Late Delivery: IVF Pioneer Wins Nobel Prize

BY CHRISTINE KILGORE

For years, the Nobel Committee for Physiology or Medicine passed over in vitro fertilization. Its members were urged by obstetricians and gynecologists, among others, to award the Nobel Prize to British biologist Robert G. Edwards, Ph.D., and to recognize IVF for its reach and impact. Yet for years — for reasons that are discussed but may never be fully detailed — the committee made other choices, leaving in vitro fertilization and its main visionary to continue waiting in the wings.

Last month, after Dr. Edwards’ wife was informed that her 85-year-old husband was being awarded the Nobel Prize for the decades of work he spent developing IVF, committee members explained that the time was right. And infertility specialists and other ob.gyns. felt vindicated.

“One to two percent of all newborns are conceived through IVF,” said Prof. Goran K. Hansson, secretary of the committee, in announcing the decision. “IVF children are as healthy as other children … and many of the IVF children born in the 1980s now have children of their own, conceived without the help of IVF.”

Reproductive endocrinologists who are now active leaders in their field have called the award “gratifying,” “exciting,” and “long overdue” at a time when some concerns that the prize was given to Dr. Edwards alone because “he had the vision for IVF.” Others assisted … but it was really Dr. Edwards who saw the vision and made it happen.”

Some believe, however, that if his collaborator Dr. Patrick Steptoe were alive (he died in 1988), he might have shared the prize. Dr. Edwards, now a professor emeritus at the University of Cambridge, England, had called Dr. Steptoe to ask him for his help in 1968, after reading of his work with laparoscopy and having come to appreciate the

“IVF has enabled us to dissect the human reproductive processes in a way we weren’t able to do in the past. … There are very few things in medicine that have changed not only how we look at reproduction but life itself,” said Dr. Zev Rosenwaks, director of the Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine at Cornell University and the New York Presbyterian Hospital, both in New York.

“From a social, ethical, human, medical, and scientific point of view,” the award was well deserved and long overdue, he said.

In comments made after the Nobel Prize announcement, Prof. Christer Höög, a member of the Nobel Committee for Physiology or Medicine, said that the prize was given to Dr. Edwards alone because “he had the vision [for IVF]. Others assisted … but it was real-

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INDICATION

Prolia™ is indicated for the treatment of postmenopausal women with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy. In postmenopausal women with osteoporosis, Prolia™ reduces the incidence of vertebral, nonvertebral, and hip fractures.

IMPORTANT SAFETY INFORMATION

Hypocalcemia: Prolia™ is contraindicated in patients with hypocalcemia. Pre-existing hypocalcemia must be corrected prior to initiating Prolia™. Hypocalcemia may worsen, especially in patients with severe renal impairment. In patients predisposed to hypocalcemia and disturbances of mineral metabolism, clinical monitoring of calcium and mineral levels is highly recommended. Adequately supplement all patients with calcium and vitamin D.

Serious Infections: In a clinical trial (N = 7808), serious infections leading to hospitalization were reported more frequently in the Prolia™ group than in the placebo group. Serious skin infections, as well as infections of the abdomen, urinary tract and ear, were more frequent in patients treated with Prolia™. Endocarditis was also reported more frequently in Prolia™-treated subjects. The incidence of opportunistic infections was balanced and the overall incidence of infections was similar between the treatment groups. Advise patients to seek prompt medical attention if they develop signs or symptoms of severe infection, including cellulitis.

Patients on concomitant immunosuppressant agents or with impaired immune systems may be at increased risk for serious infections. In patients who develop serious infections while on Prolia™, prescribers should assess the need for continued Prolia™ therapy.

Dermatologic Adverse Reactions: Epidermal and dermal adverse events such as dermatitis, eczema and rashes occurred at a significantly higher rate in the Prolia™ group compared to the placebo group. Most of these events were not specific to the injection site. Consider discontinuing Prolia™ if severe symptoms develop.

Osteonecrosis of the Jaw (ONJ): ONJ, which can occur spontaneously, is generally associated with tooth extraction and/or local infection with delayed healing, and has been reported in patients receiving Prolia™. An oral exam should
fertility of in vitro–matured oocytes. “Then the world’s master of this method, he could easily aspirate (ma-
tured) oocytes from their follicles. We teamed up for IVF and discussed in de-
tail the safety of our proposed procedures, and the underlying ethics,” Dr. Ed-
wards wrote in 2001 (Nat. Med. 2001;7:1091-4). “We agreed to work to-
gether as equals, pursue our work care-
fully, and stop if any danger emerged to pa-
tients or children, but not for vague re-
ligious or political reasons. We stayed to-
ger for 20 years, until his death. I reck-
on he taught me medicine.”

Dr. Alan H. DeCherney, editor in chief of the journal Fertility and Sterility, heard Dr. Steptoe present their experience with the first IVF baby at a conference in Venice, Italy, held shortly after Louise Brown’s birth. “I thought, this is the fu-
ture, and when I returned to Yale – where I was at the time – we immediately start-
ning putting together an IVF program.” In the meantime, the first birth outside
England of a child conceived through IVF was reported in 1980 in Australia. In
1981, the first IVF baby in the United States, Elizabeth Carr, was born in Nor-
folk, Va. By the end of 1983, 150 IVF ba-
bies had been born worldwide. Through
continual improvements in clinical IVF, the number of live births worldwide
soared, to 1 million in 2000.

The problem was, with the focus on
raising pregnancy rates and the simulta-
neous improvements in technique, the
rate of multiple pregnancies as a result
of IVF skyrocketed. Reproductive spe-
cialty organizations set standards for
maximal embryo transfers. The efforts
have paid off in terms of triplet and
higher-order multiple births, but twin
pregnancies continue to rise. Fertility specialists still feel the tug be-
tween the need to control the multiple
birth rate on one hand, and the principle
of patient autonomy and free enterprise
on the other, said Dr. Bradley J. Van
Voorhis, who directs the IVF program at
the University of Iowa Hospitals and
Clinics in Iowa City.

To resolve this dilemma, many in the
field are pinning their hopes on embryo
selection – finding the healthiest, most
viable embryos, those most likely to im-
plant. “Without question,” said Dr.
Rosenwaks, “identifying a viable em-
bryo is one of the greatest challenges for
IVF in the future.”

#### In Treating Your Postmenopausal Osteoporosis Patients at High Risk for Fracture, Help . .

**BE A FORCE AGAINST FRACTURE**

Prolia™ targets and binds to RANK Ligand, inhibiting osteoclast formation, function, and survival.

Prolia™ significantly reduced fracture risk at key sites in a phase 3 trial.²,³

<table>
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<tr>
<th>Fracture Type</th>
<th>Risk Reduction</th>
<th>p-Value</th>
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<tbody>
<tr>
<td>Vertebral Fracture</td>
<td>68% ARR 1.4%</td>
<td>p &lt; 0.001</td>
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<tr>
<td>Hip Fracture</td>
<td>40% ARR 1.3%</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Nonvertebral Fracture</td>
<td>20% ARR 1.5%</td>
<td>p &lt; 0.001</td>
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Prolia™ is a subcutaneous injection administered every 6 months in your office.

Please see Brief Summary of Prescribing Information on the following page.

**Prolia™ Postmarketing Active Safety Surveillance Program:**

The Prolia™ Postmarketing Active Safety Surveillance Program is available to collect information from prescribers on specific adverse events. Please go to www.proliasafety.com or call 1-800-772-6436 for more information about this program.

**References:**

1. Van Voorhis BJ, Van Voorhees PA, Van Voorhis VJ. “The first birth outside England of a child conceived through IVF was reported in 1980 in Australia.”

2. Prolia™ (denosumab) prescribing information, Amgen.

3. Van Voorhis BJ, Van Voorhees PA, Van Voorhis VJ. “The first birth outside England of a child conceived through IVF was reported in 1980 in Australia.”

4. Prolia™ (denosumab) prescribing information, Amgen.

5. Van Voorhis BJ, Van Voorhees PA, Van Voorhis VJ. “The first birth outside England of a child conceived through IVF was reported in 1980 in Australia.”

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7. Van Voorhis BJ, Van Voorhees PA, Van Voorhis VJ. “The first birth outside England of a child conceived through IVF was reported in 1980 in Australia.”

8. Prolia™ (denosumab) prescribing information, Amgen.

9. Van Voorhis BJ, Van Voorhees PA, Van Voorhis VJ. “The first birth outside England of a child conceived through IVF was reported in 1980 in Australia.”

10. Prolia™ (denosumab) prescribing information, Amgen.