Cystic Fibrosis Diagnosis After Age 40 on the Rise

BY TIMOTHY F. KIRN
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I
his adult cystic fibrosis clini-
dent, Dr. Jerry A. Nick has patients who were not di-
agnosed until they were 40 years of age or older.

These patients represent the tip of an iceberg of unrecognized
patients, and clinicians need to be on the lookout for these individ-
uals, Dr. Nick suggests.

His patients reflect the fact that the clinical pre-
sentation of cystic fibro-
sis can vary along a spec-
trum of severity. This has becom-
ese clearer as more and more specific genet-
ic mutations causing cystic fibro-
is have been discovered.

With that awareness, patients who were once just considered a
curious aberration are now recog-
ized as having something signif-
ic, said Dr. Nick, di-
rector of the Adult Cystic Fibrosis
Clinic of the National Jewish
Medical and Research Center.

“These cases have shown up sporadically for years,” he said in
an interview.

Dr. Nick recently published a paper on late-diagnosis patients (Am. J. Respir. Crit. Care
Med. 2005;171:621-6), comparing them with 28 patients diagnosed
early who have survived into their 40s. He has also published a
review article on long-term sur-
vival with cystic fibrosis (Curr.

Dr. Nick’s patients are some of the
oldest cystic fibrosis patients yet reported. The median age of
his late-diagnosis patients is at
present more than 52 years.

They may not be an exclusive group for long, however. Adult
diagnosis is already becoming
more common, Dr. Nick noted in
his article. In 1982, only 3% of pa-
tients enrolled in the Cystic Fi-
броsis Foundation patient reg-
istry had been diagnosed after the age of 18 years. By 2002, 10% of the new patients added to the
registry that year were diagnosed during adulthood.

Many of the late-diagnosis pa-
tients that Dr. Nick described in his article had been seeing physi-
cians for years for recurrent and
chronic lung infections, or simi-
lar symptoms. They were
thought to have asthma, or chronic obstructive pulmonary
disease, or something else.

But there is no question about their cystic fibrosis diagnosis, Dr. Nick said. The patients all meet Cystic Fibrosis Foundation
diagnostic criteria, and they have had genetic analysis, sweat chlo-
ride testing, and, or nasal po-
tential difference testing.

European centers also have be-
gan to take note of late-diagno-
sis patients, but most of the Eu-
ropean patients have been
in their 20s and 30s.

The importance of Dr. Nick’s
older patients is that they may help to identify genetic
factors associated with long-term survival. The me-
dian survival of cystic fibrosis
patients is still only 35 years of
age, despite improvements in
medical care.

By 2002, 10% of the new patients
added to the Cystic Fibrosis
Foundation registry that year were
diagnosed during adulthood.

These patients represent the tip of an iceberg, and clinicians need
to be on the lookout for these individuals, Dr. Jerry A. Nick says.

Hypertonic Saline Inhalation Helps Manage CF Symptoms

BY MARY ANN MOON
Contributing Writer

Hypertonic saline inhalation using a
nebulizer reduced pulmonary excr-
erations in patients with cystic fibrosis and decreased their absenteeism from
school, work, and their usual activities, re-
searchers found in two separate random-
ized clinical trials.

The trials provided the first evidence of the
long-term efficacy of this safe and rel-
atively inexpensive treatment. The thera-
py appears to work by increasing the vol-
ume of liquid on the airway surfaces,
which is depleted because of excessive ab-
sorption of salt from the airway lumen.

This rehydration seems to produce a sus-
tained acceleration of mucus clearance,
both groups of investigators theorize.

In the first study, 164 adults and children
with stable cystic fibrosis (CF) were ran-
domized to either a 4 ml of either
hypertonic (7%) saline plus a taste mask-
ing agent or a control solution (isotonic
saline) plus a taste-masking agent via neb-
ulizer for 48 weeks. A bron-
chodilator was administered before each
treatment to prevent or minimize nar-
rowing of CF patients’ hyperresponsive
airways during nebulizer therapy, report-
ed Dr. Mark R. Elkins, of Royal Prince Al-
fred Hospital, Sydney, Australia, and his associates.

The treatment had only a moderate ef-
fact on lung function as measured by forced vital capacity (FVC) and forced ex-
piratory volume in 1 second (FEV1), and
no apparent effect on the typical decline in
lung function over the course of the year-
long study. However, it had “dramatic” ef-
fec ts on several clinical factors, they not-

The mean number of symptom excr-
erations was 1.32 per person in the treatment
group, compared with 2.74 per control sub-
ject. The mean duration of exacerbations was
22 days in the treatment group, com-
pared with 69 days in the control group.

And the length of time spent free of ex-
creration sentions, expressed as “48-week excr-
eration-free survival rate,” was 41% in the
treatment group, compared with 16% in
controls. All of these differences were high-
ly statistically significant. Similarly, antibiotic
usage during exacerbations was much lower
in the treatment group.

Patients in the active treatment group re-
ported a mean of 7 days (range, 0.21) when
they could not participate in school, work,
or usual activities, compared with a mean
of 24 days (range, 12-48) for the controls.

The treatment group also scored signifi-
cantly higher on quality of life measures.

The treatment did not alter the levels of
Pseudomonas aeruginosa or Staphylococcus
aureus in the sputum, nor did it affect the
rate of acquisition of these organisms,
Burkholderia cepacia, Stenotrophomonas mal-
tephila, Candida albicans, aspergillus species,
or Hemophilus influenzae.

In the other clinical trial, investigators
reasoned that slowing the absorption of
nebulized hypertonic saline by premed-
ating CF patients with amiodole, a sodium
channel blocker, would enhance pa-
tient response by extending the duration of
airway rehydration.Twenty-four CF pa-
ients aged 14 years and older were ran-
domized to pretreatment with either
amiodole or a taste-masked placebo, fol-
lowed by hypertonic saline via nebulizer
times daily for 14 days. All the subjects
received a bronchodilator via inhaler 10-60
minutes before the nebulizer treatment.

The study confirmed that hypertonic
saline was well tolerated in CF patients,
lung function, and quality of life, reported Dr. Scott H. Donaldson and Dr. William D. Bennett of the University of North Carolina at
Chapel Hill Cystic Fibrosis Research and
Treatment Center and their associates.

Perhaps as important, the treatment hast-
ened the rate of mucous clearance from
the lungs and “produced a larger and more
sustained increase in the volume of airway
surface liquid” in CF patients than in
healthy controls (N. Engl. J. Med. 2006;
354:241-50).

The findings suggest inhaled hyperton-
ic saline may be an option for CF patients,
Dr. Felix Ratjen of the University of Toronto
told in an editorial comment accompa-
nying the publication of both reports.

It was previously shown that hyperton-
ic saline inhalation increased mucusi-
clar transport in CF patients—but the effect
was presumed to be short-lived because
sodium deposited on epithelial surfaces
would be taken up rapidly. The new re-
search shows that the treatment “not only had a prolonged effect on the amount of airway surface liquid in epithelial cells . . . but also resulted in a sustained improve-
ment of mucociliary transport,” Dr. Rat-

The treatment had “no apparent effect on the typical decline in
lung function over the course of the year-long study.”

However, it had “dramatic effects” on several clinical factors, study authors noted. The average number of symptoms excretions was 1.32 per person in the treatment group, compared with 2.74 per control subject. The average duration of exacerbations was 22 days in the treatment group, compared with 69 days in the control group. Treatment also reduced antibiotic use during exacerbations, which were much shorter in the treatment group. Patients who received the active treatment reported a mean of 7 days (range, 0.21) when they could not participate in school, work, or usual activities, compared with a mean of 24 days (range, 12-48) for controls.