I'm having IVF treatment, but it's not working. Is there anything else I can do? - A personal professional view.

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It's natural that when IVF treatments have not been successful and there is no apparent reason for couples to look to see if there is anything else they can try in the hope that it may make a difference. It is believed that for the most part when IVF fails it is due to flaws in the internal make-up of eggs, sperm or embryos. These occur naturally in the sperm and eggs of all men and women and are one of the main reasons why not all normally fertile couples conceive immediately upon trying and are also probably the reason for most miscarriages. These defects may be impossible to detect in the eggs or sperm being used for IVF treatment and can occur with normal-looking sperm, eggs and embryos, so there remains an element of luck so far as treatment success is concerned as to whether the right eggs or sperm may be produced or selected in any particular treatment cycle. When a treatment cycle fails it is likely, therefore, to be mainly a matter of luck in most cases.

We are often asked in our clinic about supplementary treatments that couples may have heard of or come across on the internet, whether they work and whether we are prepared to try them. In this regard all UK clinics are bound both by medical ethics and the HFEA Code of Practice only to utilise treatments for which there is evidence of benefit. Such evidence generally comes into three main categories:

1. firm evidence of benefit and established practice
2. some evidence of benefit but uncertainties exist, not established practice but probably not likely to be harmful
3. no evidence of benefit and may actually be harmful or an expensive waste of time and money

We endeavour to ensure that procedures in category 1 are incorporated into our routine practice locally. They are usually supported by professional guidelines and an expert consensus. An example of an authoritative view on medical evidence would be the guidelines produced by the UK's National Institute of Clinical Excellence (NICE) available at http://www.nice.org.uk/guidance/index.jsp?action=byID&r=true&o=10936

The status of procedures in categories 2 and 3 are more controversial and very much a matter of opinion, which may vary from specialist to specialist and clinic to clinic. My own opinion on some of the more common supplementary procedures that I am asked about is as follows:

Routine analysis of hair for 'toxic' metal concentrations and vitamin or mineral deficiencies +/- dowsing for 'geopathic stress' areas of habitation.

There is some evidence that exposure to pesticides, heavy metals such as lead or cadmium, or other environmental chemicals may be a factor in infertility in certain occupational groups. I am unable to find any reliable

scientifically-acceptable evidence to support routine testing, however, and there is a risk that this may be an expensive waste of time and money. That is not to say that certain vitamin and mineral supplements may not be helpful for some people – indeed our clinic's standard information supplement makes recommendations about some of these.

Acupuncture:
There are a number of published scientific studies showing a benefit of acupuncture as an adjunct to IVF treatment. In particular is seems to have an effect on the number of IVF pregnancies that miscarry. It is not established practice but may be beneficial in reducing stress and anxiety. Some couples in our clinic do arrange acupuncture prior to embryo transfer and we are happy to support this.

Homeopathy/herbalism:
It is difficult to comment on this since homeopathy seems to encompass a wide range of different practices. There do not appear to be any scientific studies in the standard scientific literature to indicate a benefit of any homeopathic treatments as an adjunct to IVF. Some herbal compounds do contain biologically active ingredients that may theoretically have an effect on treatments, however, and in the absence of studies and bearing in mind the lack of regulatory control over the products as medicines I would recommend to avoid them since there is a possibility that they may be just as likely to be harmful as beneficial.

Embryo biopsy and Preimplantation Genetic Diagnosis (PGD).
Some clinics offer a scientifically sophisticated procedure to remove some cells from embryos in the laboratory, test them for abnormalities (such as having the correct number of chromosomes), and then use the results to select only the 'normal' embryos for transfer. This is known as 'aneuploidy testing'. It sounds good in theory but many embryos contain a mixture of normal and abnormal cells. Removing cells may damage the embryo and reduce it's chance of implanting. It may also remove the only 'good' cells and leave the abnormal ones! The expert consensus at present is that this procedure does not improve success rates in routine practice. It is an established procedure, however, to help normally-fertile couples with certain hereditary problems conceive healthy babies.

DHEA (Dehydroepiandrosterone):
DHEA is a substance sold over-the-counter in some countries (although not to the best of my knowledge at the time of writing in the UK) as a 'food supplement'. It may be possible to obtain it in the UK from internet suppliers but anyone wishing to do so would need to check the legality of this. Claims are made for it with regard to rejuvenating and 'tonic' properties. It is in fact a substance that occurs naturally, which the human body manufactures on the way to producing sex hormones such as oestrogen and testosterone and it's biological effects are somewhat similar to testosterone. Testosterone is a 'feel-good' hormone that has effects on libido, amongst other things, but may have side-effects such as acne or unwanted hair growth. It is known to stimulate the receptors on cells in the ovaries that cause them to respond to

the FSH, which is the hormone that we use to stimulate eggs to develop. There is a study that suggests women who are liable to respond poorly to these injections (e.g. because of age) may produce higher numbers of eggs if they take DHEA in a dose of 75mg/day for a few months before treatment. It's probably not harmful if taken in this way, is inexpensive, and in such situations there may often be little to lose by trying it. Anyone wishing to do so, however, should bear in mind that obtaining it over the internet or from foreign sources may bypass the normal regulatory safety checks and procedures for medicines in the UK.

Assisted Hatching:
Embryos develop in a membrane called the 'zona' through which the cells have to break in order to continue developing and implant in the womb – usually around five days after fertilisation. This process is known as 'hatching' since in many ways it is just like a chick breaking though its eggshell. It is possible to assist this process by weakening the membrane around the embryo by a variety of means. In our clinic it can be done using a special laser microscope that very precisely creates a tiny hole in the membrane. It is not thought to be of benefit in routine practice but may be helpful in cases of recurrent implantation failure, older women or when the membrane has been measured to be unusually thick. The evidence is controversial but we may offer it in such cases.

Aspirin, heparin, steroids and immunosuppression:
It is theorised that in some cases fertility success may be reduced due to immune causes e.g. the woman may produce antibodies against some of her own cells or tissues or have abnormal numbers or function of cells involved in fighting infections. In some cases the recognition and treatment of such conditions is established practice e.g. a condition called 'antiphospholipid syndrome (APS)', for which we routinely test. The treatment for this condition involves taking a small dose of aspirin on a regular basis and giving injections of a drug called heparin to thin the blood. Some centres have gone so far as to try these measures on patients even if they do not test positive for APS, but evidence of benefit is not strong and it is not established practice.
Other conditions, such as having abnormal numbers of cells called 'natural killer (NK) cells' in the blood, are much more controversial and there is strong expert opinion that performing blood tests for these (which may be very expensive) is illogical and without firm scientific foundation. Some centres use steroid hormones and other drugs to suppress the immune response in selected cases, including those where there are abnormal NK cell numbers on blood tests. The scientific claims of benefit are very controversial, not least because some of the drugs may be very expensive and carry significant risks. The expert consensus at present would appear to be that the evidence of benefit does not support their use in routine practice and this is also my opinion at the present time. There is some evidence that the use of steroid medication such as prednisolone may be of benefit in certain other immune conditions, however, some of which may be subtle and not easy to recognise routinely. Although I wouldn't normally suggest or recommend it I am not averse to trying prednisolone as an adjunct to IVF treatment for some couples

who have done their own research into the pros and cons and are very keen to try it.

Testing sperm for DNA fragmentation and antibiotic administration:
DNA is the chemical within the sperm, eggs and indeed all living human cells that forms the 'blueprint' for the way in which they form and function. It is the DNA of the sperm and the egg that combine to create the blueprint for an embryo and the genetic characteristics of the child should one develop from that embryo. Tests, called 'DNA fragmentation tests', have been developed that purport to demonstrate the extent to which a man's sperm may contain abnormalities. There is conflicting evidence about the significance of these tests to most couples undergoing fertility treatment but at the time of writing this they seem most likely to indicate how well the sperm will fertilise eggs in IVF and how likely it will be that an IVF pregnancy will miscarry. DNA fragmentation testing may be complicated to perform and expensive and its cost-effectiveness in routine use is doubtful in my view. Having said that there is also some evidence that in some cases high DNA fragmentation may be associated with certain organisms found in the genital tract, including Chlamydia. Some of the associated organisms may be very hard to detect except with expensive tests but there is evidence that treatment with a relatively inexpensive course of antibiotics (Azithromycin and doxycycline) may improve both the DNA fragmentation and subsequent fertility. Although it is not established practice there may be an argument for a pragmatic approach to use antibiotic treatment in any case.