Cause of death in Huntington's disease

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GEORGE HUNTINGTON.

Contents

Abstract

Huntington's disease (HD) is a progressive neurodegenerative autosomal dominant disease characterized by choreatic and hypokinetic movements, disturbed behaviour, and cognitive decline. Death usually results from respiratory complications often caused by dysphagia. Previous studies about the cause of death in HD have shown that the most frequent primary cause of death is pneumonia. The pneumonia is never classified by type, eg community-acquired pneumonia (CAP), hospital-acquired pneumonia (HAP), chemical pneumonia, and aspiration pneumonia. The hypothesis on this study is that the most primary cause of death in HD is aspiration pneumonia. Therefore, date regarding 224 deceased HD patients, collected in the Leiden brainbank, were obtained. A significant difference was found for the patients who definitely/probably died from aspiration pneumonia, and the patients who died from a bacteremic pneumonia (χ^2=.001). No significant difference was found for gender and aspiration (χ^2=.931).

Keywords

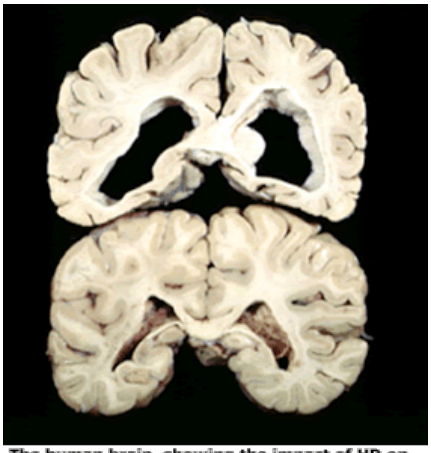
Huntington's disease, cause of death, pneumonia, aspiration, dysphagia.

Chapter 1 Introduction

Huntington's disease (HD) is a progressive neurodegenerative autosomal dominant disease characterized by choreatic and hypokinetic movements, disturbed behaviour, and cognitive decline. George Huntington (1850-1916) was the first to describe these characteristics in 1872, and he said "this disease will devastate families and perplex clinicians who care for them." [1]

History, inheritance and neuropathology

In 1983 HD was linked to the short arm of chromosome 4. In 1993 the gene was localized. HD is caused by a CAG (Cytosine Adenine Guanine) repeat expansion of the *HTT* gene. [2, 3] Since then, predictive testing to HD is available. Having one parent with the disease means a 50% chance to receive the abnormal gene. The Huntington gene shows usually a complete penetrance. [4] The mutant protein huntingtin causes neurodegeneration in the brain, particularly in the caudate nucleus and putamen. The age at onset is on average in the third and fourth decade of life and the disease duration about 15-20 years, with a range from 2-85 years [5-11].



The human brain, showing the impact of HD on brain structure in the basal ganglia region of a person with HD (top) and a normal brain (bottom).
http://kobiljak.msu.edu

Clinical features

Motor symptoms

The most prominent feature in HD, are the choreatic or hypokinetic movements. Choreatic movements are irregular, and unwanted. The movements do not only involve limbs, but also respiratory and buccolingual muscles. Chorea is comparable to dancing (chorea=dancing in Greek). Because of the increasing chorea, patients can have disturbances as: postural instability, dysarthria, dysphagia, dystonia, bradykinesia and hypokinesia. [12] All HD patients will become hypokinetic at the end of the disease. In Juvenile HD (JHD), defined as an age at onset before the age of 20 years, the motor symptoms show more rigidity, oral motor dysfunction, and tremor. [13]

Cognitive symptoms

In HD, cognitive dysfunction is prevalent. Cognitive symptoms can include: abstract thinking, problem solving, attention, and sequencing. [14] But also language aspects are affected. Utterances become increasingly shorter, comprehension difficulties do occur, such as difficulties in understanding and retaining information, slowed processing of information, difficulties in appreciating complex language and failures to appreciate the importance of prosodic changes in others speech. Furthermore, word finding, grammar construction, naming, reading and writing, and initiating speech are involved. [15-19] Cognitive decline deteriorates when the disease progresses, and may lead to problems in relations, communication problems, and misunderstanding by patients or family and caregivers.

Psychiatric symptoms

HD patients establish changes in behaviour. Apathy and impulsivity do occur in HD. Psychiatric symptoms can occur as a first manifestation of HD. [20] HD patients may develop personality

changes and other psychiatric disorders, such as depression. [21] During the course of HD, patients will suffer from dementia.

Prevalence

The prevalence of HD patients in the Netherlands is about 1500 patients, and about 6000 persons who are at risk for developing the disease.

Stages of HD

In HD, different stages are known. The period before onset is called the premanifest period. The disease starts when motor, psychiatric or cognitive symptoms become apparent. In stage 1 of the disease, patients are able to lead an independent life. Chorea can be prominent and psychiatric problems can occur. In stage 2, the patient becomes increasingly dependent. Patients can have physical disability, and chorea increases. In stage 3, the final stage, patients are mostly complete dependent, and is followed by death.

Causes of death in the literature

Previous studies about the cause of death in HD have shown that the most primary cause of death is pneumonia. [22-27]

Edmonds (1966) did a study to HD: dysphagia and death. Fourteen HD patients and 28 controls who died in the hospital were investigated for the cause of death. The immediate causes of death were: bronchopneumonia, asphyxia due to inhalation of food, starvation and cachexia. All HD patients had a history of difficulty with swallowing. In his conclusion Edmonds said that the

increased incidence of respiratory death in HD is probably the result of aspiration of fluids or foods, secondary to the involuntary movements affecting swallowing. [22]

Haines & Conneally (1986) examined causes of death in HD as reported on death certificates. 253 HD death certificates were investigated. In this study pneumonia was the most frequent primary, and primary + contributory cause of death. In this study, pneumonia was twice as likely to be listed after 1960 (51%) than before (=16%). No significant differences with the cause of death pneumonia was found between autopsy and no autopsy groups ($\chi^2 = 4.71$; P>.60). [23]

Lanska et al. (1988)[a] analyzed HD mortality in the United States. The leading cause of death in this study, were pneumonia and heart disease. Another common cause was nutritional deficiencies.[24]

Lanska et al. (1988)[b] did another study to conditions associated with HD at death, a case-control study. In this study 1978 US death certificates from patients with HD were studied. Also in this study, pneumonia, but also choking, nutritional deficiencies and chronic skin ulcers were increased in HD. In his comments, Lanska described that patients with HD develop severe difficulty in swallowing, which promotes choking, aspiration pneumonia and nutritional deficiencies [25]. He also said that because swallowing difficulties and pneumonia contribute to a large fraction of death in may be possible to modify risk factors for aspiration to influence both their morbidity and mortality [25].

Sørensen & Fenger (1992) described the causes of death in patients with HD and in unaffected first degree relatives. 395 HD patients and 282 unaffected sibs were examined from death certificates and compared with the causes of death in the general population. In this study, pneumonia was the leading cause of death for the HD patients. [26]

Baliko et al. (2004) studied 96 families with HD and investigated the frequency of suicide in this Hungarian HD population, compared to the general population. They concluded that suicide among

HD patients is more common than in the general population. No other causes of death were described in this study. [27]

The above mentioned studies demonstrates that the cause of death pneumonia is the leading cause in HD. Some studies, e.g. Edmonds (1966) and Lanska et al. (1988)[b] linked this cause of death directly to dysphagia and described that the HD patients had a history with swallowing difficulties, and the risk of aspiration pneumonia when having difficulty with swallowing. No study examined the cause of death pneumonia focusing on the type of pneumonia, which is really a necessary study, because than it is possible to, as Lanska et al. (1988)[b] said, modify risk factors for aspiration to influence both their morbidity and mortality.

Chapter 2 Thesis

During the course of HD, patients will develop dysphagia. Death usually results from respiratory complications often caused by dysphagia [22-27]. Previous studies into the causes of death in HD have shown that the most frequent primary cause of death is pneumonia [22-27]. Pneumonia can be classified to different types, such as community-acquired pneumonia (CAP), hospital-acquired pneumonia (HAP), chemical pneumonia, and aspiration pneumonia. The studies in HD however, did not classify the pneumonia by type. Therefore, it is not precisely known by which type of pneumonia HD patients die. Because most HD patients have dysphagia, especially in the advanced stage of the disease, it is most likely that aspiration would be the cause of the fatal pneumonia. It is important to distinguish the different types of pneumonia, because when aspiration pneumonia is the primary cause of death, intervention studies to dysphagia can be set up to prevent aspiration pneumonia. The hypothesis of this study is that is the primary cause of death in HD is aspiration pneumonia.

Aims of the study

The aim of the present study is to find out if aspiration pneumonia is the primary cause of death in HD.

The first part of this thesis is a description of the patients and methods we used in this study. Then, we will describe the results, and we will analyze these results. In the discussion part, the results of this thesis will be put into a broader perspective and we will give recommendations for further research.

Patients and Methods

For this study, the documents of deceased HD patients from the Leiden University Medical Center (LUMC) brainbank in the Netherlands are used. Data of 224 patients are available from 1964 till 2010. The diagnosis of HD is mostly confirmed by post-mortem pathological investigation, and for present generation since 1993 some are confirmed by DNA analysis. The primary cause of death is mostly based on clinical criteria, and if available on the total body autopsy.

From all files the following information was collected: DNA confirmation, gender, year of birth, year of death, age at onset, location of death, naturally death, autopsy of the body, described primary cause of death, described underlying causes of death, reverse pneumonias, other aspects. (App. A). When the primary cause of death was not described in the files, we have tried to discover whether there has been aspiration pneumonia when these patients deceased. Therefore, features were investigated, notably the following.

1. Is it described that the patient suffered from dysphagia.
2. Is it described that the patient suffered from repeated pneumonias.
3. Is it described what were the contents of the pulmones were.

Because suffocation is possibly directly related to aspiration, we also investigated if patients suffocated when eating.

Statistical analysis

To find out if our hypothesis: the most primary cause of death in HD is aspiration pneumonia, is true, the data will be analyzed using the Statistical Package for Social Sciences (SPSS 18.0). Causes of death will be numerically coded and will be entered in the computer file. The cause of death

pneumonia will be numerically coded to the type of the pneumonia and entered in the computer file. Chi-square distribution will be used to compare the different variables.

Chapter 3 Results and analyses of results

Patients.

The mean age at death for the patients was 55.8 years (SD 11.9 years) for males and 60.2 years (SD 13.9 years) for females (Table 1, 2). Nine files were excluded because of lacking data. The distribution for gender was uniform for all cases (Figure a). There was also an uniform distribution for gender and patients who deceased from pneumonia (Figure b).

Causes of death.

The described primary causes of death from 215 HD patients were grouped into 10 main groups, as shown in Table 3. In the Leiden HD brainbank, the most frequent, described primary cause of death was pneumonia (55.1%). This cause pneumonia was definitely more prevalent than the other causes of death. All described primary causes of death in HD were: pneumonia, 55.1% (n=81); suffocation, 4.1% (n=6); pulmonary embolism, 4.1% (n=6); cachexia, 7.5% (n=11); cardiac causes, 10.9% (n=16); other neurological disease, 2.0% (n=3); shock and sepsis, 4.8% (n=7); suicide, 1.4% (n=2); euthanasia, 3.4% (n=5); other causes, 6.8% (n=10).

In 34.4% (n=77) cases no primary cause of death was given. In 19.5% (n=15) of this group the clinical information reveiled dysphagia during the last period of their life, 10.4% (n=8) of the patients had suffered from repeated pneumonias, and in 5.2% (n=4) the autopsy report gave a description of giant cells, edema, pus, infiltrate, red lobes and voluminous contents in the bronchi and the pulmones. (Table 4, Table 5, Table 6).

In 53.1% (n=43) of all the patients with primary cause of death pneumonia, autopsy was performed (Table 7). To find out if aspiration was the cause of the pneumonia, the contents of the pulmones

were investigated. The autopsy had shown that in 42.1%, the contents of the pulmones were: gastric contents, food, and fluid in the lungs or giant cells. A giant cell is mostly a macrophage, which exists when foreign bodies, such as food, gastric contents or drink, enter the pulmones. Therefore, these patients deceased from aspiration pneumonia. In 44.7% the contents of the pulmones were: edema, pus, infiltrate or red and voluminous lungs. These patients probably died from aspiration pneumonia. In 13.2% the contents of the pulmones were: staphylococcus aureus, streptococcus viridans, candida albicans, klebsiella and the proteus vulgaris. Therefore, these patients deceased from a bacteremic pneumonia (Table 8).

A significant difference was found for the patients who definitely/ probably died from aspiration pneumonia, and the patients who died from a bacteremic pneumonia (χ^2=.001) (Table 9). For patients with the described primary cause of death pneumonia, no significant difference was found for the gender and aspiration (χ^2=.931). Therefore, both, males and females, have an equal opportunity to aspirate and to decease from aspiration pneumonia (Table 10).

The described primary cause of death suffocation was performed in 4.1% (n=6) of all patients. From this group of patients, 66.7% (n=4) aspirated food. (Table 14). 16.7% (n=1) of the patients did not aspirate, but suffocated in the sheets of the bed, and the other 16.7% (n=1) the cause for suffocation was unknown.

Chapter 4 Discussion and recommendation

Discussion

On investigating the files of the deceased HD patients, a large proportion of the files (77, = 34.4%) did not contain the primary cause of death. Therefore, it seems that the files of the deceased HD patients are relatively inaccurate in recording causes of death. Other studies to causes of death have also shown an inaccuracy rate. Haines et al. (1986) had an overall rate of 66%. [23] Alderson et al. (1967) found an overall accuracy rate of 61%. [28] Thus, our overall rate of 65.6% is not unusual. It is likely that patients without a described primary cause of death, deceased from aspiration pneumonia. Some of these patients were described with suffering form dysphagia, and repeated pneumonias in their last period of their life.

In 34.6% of the patients who deceased with primary cause of death pneumonia, it was described that patients suffered from dysphagia during morbidity. In 25.6% of these patients, it was described that these patients had repeated pneumonias. Because of these issues, these patients will have a higher risk of developing aspiration pneumonia. In 40.7% of these files, it was described that patients that patients were cachectic, dehydrated or both, when they deceased. Therefore, these patients will also have a higher risk of developing both, aspiration or bacteremic pneumonia. Previous studies to pneumonia hospitalizations and mortality, and the role of chronic conditions, health behaviors, and nutritional status have shown found that these factors increases the risk of pneumonia. [29, 30, 31] It is possible that patients with the streptococcus, deceased from a Community Acquired Pneumonia (CAP), because these bacteria remains an important cause of fatal CAP. [32] When patients have a reduced resistance, it is likely that patients deceased from a klebsiella, candida or staphylococcal pneumonia.

However, there is a potential bias in this study. Because, when patients deceased from an bacteremic pneumonia, in most cases the culture consisted the staphylococcus aureus, klebsiella and candida albicans. These bacteria and fungi exists on the skin and the mucus. When patients are aspirating their saliva, it seems very likely, that patients aspirate these bacteria and develop pneumonia, especially patients in the last stage of HD, who are mostly cachectic, in bad condition and with a poor resistance. Or, when patients having bad teeth, or an unhealthy condition of the mouth, the risk on developing pneumonia increases.

Another interesting point is, that it seems that autopsies did not increase the accuracy of reporting aspiration pneumonia. In 39.5% of the patients who deceased from pneumonia diagnosed by autopsy, the pathologists described edema, pus, infiltrate etc. in the lungs, but no cultures were taken, and therefore, the precise cause is unknown. However, it is very likely that the patients with the contents of the pulmones: edema, pus, infiltrate or red and voluminous lungs died from aspiration pneumonia. Because HD patients in the last stage of the disease have developed dysphagia, these patients are unable to chew and swallow solid food. Therefore, it is impossible to find gastric contents or food in the lungs. HD patients in the last stage of the disease mostly have liquid diets. Therefore, it is likely to find edema or infiltrate in the lungs.

Another important cause of death related to aspiration, was suffocation. In our experience, dysphagia, and aspiration is a very frightening issue for HD patients. Some patients refuse to eat solid food, because of this issue. These patients want to decrease their chance to suffocate. Other patients would like to stay eating solid foods, even when the swallowing problems became very serious. When they were advised to change their meals into ground food, or a complete liquid diet they refused, and were clear about taking the risk to suffocate.

To conclude, our data suggest that aspiration pneumonia is the primary cause of death in HD. However, because the documents of the diseases HD patients are relatively inaccurate, and because

it seems there is no structured way to document notable information when patients die with primary cause pneumonia, the outcomes are in some way incomplete.

Recommendation

We suggest that a structured document have to be developed to register information about swallowing, dysphagia, pneumonia in patients with HD.We think, it is also important to describe if patients have had any form of therapy during live, especially dysphagia-therapy or breathing-therapy.

Because aspiration pneumonia is the most primary cause of death in HD, we also suggest that intervention studies to prevent dysphagia will be set up. Therefore, it is needed that the prevalence of dysphagia in HD is known, and the exact dysphagia problems are known. We already initiated a study, and are developing the Huntington's Disease Dysphagia Scale to determine the prevalence of dysphagia in the different stages of HD.

Summary / samenvatting

Huntington's disease is a progressive neurodegenerative autosomal dominant disease characterized by choreatic and hypokinetic movements, disturbed behaviour, and cognitive decline. During the course of HD, many patients will develop dysphagia. Death usually results from respiratory complications often caused by dysphagia. In this study, we described the primary causes of death in HD focusing on pneumonia. Because swallowing difficulties do occur in patients with HD, and because of the serious consequences of dysphagia, we expected to find that the primary cause of death in HD patients is aspiration pneumonia. We did find a significant difference for the patients who definitely/ probably died from aspiration pneumonia, and the patients who died from a bacteremic pneumonia (χ^2=.001). Our data suggest, that aspiration pneumonia is the primary cause of death in HD. However, because the documents of the diseases HD patients were relatively inaccurate, and because it seems that there was no structured way to document notable information when patients die, the outcomes are in some way incomplete. We suggest that a structured document will be developed to register notable information from HD patients, about swallowing, dysphagia, pneumonia etc. during their morbidity and mortality. Another suggestion we appointed was, that it would be important to start intervention studies to prevent dysphagia. Therefore, it is needed that the prevalence of dysphagia in HD is known, and the exact dysphagia problems are known.

Samenvatting

De ziekte van Huntington is een progressieve, neurodegeneratieve, autosomale dominante aandoening, die gekarakteriseerd wordt door choreatische bewegingen, veranderingen in gedrag, en cognitieve achteruitgang. Gedurende het verloop van de ziekte ontwikkelen patiënten dysfagie.

Patiënten komen vaak te overlijden aan een pneumonie, meestal ten gevolge van dysfagie. In deze studie werd gekeken naar de doodsoorzaken bij de ziekte van Huntington, gericht op pneumonie. Omdat patiënten vaak dysfagie hebben, en omdat dysfagie ernstige gevolgen kan hebben, hadden we de verwachting in deze studie te bevestigen, dat de eerste doodsoorzaak bij de ziekte van Huntington aspiratie pneumonie is. We vonden inderdaad een significant verschil voor de patiënten die absoluut, en hoogstwaarschijnlijk aan een aspiratie pneumonie zijn overleden, en de patiënten die overleden zijn aan een bacteriele pneumonie. Onze uitkomst suggereert, dat aspiratie pneumonie de eerste doodsoorzaak is bij de ziekte van Huntington. Echter, de documenten van de overleden Huntingtonpatienten waren vrij incompleet, en er was geen gestructureerde manier van documenteren. Derhalve, bevelen wij aan dat er een gestructureerde manier van documenteren ontwikkeld wordt met daarin alle relevante informatie. Verder bevelen we aan, dat er interventie studies moeten worden opgezet om dysfagie te voorkomen.

References

1. Huntington G: On chorea. Med Surg Rep 1872; 26: 320-321.
2. Gusella JF, Wexler NS, Conneally PM et al.: A polymorphic DNA marker genetically linked to Huntington's disease. Nature 1983; 306:234-238.
3. Huntington's Disease Collaborative Research Group: A novel gene containing a trinucleotide repeat that is expanding and unstable on Huntington's disease chromosomes. Cell 1993; 72:971-983.
4. Walker FO: Huntington's disease. Lancet 2003; 369:218-223.
5. Bates G, Harper PS, Jones L: Huntington's Disease. Third edition ed. New York: Oxford University Press, 2002.
6. Albin RL, Reiner A, Anderson KD, et al.: Preferential loss of strato-external pallidal projection neurons in presymptomatic Huntington's disease. Ann Neurol 1992; 31 (4): 425-430.
7. Albin RL: Selective neurodegeneration in Huntington's disease. Ann Neurol 1995; 38: 835-836.
8. Cardoso F, Seppi K, Mair KJ, Wenning GK, Poewe W: Seminar on choreas. Lancet Neurol 2006; 5: 589-602.
9. Roos RAC, Hermans J, Vegter-van der Vlis M, van Ommen GJ, Bruyn GW: Duration of illness in Huntington's disease is not related to age at onset. J Neurol Neurosurg Psychiatry 1993; 56: 98-100.
10. Quarrel O: Huntington's disease: the facts. Oxford University Press, 1999.
11. Vonsattel JP, Myers RH, Stevens TJ, Ferrante RJ, Bird ED, Richardson EP Jr: Neuropathological classification of Huntington's disease. J Neuropathol Exp Neurol 1985; 44(6): 559-577.

12. Vonsattel JP: Neuropathology of Huntington's disease. In: Joseph AB, Young RR, eds. Movements disorders in neurology and neuropsychiatry. Cambridge (UK): Blackwell Scientific, 1992, pp 186-194.

13. Nance MA, Myers RH: Juvenile onset Huntington's disease - clinical and reseacrh perspectives. Ment Retard Dev Disabil Res Rev 2001; 7:153-157.

14. Craufurd D, Snowden JS: Neuropsychological and neuropsychiatric aspects of Huntington's disease. In: Bates GP, Harper PS, Jones LJ (eds.): Huntington's disease. Third edition ed. New York: oxford University Press, pp 62-94, 2002.

15. Podoll K, Caspary P, Lange HW, Noth J: Language functions in Huntington's disease. Brain 1988; 111:1475-503.

16. Gordon WP, Illes J: Neurolinguistic characteristics of language production in Huntington's disease: a preliminary report. Brain and Language 1987; 31:1-10.

17. Jensen AM, Chenery HJ, Copland DA: A comparison of picture description abilities in individuals with vascular subcortical lesions and Huntington's disease. Journal of Communication disorders 2006; 39(1):62-77.

18. Frank EM, McDade HL, Scott WK: Naming in dementia secondary to Parkinson's, Huntington's, and Alzheimer's diseases. Journal of Communication disorders 1996; 29(3): 183-97.

19. Wallesch CW, Fehrenbach RA: On the neurolinguistic nature of language abnormalities in Huntington's disease. Journal of Neurology, Neurosurgery and Psychiatry 1988; 51(3): 367-73.

20. Paulsen JS, Langbehn DR, Stout JC, et al.: The predict-HD investigators and coordinators of the Huntington Study Group: Detection of Huntington's disease decades before diagnosis: the Predict-HD study. J Neurol Neurosurg Psychiatry 2008; 79: 874-880.

21. Paulsen JS, Ready RE, Hamilton JM, Mega MS, Cummings JL: Neuropsychiatric aspects of Huntington's disease. J Neurol Neurosurg Psychiatry 2001; 71: 310-314.

22. Edmonds C: Huntington's chorea, dysphagia and death. Med J Aust 1966; 53: 273-274.

23. Haines JL and Conneally PM: Causes of death in Huntington's disease as reported on death certificates. Genetic Epidemiology 1986; 3:417-423.
24. Lanska DJ, Lavine L, Lanska MJ, Schoenberg BS: Huntington's disease mortality in the United States. Neurology 1988[a]; 38: 769.
25. Lanska DJ, Lanska MJ, Lavine L, Schoenberg BS: Conditions associated with Huntington's Disease and death. A case control study. Archives Neurology 1988[b] ; 45(8):878-880.
26. Sorensen & Fenger: Causes of death in patients with Huntington's disease and in unaffected first degree relatives. Journal of Medical Genetics 1992; 29: 911-914.
27. Baliko L, Csala B, Czopf J: Suicide in Hungarian Huntington's disease patients. Neuroepidemiology 2004; 23:258-260.
28. Alderson MR, Meade TW: Accuracy of diagnosis on death certificated compared with that in hospital records. Br J Prev Soc Med 1967; 21: 22-29.
29. LaCroix AZ, lipson S, Miles T, White L: Prospective study of pneumonia hospitalizations and mortality of U.S. older people: the role of chronic conditions, health behaviors and nutritional status. Pub Health Rep 1989, 104:350-369.
30. Fedson DS, Baldwin JA: Previous hospital care as a risk factor for pneumonia. Implications for immunization with pneumococcal vaccine. JAMA 1982, 246: 1989-1995.
31. Muder RR: Pneumonia in residents of long-term care facilities: epidemiology, etiology, management, and prevention. Am J Med 1998, 105: 319-330.
32. Örtqvist Å, Kalin M, Julander I, Mufson MA: Deaths in bacteremic pneumococcal pneumonia. Chest 1993; 103: 710-716.

Tables

Table 1: Frequency for gender

Gender

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	male	111	49,6	51,6	51,6
	female	104	46,4	48,4	100,0
	Total	215	96,0	100,0	
Missing	System	9	4,0		
Total		224	100,0		

Table 2: Mean age for gender

Gender	Mean	N	Std. Deviation
male	55,8108	111	11,90837
female	60,2019	104	13,92029
Total	57,9349	215	13,07653

Legend: N, Number of subjects; Std. Deviation, Standard Deviation

Table 3: Described immediate causes of death in HD

Cause1

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	pneumonia	81	36,2	55,1	55,1
	suffocation	6	2,7	4,1	59,2
	lungemobolus	6	2,7	4,1	63,3
	cachexie	11	4,9	7,5	70,7
	cardial	16	7,1	10,9	81,6
	neurological	3	1,3	2,0	83,7
	shock/sepsis	7	3,1	4,8	88,4
	suicide	2	,9	1,4	89,8
	euthanasie	5	2,2	3,4	93,2
	other	10	4,5	6,8	100,0
	Total	147	65,6	100,0	
Missing	System	77	34,4		
Total		224	100,0		

Table 4: Unknown cause of death: described dysphagia

Dysphagia					
	Frequency	Percent	Valid Percent	Cumulative Percent	
Valid	yes	15	19,5	100,0	100,0
Missing	System	62	80,5		
Total	77	100,0			

Table 5: Unknown cause of death: described repeated pneumonias

Reversedpneumonia					
	Frequency	Percent	Valid Percent	Cumulative Percent	
Valid	yes	8	10,4	10,4	10,4
	unknown	69	89,6	89,6	100,0
	Total	77	100,0	100,0	

Table 6: Unknown cause of death: described contents of the pulmones

Pulmones					
	Frequency	Percent	Valid Percent	Cumulative Percent	
Valid	giant cells	2	2,6	50,0	50,0
	edema/pus/mucus/ infiltrate/red lobes/ voluminous	2	2,6	50,0	100,0
	Total	4	5,2	100,0	
Missing	System	73	94,8		
Total	77	100,0			

Table 7: Cause of death pneumonia: autopsy performed

Autopsy					
	Frequency	Percent	Valid Percent	Cumulative Percent	
Valid	yes	43	53,1	53,1	53,1
	no	38	46,9	46,9	100,0
	Total	81	100,0	100,0	

Table 8: Cause of death pneumonia: contents of the pulmones

Pulmones					
	Frequency	Percent	Valid Percent	Cumulative Percent	
Valid	gastric contents	6	14,0	15,8	15,8
	food/fluid	6	14,0	15,8	31,6
	giant cells	4	9,3	10,5	42,1
	edema/pus/mucus/ infiltrate/red lobes/ voluminous	17	39,5	44,7	86,8
	influenza/virus/other bacteries	5	11,6	13,2	100,0
	Total	38	88,4	100,0	
Missing	System	5	11,6		
Total	43	100,0			

Table 9: Cause of death pneumonia: chi square distribution for aspiration pneumonia yes/probably/no

Aspiration			
	Observed N	Expected N	Residual
yes	19	16,0	3,0
probalby	25	16,0	9,0
no	4	16,0	-12,0
Total	48		

Test Statistics	
	Aspiration
Chi-square	14,625[a]
df	2
Asymp. Sig.	0,001
a. 0 cells (,0%) have expected frequencies less than 5. The minimum expected cell frequency is 16,0.	

Legend: N, Number of subject;. df, degrees of freedom; Asymp. Sig, Asymptotic Significance

Table 10: Cause of death pneumonia: chi square distribution for aspiration pneumonia and gender

Aspiration * Gender Crosstabulation				
Count				
	Gender	Total		
	male	female		
Aspiration	yes	10	9	19
	probalby	13	12	25
	no	2	2	4
Total	25	23	48	

Chi-Square Tests			
	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	,009[a]	2	0,995
Likelihood Ratio	0,009	2	0,995
Linear-by-Linear Association	0,008	1	0,931
N of Valid Cases	48		
a. 2 cells (33,3%) have expected count less than 5. The minimum expected count is 1,92.			

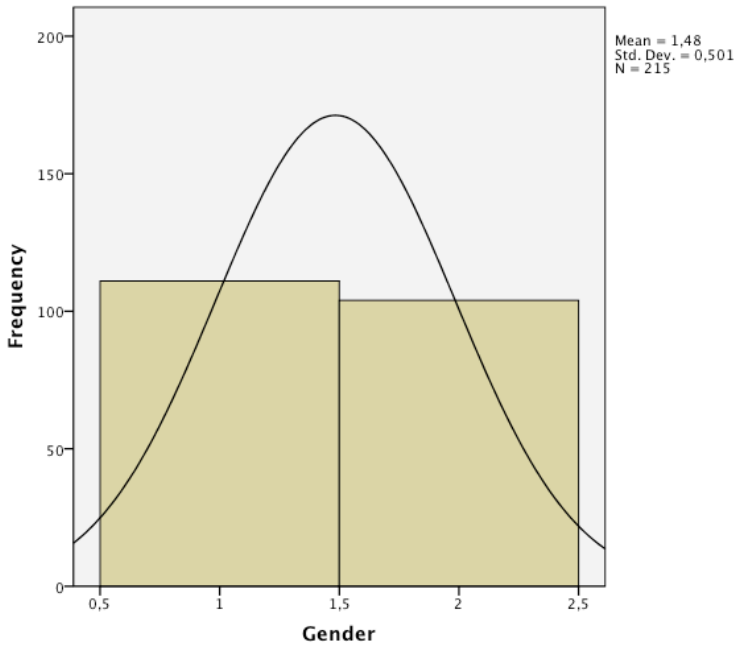
Legend: df, degrees of freedom; Asymp. Sig, Asymptotic Significance; N, Number of subjects

Table 11: Cause of death suffocation

Aspiration					
	Frequency	Percent	Valid Percent	Cumulative Percent	
Valid	yes	4	66,7	100,0	100,0
Missing	System	2	33,3		
Total	6	100,0			

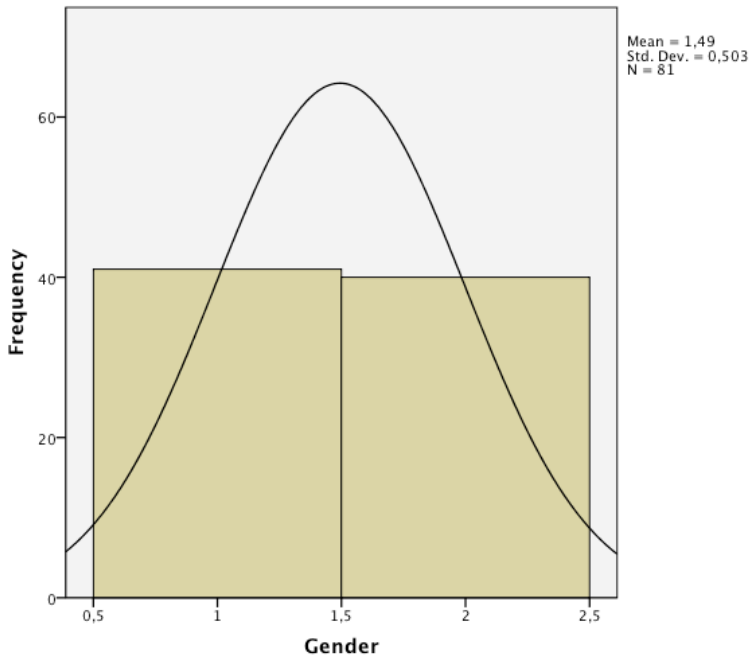
Figures

Figure a: ***Distribution for gender in all cases***



Legend: Std. Dev, Standard Deviation; N, Number of patients

Figure B: Distribution for gender in cases with patients with primary cause of death pneumonia



Legend: Std. Dev, Standard Deviation; N, Number of patients

Appendix A

Investigation causes of death in HD patients. Brainbank LUMC.

Patient	Genetisch bepaald	M/F	Geboortejaar	Jaar overlijden	Age onset	Locatie overlijden	Natuurlijke dood	Autopsie	Doodsoorzaak 1	Doodsoorzaak 2,...	Recidiverende pneumonien	Opvallendheden
1												
2												
3												
4												
5												
6												
7												
8												
9												
10												

Legend: M/F, Male/Female

Curriculum vitae

Name: Heemskerk- van den Berg, Willemien Antoinette
First name: Anne-Wil
Day of birth: 19 February 1979

Positions and employment
2008 - Utrecht University: master Clinical Language and Hearing Science
2007 - 2008 Utrecht University: premaster Clinical Language and Hearing Science
1998 – 2002 Rotterdam University: bachelor Speech & Language Therapy

2009 - Dept neurology, researcher Leiden University Medical Center
2009 - Lead facilitator Working Group Speech and Language Therapy on behalf of Standards of Care, European Network on Huntington's Disease (EHDN)
2008 – Participant Working Group EHDN Functional Abilities
2007 – Participant Working Group EHDN Symptomatic Research and Therapy
2003 – Speech & Language Therapist Huntington Centre Topaz Overduin, Katwijk
2003 – 2008 Speech & Language Therapist Diaconessenhuis, Leiden
2003 – 2004 Speech & Language Therapist Nursinghome Bosbeek, Sint Jacob, Heemstede
2002 – 2003 Teacher, subject: presentation skills, Rotterdam University
2001 – 2002 Freelance teacher Volksuniversiteit, Amsterdam

Courses
2005 Implementation fluid and nutrition policy in nursinghomes, Zoetermeer
2004 Swallowing disorders in neurologic diseases, Amsterdam
2004 Speech & Language Therapy in Parkinson's disease, Heerlen
2002 Dutch sign language, Effatha, Zoetermeer.

Congresses / seminars / symposium
2009 congress: World Congress on Huntington's Disease. Vancouver, Canada
2009 symposium: The last phase in life, the client central. Dutch Huntington Association. Ede
2008 congress: European Huntington Disease Network. Lisbon
2007 congress: World Congress on Huntington's Disease. Dresden
2007 seminar: The larynxcarcinoom in the Netherlands. Zoetermeer
2007 seminar: Evidence based practice. Ede
2005 seminar: Barriers in Huntington's disease. Dutch Huntington Association. Ede
2005 congress: World Congress on Huntington's Disease. Manchester UK
2005 symposium: Communication and nutrition in Huntington's disease. Dutch Huntington Association. Utrecht
2004 congress: Crossroads in aphasia rehabilitation. Rotterdam
2004 symposium: Facial palsy and then..... LUMC Leiden

Oral presentations
2009 Speech and Language Therapy in Huntington's Disease. World Congress on Huntington's Disease. Vancouver, Canada

2009 Dysarthria and Language in Huntington's disease. EHDN Working group Speech & Language Therapy. Leiden
2009 Nutrition and dysphagia in the last phase in Huntington's disease. Symposium: The last phase in life, the client central. Dutch Huntington Association. Ede
2005 – 2006 Dysphagia in Huntington's disease. Huntington Centre Topaz Overduin. Katwijk
2005 Speech & Language Therapy in Huntington's disease. Dutch Huntington Association. Utrecht
2005 Communication, nutrition and ethical dilemma's in Huntington's disease. Dutch Huntington Association. Ede

Poster presentations
2009 Matheson KY., Simpson SA., Heemskerk AW., Hamilton A. Speech and Language Therapy in Huntington's Disease: literature review. World Congress on Huntington's Disease Vancouver, Canada
2008 Heemskerk AW. Speaking in fragments. European Congress on Huntington's Disease. Lisbon, Portugal
2007 Heemskerk AW. About 80% of the speech therapists are not familiar with the right treatment for HD-patients. World Congress on Huntington's Disease. Dresden, Germany
2005 Claus H., Liem L., Heemskerk AW., Bunnig K. Examples of multidisciplinary treatment in a residential setting. World Congress on Huntington's Disease. Manchester, UK