in straws for insemination.

Insemination technique

Insemination is performed on one or two occasions in each cycle on the day before and the day of presumed ovulation. A maximum of six consecutive treatment cycles are given, and this constitutes a course. The straws are placed in the insemination gun and instilled directly into the cervical canal. Occasionally the entire semen sample is instilled into a plastic insemination cap placed on the cervix. The patient rests for at least 20 minutes in the dorsal position with the knees bent after the insemination.

TIMING OF INSEMINATION

The biggest single factor in unsuccessful inseminations is the timing of ovulation. Ovulation is often delayed in otherwise normal

patients by the emotional upset at the time of insemination. Various workers^{15 16} have recommended the use of human chorionic gonadotrophin intramuscularly in an effort to ensure ovulation at the correct time, and 5000 IU has been used on the day before insemination in some women with slightly irregular cycles. Study of the basal body temperature chart, the cervical mucus, and spinnbarkeit have also helped to time ovulation and insemination.

Results of treatment

During the review period 261 couples were referred for AID. The reasons for these requests (table I) are similar to those reported by Chong and Taymor.¹⁷

TABLE I—Classification of patients referred for donor insemination

Classification	No of patients
Azoospermia	144
Severe oligospermia	78
Zero motility of spermatozoa	9
Paraplegia with ejaculatory failure	8
Rhesus incompatibility	4
Genetically inherited problems	4
Post-vasectomy	2
Seminoma of testes (radiotherapy)	2
Epispadias	2
Incomplete data (no treatment given)	8
Total	261

After the initial interview 54 (21%) did not wish to proceed with investigation and treatment or were judged to be unsuitable. Altogether 207 patients were accepted for AID. Of these, 10 patients became pregnant before AID was performed. Eight of these husbands had oligospermia (counts of less than $10 \times 10^6/\text{ml}$ usually accompanied by poor sperm motility), one was a paraplegic with failure of ejaculation, and one had absent vasa deferentia. This is in keeping with the findings of Goss¹⁸ and Phillipp¹⁹ that between 15 and 30% of babies are not the products of the husband.

Altogether 197 patients' names were placed on a waiting list. Of these, 120 have completed or are currently undergoing treatment, and 77 patients remain on the list for future insemination. Of the 120 treated patients, 13 did not complete the course of six cycles of treatment either for personal reasons, house removals, or because of illness, and they have been excluded from further consideration. Fifty patients have received the course of six treatment cycles without success. Two of these patients have received two courses, the second being started 12 months after the first. Altogether 36 patients have become pregnant, and four of these have returned for further insemination and two are pregnant for the second time. Twenty-one patients are currently receiving treatment.

PREGNANCIES

Of the 86 patients who have completed the treatment schedule, 36 have become pregnant, two on two occasions—that is, 38 pregnancies altogether—a 44% success rate. The treatment cycles in which pregnancy occurred are spread evenly over the six cycles and suggest that extension of the treatment period would result in a higher rate of success (table II). There were 21 pregnancies when fresh semen was used, 15 when frozen semen was used, and two when both fresh and frozen semen were used in the same cycle.

After pregnancy is diagnosed the patient is referred back to her gynaecologist or general practitioner who will undertake her antenatal care. The patient is asked to let us know the outcome of the pregnancy but long-term follow-up of the child is not undertaken. An AID programme in Nottingham²⁰ includes follow-up photographs of the child at 1, 3, and 7 years of age.

TABLE II—Pregnancy and duration of treatment

Cycle No	1	2	3	4	5	6
No of pregnancies	6	10	5	7	2	8

Factors affecting fertility

Of the 86 patients treated, 29 (34%) had problems affecting their fertility. Eight patients had a blockage of the fallopian tube on one side; four of them, however, became pregnant. Of the 36 patients who became pregnant, four had non-ovulatory cycles and were treated with clomiphene citrate, two became pregnant in the sixth cycle, one in the fifth cycle, and one in the fourth cycle. Five pregnancies occurred in patients with irregular cycles after human chorionic gonadotrophin had been given to time ovulation and insemination more accurately. Of the 50 patients who received six cycles of treatment without success, eight had non-ovulatory cycles and were treated with clomiphene citrate. Two of these received 12 cycles of treatment without success. Four patients had grossly irregular although apparently ovular cycles and were treated with human chorionic gonadotrophin.

Dixon and Buttram²¹ noted a trend towards diminished fertility with increasing age. We show a similar trend, although the results obtained are not statistically significant. Eight (47%) of the 17 patients aged under 25, 20 of the 39 (57%) aged 25–29, and eight (29%) of the 27 aged 30 and over became pregnant. Chong and Taymor¹⁷ found that the pregnancy rate was not influenced by age.

Discussion

The number of patients requesting artificial insemination has increased substantially during the past few years and from our experience still seems to be increasing. There are, however, numerous administrative problems with scheduling appointments at the appropriate time in the cycle and in obtaining suitable donors. This, taken with the high work load in departments of obstetrics, gynaecology, and endocrinology, must limit the number of patients who can be treated in this way. It is therefore important to examine ways in which the rate of success could be improved. The overall success rate (46%) is similar to that of Dixon and Buttram,²¹ who had a rate of 44.9% using fresh semen only. Our figures are lower than those of previously reported series.^{17 22 23} There is an impression that frozen semen is not as fertile as fresh semen. This may be due to the decrease in motility obtained after freezing and thawing processes. The percentage recovery previously reported was about 55–75%.^{24 25} As well as the decrease in motility, Behrman²⁶ has shown that frozen sperm must be inseminated within 24 hours of ovulation for pregnancy to occur. He postulates that this is due to an alteration of cell physiology that is independent of motility.

The percentage success rates when both frozen and fresh semen are used has been calculated (table III) and results indicate that pregnancy does not occur so readily when frozen semen is used. Despite the limitations imposed we do not

TABLE III—Type of semen used to induce pregnancy

	No of cycles	No of cycles for pregnancy	Pregnancy: No of cycles
Frozen semen	301	69	4.36
Fresh semen	122	38	3.2
Fresh and frozen semen	20	6	3.3

believe it possible to conduct an extensive AID service using fresh semen exclusively, particularly within the National Health Service. Our success rate could probably be improved by increasing the number of inseminations per cycle. At present the average is only 1.2 per cycle as compared with other workers who average 2 to 3 inseminations per cycle.^{17 18} Further success might be achieved by refusal to contemplate the procedure if any bar to fertility was present. Although this might improve the success rate, it would deprive many women of the chance to have a baby that a little extra effort might have made possible.

In December 1972 the CIBA Foundation held a symposium on the law and ethics of donor artificial insemination. The conclusion was that "AID is here to stay"²⁷ and that the law has got to consider AID not in a prohibitory way and perhaps only in a regulatory way so far as is required to make the technique acceptable to society.

We thank Miss D S Gosling for secretarial help.
ADDENDUM—Since this paper was written, further pregnancies have been achieved. Fifty pregnancies have resulted among the 107 patients who have completed the treatment schedule. This has increased the success rate by 2% to 46.7%.

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(Accepted 7 March 1976)

Personal Paper

Landry Guillain-Barré syndrome: personal experience of acute ascending paralysis

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British Medical Journal, 1977, **1**, 1330-1332

On a Saturday afternoon in May 1964, while watching the FA cup final on television, I developed headache, became feverish, and was, I thought, suffering from influenza. The next day I developed photophobia and the headache persisted. These symptoms were accompanied by intense cramp-like pains in the thighs, calves, and the soles of my feet. The pain was intense during the night and sleep became virtually impossible. At times I involuntarily cried out with pain.

As my condition did not improve during the next two weeks, I was admitted to St George's Hospital, Tooting, for investigation and treatment. Infectious mononucleosis was diagnosed. I was thought to have had a lymphocytic encephalitis, the pains being due to affected posterior nerve roots.

During the next 10 years I suffered pain, mostly in the shoulders, thighs, calves, and soles of the feet, usually in the afternoons and evenings. I also had headaches or abdominal pain, and there were days when I felt extremely lethargic. These attacks became less common and less painful over the years. But in October 1974 the attacks became more severe.

An examination showed no clinical abnormality, and blood studies gave normal results.

Onset of Guillain-Barré syndrome

On Sunday 10 November 1974 I was driving to see a patient when pains in the shoulders forced me to take two paracetamol tablets. The consultation was complex and prolonged and I did not return home until 8 pm. That night sleep proved impossible because of pains mainly in the legs and feet. A bath at 3 am brought no relief, and by 5.30 am I was up and taking my dog for a walk. I experienced paraesthesiae in both feet and became apprehensive. I went to work as usual but have since been told that my gait was awkward and unsteady. When I went to see my doctor at about 5 pm I felt mildly unsteady with stiff calves. He found only very sluggish tendon reflexes in the legs and Rombergism but he arranged a consultation with a neurologist. I returned to work, but that night I again had little sleep.

Next morning the paraesthesiae had spread to both hands, in the distribution of the ulnar nerve. I drove to work but walking was awkward, my balance was uncertain, and I had to use a stick. By mid-morning I felt so unwell that the prospect of a busy outpatient clinic was too daunting and a colleague agreed to do it for me. I returned home during the afternoon feeling generally weak and unwell and was in bed by 6.30 pm. After that I remember only very severe pains, my wife ringing our general practitioner, and being given an injection of heroin and intravenous diazepam.

The next morning I recall telephoning the neurologist, who told me that I should be admitted to hospital immediately since he thought that I had the Guillain-Barré syndrome. Events seemed to

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