

represent the general population. In this study there seems to be a predominance of study subjects with a past history of pelvic inflammatory disease and intrauterine devices usage. Given a prevalence of bilateral tubal obstruction closer to 10% or less, the PPV drops even further to 18.92%, and the NPV soars to 95.72%:

		HSG		
		+	-	
LH	+	17	6	23
	-	19	35	54
		36	41	77

Adelusi study (Prevalence 29.87%).

Sensitivity 73.91% (CI = 51.59 to 89.77).

Specificity 64.81% (CI = 50.62 to 77.32).

PPV = 47.22%.

NPV = 85.37%.

Normal population (Prevalence 10%).

PPV = 18.92%.

NPV = 95.72%.

CI, 95% Confidence interval.

Using the Adelusi data, but substituting a normal prevalence for tubal disease increases the value of an HSG demonstrating bilateral tubal patency and reduces the value of an HSG demonstrating bilateral obstruction. The introduction of normal population prevalence into the analysis is a critical factor because the predictive values will vary with prevalence of the disorder that one is attempting to identify. The calculation of predictive values with adjustments for population prevalence is omitted frequently in the analysis of tests or other diagnostic interventions that are used to predict an outcome. If corrections are not made for prevalence, it is difficult to generalize a specific study to the population at large. Some investigators anxious to market an imperfect test ignore predictive values altogether and discuss only the sensitivity and specificity of the test or diagnostic intervention. Because post-test probability estimates (sensitivity and specificity) are sample statistics and are subject to random error, they can be strengthened even further by an estimate of their uncertainty in the form of confidence intervals (1). An eloquent plea for more standardized and appropriate measures of test accuracy was made over 8 years ago by John A. Swets in the journal *Science* (2). The issues that he addressed at that time are even more urgent in these times of rationed health care. Readers should be indebted to Adelusi and his colleagues for this study because it helps to point out, clarify, and stimulate further discussion about the relative value of tubal studies and the appropriate assessments of their predictive value.

Some of the same points were brought out in a

recent interview with John Collins from McMasters University in the October 11, 1995 issue of *JAMA*. In that issue with the discussion centering around a hypothetical patient, Dr. Collins pointed out the overall value of a hysterosalpingogram demonstrating bilateral tubal patency. Using an analysis of prior literature, he pointed out that a hysterosalpingogram demonstrating bilateral patency has a negative predictive value of 96% when the prevalence of tubal obstruction in the population is 10% (3, 4). This figure for NPV is essentially the same as the one derived from the Adelusi data after adjustment for normal prevalence. The high negative predictive value for HSG in a population of normal subjects presenting with infertility virtually eliminates the need for LH in those patients. Laparoscopic hydrotubation under those circumstances would provide little, if any, additional information. In reviewing Adelusi's study, one notices that the hysteroogram frequently provides other important information concerning intrauterine malformations. One will be seeing more studies similar to Adelusi and colleagues as managed care becomes a universal reality and providers become more critical of each diagnostic intervention. We are grateful to the correspondents and authors for running an important topic by us one more time.

Paul G. McDonough, M.D., Editor, Letters

REFERENCES

1. Monsour MJ, Evans AT, Kupper LL. Confidence intervals for post-test probability. *Stat Med* 1991;10:443-56.
2. Swets JA. Measuring the accuracy of diagnostic systems. *Science* 1988;240:1285-93.
3. Collins JA. A couple with infertility: clinical crossroads (conferences with patients and doctors at Boston Beth Israel Hospital). *J Am Med Assoc* 1995;274:1159-64.
4. McGuinness SD, Djahanbakhch O, Grudzinskas JG. Assessment of the fallopian tube. *Obstet Gynecol Survey* 1992;47:587-603.

Trying to Make Heads or Tails Out of Antisperm Antibody Data

To the Editor:

Yeh et al. (1) evaluated the effects of immunoglobulin M (IgM) isotype of antisperm antibodies (ASA), which have been ignored by most other researchers (including our group), and found that if IgM is bound to as little as 6% of the sperm tested there is an association with reduced fertilization after IVF. Unfortunately their discussion did not speculate how such a small percentage of ASA-bound sperm could

reduce the fertilization rate. Their finding of the negative effect of IgA with $\geq 68\%$ binding to sperm head is more understandable but also raises questions. There seems to be different conclusions depending on the study as to which isotype and what location is important (2, 3). However, when small series are evaluated, conclusions as to what is important or not when subdivided into many categories can lead to nonreproducible results. For example, using our own data with ASA $\geq 68\%$ we found fertilization $< 30\%$ as follows: IgG tail only, 7/12 (58%); IgG head and tail, 7/11 (63.6%); IgA tail only, 10/31 (32.2%); and IgA including head, 11/30 (36.6%). The pregnancy rates (PRs) per transfer for the four groups were as follows: 16.6%, 0%, 19.3%, and 23.5%. Thus, our results show a more detrimental effect with IgG not IgA, especially in light of the 0% PR with IgG head and tail. We believe that because there is so much variance in all these small series that there is probably no importance of the isotype or location of the ASA, at least with IVF. Though we suspect that the presence of ASA on the sperm is an infertility factor when postcoital tests are poor, this may be overcome by properly timed IUI (4). Because we require at least six IUI cycles before doing IVF for male ASA, possibly those making it to IVF may have cryptic male or female infertility factors unrelated to the ASA or possibly the ASA is acting as a marker rather than as an etiologic factor. This hypothesis may be supported by data showing improved PRs in IVF after treatment of sperm bound with ASA with chymotrypsin-galactose without reducing percentage of antibody binding (5). We think Yeh et al. should be encouraged to continue their studies but should prospectively match each couple where ASA is present on the sperm with a couple with similar infertility history and characteristics but negative for ASA. This study should compare not only fertilization rates but PRs also (which was missing from their present manuscript).

*Diane Katsoff, M.L.T.
Jerome H. Check, M.D.
The University of Medicine and Dentistry
of New Jersey
Robert Wood Johnson Medical School at
Camden
Cooper Hospital/University Medical Center
Department of Obstetrics and Gynecology
Division of Reproductive Endocrinology
and Infertility
Camden, New Jersey
Melrose Park, Pennsylvania
July 31, 1995*

REFERENCES

1. Yeh WR, Acosta AA, Seltman HJ, Doncel G. Impact of immunoglobulin isotype and sperm surface location of antisperm antibodies on fertilization in vitro in the human. *Fertil Steril* 1995;63:1287-92.
2. Clarke GN, Lopata A, McBain JC, Baker HWG, Johnston WIH. Effect of sperm antibodies in males on human in vitro fertilization (IVF). *Am J Reprod Immunol Microbiol* 1985;8:62-6.
3. Witkin SS, Viti D, David SS, Stangel J, Rosenwaks Z. Relation between antisperm antibodies and the rate of fertilization of human oocytes in vitro. *J Assist Reprod Genet* 1992;9:9-13.
4. Check JH, Bollendorf A. Effect of antisperm antibodies on postcoital results and effect of intrauterine insemination on pregnancy outcome. *Arch Androl* 1992;28:25-31.
5. Katsoff D, Check JH, Bollendorf A, Benfer K. Chymotrypsin-galactose treatment of sperm with antisperm antibodies results in improved pregnancy rates following in vitro fertilization. *Am J Reprod Immunol* 1995;33:149-54.

Reply of the Authors:

We have tried to make head or tails of antisperm antibody (ASA) data in assisted reproduction for several years. The Yeh et al. (1) article is companion and complementary to a previous one (2). In this earlier manuscript, as Drs. Katsoff and Check suggest, we assessed pregnancy rates and matched test and control patients. Furthermore, considering the methodological difficulties encountered in the analysis of ASA data, we endorsed the idea of a uniformed Registry to "provide a series with enough statistical power to adequately address those issues." Until then, though, we will be forced to try to make sense out of small series. Granted, there is much variance among the series published and true, small series can provide biased information. However, we do not think isotype and location of ASA are not important in the IVF outcome. Although agreement on the specifics has not been reached, the majority of the studies show they do influence IVF (3).

In our most recent paper (1), we speculated on some reasons why immunoglobulin M (IgM) might be particularly detrimental to fertilization. We did not include putative explanations for low-percentage ASA binding to decrease fertilization rates because we believed more data were needed to scientifically support those hypotheses. Among them was the possibility that undetectable amounts of IgM, which possesses high complement binding capacity, impaired sperm performance in IVF, or that sperm-bound IgM binding were an epiphenomenon reflecting sperm plasma membrane abnormalities which, *per se*, were responsible for the decreased fertilization rates. Further, despite the absence of leu-

kocytospermia, the presence of IgM ASA may reflect a subclinical infection of the male genital tract, which through the effect of cytokines could affect sperm function. Finally, it would also be possible that reactive oxygen species and peroxides generated by ASA-bound spermatozoa may inflict an oxidative damage on ASA-free sperm and/or pre-embryos. In any case, we interpret the presence of ASA as a marker of possible sperm damage regardless of whether they are the cause of such damage or only an epiphenomenon.

We agree that some of the information in the literature is conflicting. Our own results seem to be different from Drs. Katsoff and Check's data. We assume that the figures mentioned in the above letter are unpublished because no reference is given for them and they do not appear in the authors' cited articles. In any event, again, methodological differences, e.g., isotype location groups and main endpoint, make these two sets of data not entirely comparable. In sum, we believe that answers will not be obtained until National or International Registries come into effect.

*Anibal A. Acosta, M.D.
Gustavo Doncel, M.D. Ph.D.
Eastern Virginia Medical School
Norfolk, Virginia
September 1, 1995*

REFERENCES

1. Yeh WR, Acosta AA, Seltman HJ, Doncel G. Impact of immunoglobulin isotype and sperm surface location of antisperm antibodies in fertilization in vitro in the human. *Fertil Steril* 1995;63:1287-92.
2. Acosta AA, van der Merwe JP, Doncel G, Kruger TF, Sayilgan A, Franken DR, et al. Fertilization efficiency of morphologically abnormal spermatozoa in assisted reproduction is further impaired by antisperm antibodies on the male partner's sperm. *Fertil Steril* 1994;62:826-33.
3. Lundin K, Hamberger L. Antisperm antibodies and assisted reproduction. *Asst Reprod Rev* 1995;5:120-6.

Lipids and Finasteride

To the Editor:

I have read with great interest the manuscript by Ciotta and colleagues (1), happy to learn about their positive and encouraging experience using finasteride in young women with idiopathic hirsutism.

However, I was puzzled somewhat by the discrepancy between the authors' finding, whereby "The re-

sponse of 17-OHP to ACTH stimulation test, performed during the follicular phase of the cycle, was normal in all patients," and the significantly abnormal concentrations of 17-hydroxyprogesterone (17-OHP) in both the placebo and the finasteride-treated groups, 384.2 ± 36.6 and 408.9 ± 23.9 $\mu\text{g/mL}$, respectively (1), possibly suggesting 21-hydroxylase deficiency.

Moreover, even in their group of "normal" women, the concentration of 17-OHP, as written (1) was abnormal (370.4 $\mu\text{g/mL}$), whereas normal concentrations of 17-OHP are 100 to 300 ng/dL (1-3 ng/mL or 3-9 nmol/L) (2), but certainly not 270.6 to 430.5 $\mu\text{g/mL}$ as written in the manuscript by Ciotta et al. (1). I assume this mistake is due to a failure to convert properly the "conventional units" to "SI units" but I believe this misunderstanding should be specified correctly to prevent the readers from misinterpretation of the important data.

Also, did the authors measure the lipid and lipoprotein profile before starting the finasteride treatment and during the treatment period? Was there any difference in lipoprotein levels between the finasteride- and placebo-treated groups? This may be of particular interest because hirsute, hyperandrogenic women may have abnormal levels of cholesterol, triglycerides, and especially low-density (LDL) and high-density lipoproteins (HDL). Because the total concentration of T was significantly increased in association with finasteride treatment, one may speculate that long-term treatment may affect the LDL-HDL ratio due to an increase in T levels. A reassessment of such possible long-term side effects would be more than welcome.

*Zeev Blumenfeld, M.D.
Reproductive Endocrinology and
Infertility Section
Department of Obstetrics and
Gynecology
Rambam Medical Center
The Rappaport Faculty of Medicine
Technion-Israel Institute of Technology
Haifa, Israel
September 15, 1995*

REFERENCES

1. Ciotta L, Cianci A, Calogero AE, Palumbo MA, Marletta E, Sciuto A, et al. Clinical and endocrine effects of finasteride, a 5 α -reductase inhibitor, in women with idiopathic hirsutism. *Fertil Steril* 1995;64:299-306.
2. Speroff L, Glass RH, Kase NG, editors. Clinical assays. Clinical gynecologic endocrinology and infertility. 5th ed. Baltimore: Williams & Wilkins, 1994: 969.