For more than a century, scientists have built upon the basic principles of heredity that
Austrian monk Gregor Mendel gleaned from his painstaking studies of garden peas. One of the
most strongly held beliefs has been that genes – whether normal or abnormal – passed from
generation to generation essentially unchanged. Now that assumption is being challenged.

Last week scientists announced that in people with a form of muscular dystrophy, they had
identified a segment of DNA that can lengthen substantially with each succeeding generation.
Most disturbing, as the fragment lengthens, the illness becomes more severe. “This is not your
garden-variety genetic defect,” say Dr Leon Charash, who chairs the medical advisory
committee of the Muscular Dystrophy Association.

The startling discovery, reported in the British science magazine “Nature” by an international
trio of research teams, marks only the third time such a genetic phenomenon has been found.
Last year researchers revealed a similar process in two much rarer inherited diseases: fragile
X syndrome, a form of mental retardation; and spinal and bulbar muscularatrophy, a wasting
disease.

While forcing scientists to revise their thinking about heredity, the findings are also raising
ethical quandaries. “It now appears we can identify people who may be asymptomatic but
whose risk for transmitting a devastating illness is very high compared with the rest of the
population,” observes geneticist David Housman of the Massachusetts Institute of Technology,
a member of one of the research teams. “Should they be informed?” A man or woman with
such a defect will have to consider the brutal fact that not only is there a fifty-fifty chance that a
child will inherit the illness, but also that the disease may be progressively worse in that child,
the grandchildren and the great-grandchildren.

Over the years researchers have discovered that the DNA that makes up the 46 chromosomes
in the human cell is not as stable as once thought. Mutations in DNA have long been known to
occur, but they usually involve relatively small changes in genetic material. For example,
between parent and child, there may be a switch in the sequence of nucleotide bases that are
the building blocks of DNA. Sometimes an entire gene can jump to another place on a
chromosome. “But you don’t usually see a big increase in the absolute number of bases within
a single gene,” says Greg Lennon, a geneticist at Lawrence Livermore National Laboratory in
California, and a member of one of the teams that made last week’s announcement. Moreover,
mutations tend to occur at a slow pace. “The rate is so low from one generation to the next –
maybe 1 in 10,000 – as to be negligible,” notes M.I.T.’s Housman.

In myotonic dystrophy, the most common form of muscular dystrophy, the change can be far
from negligible: a fragment of DNA on chromosome 19 appears to repeat itself more frequently
with every generation. Just what triggers the repetition is a mystery. Researchers surmise that
a hitch occurs while DNA is being copied in the cell, much as the same bar of music repeats
on a scratched record. The DNA repeat gets worse with each generation, just as with each
playing of a flawed record, the music stutters for a longer period. “Presumably the replication
error occurs in the sperm or egg before conception,” says molecular geneticist Pieter de Jong,
who headed the Livermore team.

Scientists expect to find more stuttering genes. “Any time a disease gets worse through
generations, we’re going to suspect that this happens,” notes Lennon. Researchers are also
intrigued by the possibility that gene growth occurs as cells replicate in the body during a
person’s lifetime. That would have implications for ailments such as cancer. The search begun
by Mendel, for the secrets of heredity is far from complete.