LETTERS TO THE EDITOR

George Huntington: the man behind the eponym

In their portrait of George Huntington, Dur- 
bach and Hayden\(^1\) stated that all biographical 
 sources available were investigated. How- 
er, they did not mention a relevant paper on 
George Huntington (1850–1916) and George 
Sumner Huntington (1861–1927).\(^2\)

The latter was a well known American anato- 
mist of the late 19th century and the first 
decades of the 20th century. Since 1908, 
biographical data of these two doctors have 
been confused repeatedly.\(^3\) Furthermore, it 
appeared that biographical publications 
concerning both George Huntington and 
George Sumner Huntington contained 
numerous inaccuracies.\(^4\) We have corrected 
the record, provided additional information, 
and investigated the lineage of both doctors 
since 1633 to elucidate their relationship.\(^5\)

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1 Durbach N, Hayden MR. George Huntington: 

2 van der Weiden RMF. George Huntington and 
George Sumner Huntington. A tale of two 

DNA storage and 
duplicate sampling: 
lessons learnt from 
testing for Huntington’s 
disease

Testing for late onset diseases such as Hun- 
tington’s disease (HD) may lead to a small 
number of discrepancies in results, mostly 
because of non-paternity and faulty DNA 
sampling, storage, or extraction.\(^6\) Our experi- 
ence in the Northern Ireland (NI) HD pre- 
dictive testing programme illustrates how 
double sampling of DNA may help reduce 
errors.

Since starting predictive testing in 1990, 
over 150 at risk HD patients have been 
counselled, of whom 30 have completed 
the programme and received results.\(^7\) One 
serious error relating to blood sampling 
ocurred, but not as a direct result of our own 
testing programme. It involved the family 
shown in the figure. Both parents were 
dead and no stored DNA samples were available. 
Sibs II.5 and II.6, resident in NI, requested 
predictive testing. The other sibs (II.1–II.4), 
including two affected members, were resi- 
dent elsewhere. DNA from the two affected 
members (II.1 and II.2) was sent to our 
molecular genetic laboratory. (These original 
samples were taken in a regional hospital 
elsewhere by a consultant clinical geneticist, 
were sent to the regional DNA laboratory in 
a different hospital, and the extracted DNA 
thann sent to another regional molecular gen- 
etics laboratory, as the original centre did not 
test for HD.) In Belfast, the samples were 
Southern blotted with probe YNZ32,\(^8\) with

samples run in adjacent lanes and with mix- 
ing of samples to allow clear resolution of all 
four alleles. This showed incompatible 
alleles in each of the two affected sibs, sug- 
gesting either non-paternity, recombination, 
or sample mix up. Non-paternity was con- 
firmed using YNH24 probing, which showed 
five alleles in the family, with II.2 having a 
fifth allele not present in the other sibs. 
Repeat samples were requested, and DNA 
from the original stock solutions was received, 
along with a DNA sample from sib II.4, who had 
recently requested predictive 
testing at that centre. WC, in return, sent two 
DNA samples from our patients II.5 and II.6 to 
the regional centre elsewhere for concur- 
rent testing.

Repeat testing of the two affected samples 
again showed incompatible allele types 
(figures). A request was made for the 
two patients to be re-bled. During this time 
patient II.1 had died and only a new DNA 
sample was received from II.2. This sample 
was different from the original II.2 sample 
and was consistent with the allele type in 
patient II.1 and with paternity testing. 
The revised results were immediately 
telephoned to the regional centre involved, 
who were already planning to disclose their results 
on sib II.4 which had appeared to be informa- 
tive using another probe. Results in both 
centres were rechecked and the result on 
patient II.4, using a combination of YNZ32 
and another probe, indicated an exclusion 
test result. Our own patients II.5 and II.6 remained 
inuninformative on linkage based testing 
because of the lack of parental samples.

This problem clearly illustrates the 
importance of accurate sample taking, 
labelling, and storage. In this case the problem 
had probably arisen, not through initial faulty 
sample taking and labelling, but through 
sample labelling error either at DNA 
extracion or during labelling and transport 
of the samples between different genetic 
centres. Our own testing protocol, based on 
UK guidelines,\(^9\) was modified to include 
taking two samples on two separate occasions 
from each person entering the programme 
where the families were small. Sample results 
are now confirmed by analysis of the second 
sample before the disclosure session. 
This precaution reduces the risk of a similar 
problem occurring, and does not add greatly 
to the number of samples analysed. Since 
the introduction of the duplicate sampling 
in 1992, one pair of samples has since been 
identified as having been strongly labelled 
after DNA extraction. With the use of 
multiallelic DNA probes, some cases of 
sample or paternity error have been identi- 
fied directly on allele mismatch. However, 
even with the use of multiallelic probes and 
paternity testing, errors may still not be 
detected, and computer simulated linkage 
analyses in HD found a 69% rate of inconsist- 
tency in some families.\(^10\) With the availability 
of direct testing for the FT15 gene,\(^11\) samples 
can now be tested without stored DNA. 
Such a procedure still carries a risk of 
sample error, and new samples should be 
used when possible.

The application of DNA testing in late 
Onset disorders such as Huntington’s disease 
or cancer is likely to increase over the next 10 
years. We strongly recommend the use of 
two separate DNA samples from key affected 
members in small families undergoing pre- 
dictive testing for late onset genetic diseases, 
particularly where samples are transported 
from other medical or nursing staff. Strict 
adherence to DNA storage guidelines\(^12\) 
will further reduce avoidable error in HD 
and other predictive testing programmes.

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