THE DIFFICULTIES IN MAKING A DIAGNOSIS OF CJD

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GENERAL INTRODUCTION

WHAT TIME DOES IT TAKE TO DIAGNOSE SPORADIC CJD?

COULD THIS TIME BE SHORTER?

TWO ILLUSTRATIVE HISTORIES

CONCLUSIONS
GENERAL INTRODUCTION
PRELIMINARY COMMENT 1
DIFFERENT PERSPECTIVES
DIFFERENT PERSPECTIVES
PRELIMINARY COMMENT 2

SETTING
PRELIMINARY COMMENT 3

DISEASE TYPE
DIFFERENT FORMS OF CJD

• GENETIC CJD

• IATROGENIC CJD

• SPORADIC CJD

• VARIANT CJD
DIFFERENT FORMS:
DIFFERING DIAGNOSTIC CONSIDERATIONS

• GENETIC CJD

• IATROGENIC CJD

• SPORADIC CJD

• VARIANT CJD
DIFFERENT FORMS:
DIFFERING DIAGNOSTIC CONSIDERATIONS

• GENETIC CJD

• IATROGENIC CJD

• SPORADIC CJD  sCJD

• VARIANT CJD
3 ESSENTIAL PROBLEMS IN DIAGNOSIS

• RARE DISEASE
3 ESSENTIAL PROBLEMS IN DIAGNOSIS

• RARE DISEASE

• NO SIMPLE, NON-INVASIVE, CLINICAL TEST
3 ESSENTIAL PROBLEMS IN DIAGNOSIS

• RARE DISEASE

• NO SIMPLE, NON-INVASIVE, CLINICAL TEST

• DISEASE: UNTREATABLE & FATAL
THE ESSENTIAL PROBLEMS IN DIAGNOSIS

• RARE DISEASE

MOST DOCTORS HAVE LIMITED EXPERTISE
THE ESSENTIAL PROBLEMS IN DIAGNOSIS

• RARE DISEASE

MOST DOCTORS HAVE LIMITED EXPERTISE

THE DIAGNOSIS IS INHERENTLY UNLIKELY
THE ESSENTIAL PROBLEMS IN DIAGNOSIS

• NO SIMPLE, NON-INVASIVE, CLINICAL TEST

RELIANCE ON CLINICAL EVOLUTION OVER TIME
THE ESSENTIAL PROBLEMS IN DIAGNOSIS

• NO SIMPLE, NON-INVASIVE, CLINICAL TEST

  RELIANCE ON CLINICAL EVOLUTION OVER TIME

  INVASIVE TESTS CARRY RISKS
THE ESSENTIAL PROBLEMS IN DIAGNOSIS

• DISEASE: UNTREATABLE & FATAL

WANT TO BE CERTAIN OF DIAGNOSIS BEFORE GIVING IT
THE ESSENTIAL PROBLEMS IN DIAGNOSIS

• DISEASE: UNTREATABLE & FATAL

WANT TO BE CERTAIN OF DIAGNOSIS BEFORE GIVING IT

DESIRE TO GIVE PEOPLE TIME NOT ‘USED’ UP BY TESTS
ANOTHER PROBLEM

“I DON’T KNOW WHY IT WASN’T DIAGNOSED EARLIER.....
WHEN I READ ABOUT THE DISEASE, THE SYMPTOMS WERE TYPICAL.”
ANOTHER PROBLEM

“I DON’T KNOW WHY IT WASN’T DIAGNOSED EARLIER.....
WHEN I READ ABOUT THE DISEASE, THE SYMPTOMS WERE TYPICAL.”

BUT THIS IS A RETROSPECTIVE VIEWPOINT
PRESENTING SYMPTOMS MAY SUGGEST SEVERAL CAUSES
WHAT TIME DOES IT TAKE?

SYMPTOMS

DIAGNOSIS
of sCJD
‘DELAY’
COULD THIS TIME BE SHORTER?

SYMPTOMS

DIAGNOSIS
of
sCJD
WHAT TIME DOES IT TAKE TO DIAGNOSE SPORADIC CJD?
UK SPORADIC CJD

MEDIAN TIME ONSET-DIAGNOSIS

~3-4 MONTHS
WHY DOES IT TAKE THIS TIME?
WHY DOES IT TAKE THIS TIME?

SYMPTOMS

‘SOMETHING WRONG’

DIAGNOSIS
WHY DOES IT TAKE THIS TIME?

SYMPTOMS

GET MEDICAL ADVICE

DIAGNOSIS
WHY DOES IT TAKE THIS TIME?

SYMPTOMS

OUTCOME
OF INITIAL
MANAGEMENT

DIAGNOSIS
WHY DOES IT TAKE THIS TIME?

SYMPTOMS

SEE SPECIALIST

DIAGNOSIS
WHY DOES IT TAKE THIS TIME?

SYMPTOMS

RESULTS
OF SPECIALIST
TESTS

DIAGNOSIS
WHY DOES IT TAKE THIS TIME?
WHY DOES IT TAKE THIS TIME?

SYMPTOMS

CONSULTATION WITH SURVEILLANCE SYSTEM

DIAGNOSIS
WHY DOES IT TAKE THIS TIME?

SYMPTOMS

FINAL CLINICAL DIAGNOSIS

DIAGNOSIS
TIME

UK SPORADIC CJD

MEDIAN TIME ONSET-DIAGNOSIS

~3-4 MONTHS
COULD THIS TIME BE SHORTER?
SYMPTOMS

'SOMETHING WRONG'

GET MEDICAL ADVICE

DIAGNOSIS

SYMPTOMS MAY BE NON-SPECIFIC
SYMPTOMS MAY BE NON-SPECIFIC
SYMPTOMS MAY HAVE POSSIBLE EXPLANATION
SYMPTOMS MAY BE NON-SPECIFIC
SYMPTOMS MAY HAVE POSSIBLE EXPLANATION

SOME WAITING IS SENSIBLE & REASONABLE
SYMPTOMS MAY BE NON-SPECIFIC
SYMPTOMS MAY HAVE POSSIBLE EXPLANATION

SOME WAITING IS SENSIBLE & REASONABLE

TIME VARIES FROM PATIENT TO PATIENT
SYMPTOMS

‘SOMETHING WRONG’

GET MEDICAL ADVICE

DIAGNOSIS

MEDIAN TIME: 2 ¼ WEEKS

[1 DAY-SEVERAL MONTHS]

UK SPORADIC CJD 2006
SYMPTOMS

‘SOMETHING WRONG’  GET MEDICAL ADVICE  SEE SPECIALIST

DIAGNOSIS

MEDIAN TIME: 6-8 WEEKS

[1 DAY-SEVERAL MONTHS]

UK  SPORADIC CJD  2006
SYMPTOMS

‘SOMETHING WRONG’
GET MEDICAL ADVICE
SEE SPECIALIST
CJD POSSIBLE OR LIKELY

MEDIAN TIME: 8-12 WEEKS
[FEW WEEKS – SEVERAL MONTHS]

UK SPORADIC CJD 2006
SYMPTOMS

'SOMETHING WRONG'
GET MEDICAL ADVICE
SEE SPECIALIST
CJD POSSIBLE OR LIKELY
REFERRAL TO NCJDSU

DIAGNOSIS

MEDIAN TIME: 12-16 WEEKS
[FEW WEEKS – SEVERAL MONTHS]

UK SPORADIC CJD 2008
UK SPORADIC CJD

MEDIAN TIME ONSET-DIAGNOSIS

~3-4 MONTHS
THIS TIME TO DIAGNOSIS IS NOT VERY DIFFERENT FROM THAT FOR MANY NEUROLOGICAL DISEASES
THIS TIME TO DIAGNOSIS IS NOT VERY DIFFERENT FROM THAT FOR MANY NEUROLOGICAL DISEASES

WHY IS IT A PARTICULAR PROBLEM IN sCJD?
sCJD IS TYPICALLY VERY RAPIDLY PROGRESSIVE
DURATION OF ILLNESS IN sCJD (n=1084, UK)
DURATION OF ILLNESS IN sCJD
(n=1084, UK)
RATE OF PROGRESSION IN sCJD

RAPID: TYPICAL

• DIAGNOSTIC PROCESS TAKES TIME

• INCREASING & SEVERE DISABILITY & NO DIAGNOSIS

• DIAGNOSIS MAY BE ONLY SHORTLY BEFORE DEATH
### SPORADIC CJD in the UK
### MEDIAN TIME IN MONTHS

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THERE IS NO SIMPLE, NON-INVASIVE, CLINICAL DIAGNOSTIC TEST
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THERE ARE TESTS THAT ARE HELPFUL IN SUPPORTING THE DIAGNOSIS
AIDS TO DIAGNOSIS FOR sCJD

- EEG
AIDS TO DIAGNOSIS FOR sCJD

• EEG

• CSF 14-3-3 PROTEIN TEST
AIDS TO DIAGNOSIS FOR sCJD

• EEG

• CSF 14-3-3 PROTEIN TEST

• BRAIN MRI
AIDS TO DIAGNOSIS FOR sCJD

• EEG

• CSF 14-3-3 PROTEIN TEST

• BRAIN MRI

NONE OF THESE SHOW ABNORMALITIES UNIQUE TO sCJD
OTHER DIAGNOSES POSSIBLE
SOME OF WHICH ARE POTENTIALLY **TREATABLE**

CERTAIN BLOOD TESTS
MRI SCANS
SPINAL FLUID EXAMINATIONS

ALL TAKE TIME TO DO
MAY TAKE TIME FOR RESULTS
AIDS TO DIAGNOSIS FOR sCJD

• EEG

• CSF 14-3-3 PROTEIN TEST

• BRAIN MRI
VITAL FOR DIAGNOSIS OF/EXCLUSION OF OTHER DISEASES

- EEG
- CSF 14-3-3 PROTEIN TEST
- BRAIN MRI
DURATION OF ILLNESS IN sCJD
(n=1084, UK)
RATE OF PROGRESSION IN sCJD

SLOWER: ATYPICAL

- OFTEN ATYPICAL CLINICAL FEATURES
- DIAGNOSTIC AIDS (EEG, CSF, MRI) MAY BE LESS HELPFUL
- RARE FORMS OF ALREADY RARE ILLNESS
SYMPTOMS

DIAGNOSIS

‘SOMETHING WRONG’
GET MEDICAL ADVICE
SEE SPECIALIST
CJD POSSIBLE OR LIKELY
REFERRAL TO NCJDSU

DIFFICULT TO SEE HOW COULD (OR SHOULD) TO REDUCE TIME HERE
WHAT ABOUT HERE?
WHY SPECIALIST DIAGNOSIS TAKES TIME

• NON-SPECIFIC PRESENTATION
WHY SPECIALIST DIAGNOSIS TAKES TIME

• NON-SPECIFIC PRESENTATION

• RARE ILLNESS: INHERENTLY UNLIKELY
WHY SPECIALIST DIAGNOSIS TAKES TIME

• Non-specific presentation

• Rare illness: inherently unlikely

• Rare illness: unfamiliarity with it
WHY SPECIALIST DIAGNOSIS TAKES TIME

• NON-SPECIFIC PRESENTATION

• RARE ILLNESS: INHERENTLY UNLÍKEY

• RARE ILLNESS: UNFAMILIARITY WITH IT

• FATAL & UNTREATABLE: WANT TO BE CERTAIN
WHY SPECIALIST DIAGNOSIS TAKES TIME

• NON-SPECIFIC PRESENTATION

• RARE ILLNESS: INHERENTLY UNLIKELY

• RARE ILLNESS: UNFAMILIARITY WITH IT

• FATAL & UNTREATABLE: WANT TO BE CERTAIN

• NO SIMPLE DIAGNOSTIC TESTS
WHY SPECIALIST DIAGNOSIS TAKES TIME

- NON-SPECIFIC PRESENTATION
- RARE ILLNESS: INHERENTLY UNLIKELY
- RARE ILLNESS: UNFAMILIARITY WITH IT
- FATAL & UNTREATABLE: WANT TO BE CERTAIN
- NO SIMPLE DIAGNOSTIC TESTS
AWARENESS OF DISEASE

IN THE UK (& ELSEWHERE)

BSE & VARIANT CJD

HAVE INCREASED AWARENESS
OF CJD IN GENERAL
WHAT DO UK NATIONAL SURVEILLANCE DATA TELL US ABOUT SPECIALIST DIAGNOSIS?
REFERRALS TO NCJDRSU: SUSPECTED CASES

[NOT ALL TURN OUT TO HAVE CJD]
NUMBER OF REFERRALS TO THE UK NCJDSU
1996-2009
NUMBER OF REFERRALS TO THE UK NCJDSU
1996-2009
NUMBER OF REFERRALS TO THE UK NCJDSU
1996-2009
NUMBER OF REFERRALS TO THE UK NCJDSU 1996-2009
SPORADIC CJD CASES

ACTUAL CONFIRMED CASES
UK NCJDSU: NUMBER OF sCJD CASES* 1996-2009

*DEFINITIVE & PROBABLE
REFERRAL (SUSPECT) RATES VARIED & FELL

INCREASING NUMBER OF CONFIRMED CASES

WHAT DOES THIS TELL US?
NUMBER OF REFERRALS TO THE NCJDSU & UK sCJD CASES 1996-2009

Number of Referrals  Number of sCJD cases
NUMBER OF REFERRALS TO THE NCJDSU & UK sCJD CASES 1996-2009

BETTER RECOGNITION OF CJD CASES BY NEUROLOGISTS
REDUCTION IN REFERRAL OF NON-CASES
UK CLINICIANS HAVE IMPROVED IN DIAGNOSIS OF SPORADIC CJD

AWAreNESS
EDucATION
DIAGNOSTIC TESTS*

*CSF 14-3-3 and BRAIN MRI
SPORADIC CJD in the UK
ONSET-NOTIFICATION
SPORADIC CJD in the UK
ONSET-NOTIFICATION

MEDIAN TIMES IN MONTHS

1990: 3.5 months
1998: 3.5 months
2008: 3.5 months
SPORADIC CJD in the UK
ONSET-NOTIFICATION

MEDIAN TIMES IN MONTHS

1990
1998
2008
UK CLINICIANS HAVE IMPROVED IN DIAGNOSIS OF SPORADIC CJD

BUT

NOT IMPACTED GREATLY ON TIME TO NOTIFICATION
UK CLINICIANS HAVE IMPROVED IN DIAGNOSIS OF SPORADIC CJD

BUT

NOT IMPACTED GREATLY ON TIME TO NOTIFICATION AND IN TIME TO DIAGNOSIS
SOME FURTHER INDIRECT EVIDENCE THAT THE DIAGNOSIS OF SPORADIC CJD IS DIFFICULT
SUSPECTED sCJD REFERRALS SEEN BY NCJDSU in 2008
NUMBER DEFINITE or PROBABLE
AT TIME SEEN BY NCDSU STAFF

TOTAL: 85

~55% sCJD

STILL ?

NOT CJD

~55% sCJD
SUSPECTED sCJD REFERRALS SEEN BY NCJDSU in 2008
NUMBER DEFINITE or PROBABLE
AT TIME SEEN BY NCJDSU STAFF

TOTAL: 85

~55% sCJD

STILL ?

NOT CJD

NCJDSU STAFF VERY EXPERIENCED IN CJD
STILL UNCERTAIN IN NEARLY 1/4
SUSPECTED sCJD REFERRALS SEEN BY NCJDSU in 2008 NUMBER DEFINITE or PROBABLE AT TIME SEEN BY NCDSU STAFF

68% FINALLY DEFINITE or PROBABLE sCJD

13/19 CASES STILL UNCERTAIN AT TIME NCJDSU VISITED WERE IN FACT sCJD
SUSPECTED sCJD REFERRALS TO NCJDSU in 2008

**FINAL OUTCOME**

**TOTAL: 135**

* DEF or PROB

~64%*

~33%

REFERRED SUSPECTS TO NATIONAL SURVEILLANCE

~1/3 TURN OUT NOT TO BE CJD OF ANY KIND
OTHER DIAGNOSES POSSIBLE
(SOME POTENTIALLY TREATABLE)

PASSAGE OF TIME AS DIAGNOSTIC TEST ITSELF
TWO ILLUSTRATIVE HISTORIES
<table>
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<tr>
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<th>Time</th>
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<tr>
<td>1st seeking advice</td>
<td>3 weeks</td>
</tr>
<tr>
<td>Referred neurologist</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Seen by neurologist</td>
<td>5 weeks</td>
</tr>
<tr>
<td>Admitted to hospital</td>
<td>6 weeks</td>
</tr>
<tr>
<td>Brain MRI</td>
<td>6 1⁄2 weeks</td>
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<tr>
<td>Notified NCJDSU</td>
<td>8 weeks</td>
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<tr>
<td>Seen NCJDSU</td>
<td>9 weeks</td>
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<tr>
<td>Died</td>
<td>11 weeks</td>
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Male 83 (Definite sCJD)

CJD first suggested

- 1<sup>st</sup> seeking advice 3 weeks
- Referred neurologist 4 weeks
- Seen by neurologist 5 weeks
- Admitted to hospital 6 weeks
- Brain MRI 6 ½ weeks
- Notified NCJDSU 8 weeks
- Seen NCJDSU 9 weeks
- Died 11 weeks
67 yr old Female (Definite sCJD)

- 1st saw a doctor: 8 weeks
- Hospital admission: 14 weeks
- Referred neurologist: 14 weeks
- Seen by neurologist: 15 weeks
- Notified to NCJDSU: 16 weeks
- Seen by NCJDSU: 16 weeks
- Died: 20 weeks
67 yr old Female (Definite sCJD)

- 1st saw a doctor: 8 weeks
- Hospital admission: 14 weeks
- Referred neurologist: 14 weeks
- Seen by neurologist: 15 weeks
- Notified to NCJDSU: 16 weeks
- Seen by NCJDSU: 16 weeks
- Died: 20 weeks

Very non-specific early symptoms
No cognitive problems until 12 weeks
67 yr old Female (Definite sCJD)

CJD first suspected

- 1st saw a doctor: 8 weeks
- Hospital admission: 14 weeks
- Referred neurologist: 14 weeks
- Seen by neurologist: 15 weeks
- Notified to NCJDSU: 16 weeks
- Seen by NCJDSU: 16 weeks
- Died: 20 weeks
CLINICAL DIAGNOSIS IS DIFFICULT

• NON-SPECIFIC PRESENTATION

• OTHER DISEASES NEED TO BE EXCLUDED

• NO SIMPLE DIAGNOSTIC TEST

• PASSAGE OF TIME MAY BE IMPORTANT
## SPORADIC CJD in the UK
### MEDIAN TIME IN MONTHS

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COULD THIS TIME BE SHORTER?
COULD THIS TIME BE SHORTER?

PROBABLY NOT AS THINGS STAND
COULD THIS TIME BE SHORTER?

PROBABLY NOT AS THINGS STAND

SIMPLE DIAGNOSTIC TEST WOULD HELP
DIAGNOSIS TAKES TIME

UNCERTAINTY
DIAGNOSIS TAKES TIME

UNCERTAINTY AFFECTS PATIENT FAMILY & FRIENDS
DIAGNOSIS TAKES TIME

UNCERTAINTY AFFECTS PATIENT FAMILY & FRIENDS CLINICAL STAFF
STAFF OF THE NCJDSU
STAFF OF THE NCJDSU
REFERRING DOCTORS
STAFF OF THE NCJDSU
REFERRING DOCTORS
PATIENTS & THEIR FAMILIES