



AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE

## A PRACTICE COMMITTEE REPORT

### *A Committee Opinion*

# THE ROLE OF ASSISTED HATCHING IN IVF: A REVIEW OF THE LITERATURE

## BACKGROUND

**I**n vivo hatching of the blastocyst is a critical component of the physiologic events culminating in implantation. Conversely, the failure to hatch (whether due to intrinsic abnormalities of the blastocyst, zona pellucida or endometrium) may be one of the many factors limiting human reproductive efficiency. The clinical application of assisted hatching has been proposed as one approach toward the enhancement of implantation and pregnancy rates following in vitro fertilization (IVF). In 1989, Cohen and associates reported an increased implantation rate following mechanical opening (partial zona dissection-PZD) of the zona pellucida in embryos resulting from IVF.<sup>3</sup> These investigators postulated that the opening of the zona might enhance the subsequent hatching process. Cohen et al subsequently published a randomized, prospective trial of selected assisted hatching 72 hours post-retrieval (zona drilling with acidified Tyrode's medium), which suggested an improvement in implantation rates when the procedure was *selectively* applied to embryos with a poor prognosis (based on zona thickness, blastomere number, fragmentation rates, maternal age, etc.).<sup>2</sup> Since these early reports, many ART programs have incorporated the use of assisted hatching in an effort to improve clinical outcomes for their patients.

The assisted hatching procedure is generally performed on day 3, and entails the creation of a gap in the zona either by drilling with acidified Tyrode's medium,<sup>6-7</sup> PZD with a glass microneedle,<sup>4</sup> laser photoablation<sup>10</sup> or use of a piezomicromanipulator<sup>9</sup>. The assisted hatching procedure has been implicated in an increased rate of monozygotic twinning.<sup>5</sup>

Success rates following the use of assisted hatching in different ART programs have varied considerably. It is, however, difficult to compare reports from different clinics due to differences in their patient populations, experience, technique of hatching and study design. Table 1 summarizes the reports of six programs from 1996 to the present. These studies utilized three different hatching techniques, all of which had at least one report of a significant improvement in clinical pregnancy and implantation rates following its use.

Three of these studies demonstrated no benefit with the use of assisted hatching.<sup>2,4,6</sup> All were prospective, randomized trials. Of note, all of these three negative studies were performed in the context of a broad patient population (i.e. all patients, all good prognosis patients, and offered to all patients 36 years and older).

A **Committee Opinion** offers consensus-based (or evidence-based when there is sufficient evidence available) guidance relative to a given practice activity. This guidance, in addition to scientific and clinical information, may take into account issues of ethical and financial concerns.

Three additional prospective, randomized studies were performed on a specific patient population, namely those with multiple IVF failures (Chao,<sup>1</sup>Magli,<sup>8</sup> Nakayama<sup>9</sup>). These studies reported a significant increase in clinical pregnancy and implantation rates following assisted hatching.

### RECOMMENDATIONS

Review of these reports suggests that assisted hatching may be clinically useful and that individual ART programs should evaluate their own patient populations in order to determine which subgroups may benefit from the procedure. The routine or universal performance of assisted hatching in the treatment of all IVF patients appears, at this point, to be unwarranted.

### REFERENCES

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Reference	No. Cycles	Type of Assisted Hatching (AH)	Type of Patients	Pregnancy and Implantation Rates in AH Group	Pregnancy and Implantation Rates in Control Group	Conclusions
Hellebaut et al., 1996	120	Partial zona dissection	“all patients”	42.1%/17.9%	38.1%/17.1%	No significant increase in clinical pregnancy and implantation rate
Chao et al., 1997	64	Partial zona dissection	Multiple IVF failures	42.4%/11.0%	16.1%/3.7%	Significant improvement in clinical pregnancy and implantation rates
Hurst et al., 1998	20	Acid Tyrode’s medium	“good prognosis”	23.0%/9/6%	43.0%/10.7%	No significant increase in rates of clinical pregnancy or implantation
Lanzendorf et al., 1998	89	Acid Tyrode’s medium	Patients ≥36 years old	39.0%/11.1%	41.7%/11.3%	No significant increase in rates of clinical pregnancy or implantation
Magli et al., 1998	248	Acid Tyrode’s medium and fragment removal	Patients ≥38 and/or 3 or more failed cycles	33.0%/13.3%	12.0%/4.1%	Significant increase in clinical pregnancy and implantation rate
Nakayama et al., 1999	248	piezomicro-manipulator	2 or more failed cycles and treatment for >4 years	19.4%/10.1%	5.9%/2.6%	Significant increase in clinical pregnancy but only in patients who had good quality embryos at time of transfer

TABLE 1. Prospective randomized assisted hatching studies performed from 1996 to 1999.

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