Hereditary Multiple Exostosis and Pain

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Abstract: This study was undertaken to characterize pain in individuals with hereditary multiple exostosis (HME). Two hundred ninety-three patients with HME completed a questionnaire designed to assess pain as well as its impact on their life. Eighty-four percent of participants reported having pain, indicating that pain is a real problem in HME. Of those with pain, 55.1% had generalized pain. Two factors were found to be associated with pain outcome: HME-related complications and surgery. Individuals who had HME-related complications were five times more likely to have pain, while those who had surgery were 3.8 more likely to have pain. No differences were found between males and females with respect to pain, surgery, or HME-related complications. The results of this study indicate that the number of individuals with HME who have pain has been underestimated and that pain is a problem that must be addressed when caring for individuals with HME.

Key Words: hereditary multiple exostosis, pain, exostoses, osteochondromas, support group

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Hereditary multiple exostosis (HME) is a skeletal disorder characterized by the presence of numerous bony outgrowths (osteochondromas or exostoses) that develop next to the growth plates of all the long bones.[1] HME is an autosomal dominant condition with a prevalence of approximately 1 in 50,000 individuals.[2] It has been estimated that 66% to 90% of individuals with HME have a family history of the condition.[1,2]

The most striking feature of HME is the numerous cartilage-capped exostoses, which are associated with the all of the skeleton. In addition to having exostoses, individuals with HME can have other skeletal and nonskeletal complications, including limb discrepancy, bony deformities, mild short stature, blood vessel compression, peripheral nerve compression, and spinal cord compression.[1,3–5] The most severe complication of HME is the malignant transformation of an exostosis. Recent studies estimate the lifetime risk of malignant degeneration to be about 2% for individuals with HME.[2,5] Many individuals with HME undergo surgery as a result of HME-related complications, with 66% to 74% of individuals undergoing at least one operation for their exostoses and the average number of surgeries being two to three.[2,5]

There is little information in the current literature concerning pain in individuals with HME. While the presence of pain has been documented in HME, its overall severity and effects on individuals have not been thoroughly assessed. This study was undertaken to characterize pain in individuals with HME to determine what proportion of individuals with HME have pain, whether the pain is isolated or generalized, whether there are differences in pain between genders and age groups, and to what extent the pain in individuals with HME is associated with surgery for HME-related complications.

MATERIALS AND METHODS

A four-part questionnaire was designed for this study. Part 1 was a demographic section. Part 2 addressed the participant's HME-related medical history and was partly based on the data collection sheet used in the study by Wicklund et al.[5] Part 3 addressed pain and assessed whether the participant had pain and if and how pain interferes with his or her life, using numeric rating scales and a pain drawing.[6–9] Part 4 was a family history section. The complete study questionnaire is in Appendix A.

Questionnaires were mailed to 755 individuals with HME, 700 ascertained through the MHE Coalition and 55 through the Shriners Hospital for Children, Houston. For young children, the questionnaire was completed with the help of a parent or family member. A total of 293 questionnaires were returned (39% response rate). Of the 293 participants, 38 (13%) were ascertained through the Shriners Hospital and 255 (87%) through the MHE Coalition. All participants included in the study indicated that they had a diagnosis of HME and were known to have multiple exostoses. All information was kept confidential and analyzed using unique identifiers.

Data were analyzed using the SPSS statistical analysis software program version 10.0 (SPSS Inc, Chicago, IL). Frequencies were calculated for all variables and testing for statistical significance was performed using chi-square

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hypothesis testing, *t* test, and logistic regression. Statistical significance was considered at $P \leq 0.05$. This study was approved by the Institutional Review Board of the University of Texas Health Science Center-Houston.

RESULTS

Demographics

Of the participants, 132 (45.1%) were male and 161 (54.9%) were female. The mean age was 28.2 years. Seventy-six percent of the participants indicated that they were members of the MHE Coalition (not all participants ascertained through the MHE Coalition were members of the support group); of those, 12.0% are active on a daily basis, 19.8% are active on a weekly to monthly basis, 20.3% are active every few months, 4.6% are active on a yearly basis, and 43.4% are non-active members (Table 1). Activity in the support group is defined as e-mailing or contacting other members of the support group, visiting the website, and receiving the newsletter.

HME-Related Medical History

The mean age at first exostosis was 4 years and the mean age at diagnosis of HME was 7 years. Eighty percent of participants reported having surgery for their exostoses, with a median of two surgeries (range 0–45). Seventy-four percent of participants reported having complications secondary to having exostoses, with most having compression of tendons, muscles, ligaments, or nerves. Thirty-five percent of participants reported having other complications such as pain when breathing, bone deformities, and spinal cord compression. Twelve individuals (4.1%) reported malignant degeneration of an exostosis, with the most common location being the pelvis (Table 2). Eight individuals reported having a chondrosarcoma, three had an osteosarcoma, and one had a Ewing sarcoma.

Pain

Eighty-four percent of the participants reported having pain (Tables 3 and 4). Of those reporting pain, 55.1% were determined to have generalized pain and 44.9% to have isolated pain. A participant was determined to have generalized pain if he or she described having pain throughout the body (multiple locations in different parts and sides of the body) and not localized to areas where he or she had exostoses. Questions about the location of pain and the location of exostoses as well as the pain drawing were used to determine whether an individual has generalized pain. When asked how frequently they experience pain in an average month, 45.3% reported having pain daily, 12.2% 20 to 29 days per month, 14.3% 10 to 19 days per month, and 28.2% 1 to 9 days per month. Twenty participants (0.07%) reported being on disability or unable to work due to pain. For those who were able to work, the average number of days of work missed in a month was 1 day. Eighty-seven percent of participants with

TABLE 1. Demographics

	No. (%)
Ascertainment (n = 293)	
Shriners Hospital	38 (13.0%)
MHE Coalition	255 (87.0%)
Sex (n = 293)	
Male	132 (45.1%)
Female	161 (54.9%)
Age (years) (n = 290)	
0–10	62 (21.4%)
11–20	60 (20.7%)
21–30	41 (14.1%)
31–40	52 (17.9%)
41–50	31 (10.7%)
51–60	30 (10.3%)
>60	14 (4.8%)
Support Group Membership (n = 292)	
Member	221 (75.7%)
Non-Member	71 (24.3%)
Frequency of Support Group Participation (n = 218)	
Daily	26 (12.0%)
Weekly	34 (15.7%)
Monthly	9 (4.1%)
Every few months	44 (20.3%)
Once a year	10 (4.6%)
Not active	95 (43.3%)

TABLE 2. HME-Related Medical History

	No. (%)
Surgery (n = 293)	
Yes	235 (80.2%)
No	58 (19.8%)
Number of Surgeries (n = 293)	
0	58 (19.8%)
1–5	150 (51.2%)
6–10	50 (17.1%)
11–15	18 (6.1%)
16–20	5 (1.7%)
>20	12 (4.1%)
HME-Related Complications (n = 293)	
Yes	217 (74.1%)
No	76 (25.9%)
Compression of Tendons, Muscles, Ligaments (n = 293)	
Yes	188 (64.2%)
No	105 (35.8%)
Compression of Blood Vessels (n = 293)	
Yes	49 (16.7%)
No	244 (83.3%)
Compression of Nerves (n = 293)	
Yes	127 (43.3%)
No	166 (56.7%)
Other Complications* (n = 293)	
Yes	102 (34.8%)
No	191 (65.2%)
Malignant Degeneration of an Exostosis (n = 293)	
Yes	12 (4.1%)
No	281 (95.9%)

*Complications such as pain when breathing due to an exostosis, spinal cord compression, and bone deformities.

TABLE 3. Pain Ratings*

Pain Rating	Current Pain Number (%)	Average Pain Number (%)
None (rating of 0)	59 (24.1%)	1 (0.4%)
Mild (rating of 1–3)	73 (29.8%)	56 (23.2%)
Moderate (rating of 4–6)	64 (26.1%)	118 (49.0%)
Severe (rating of 7–10)	49 (20.0%)	66 (27.3%)

*Data only for individuals with pain.

pain have had at least one surgery as a result of having exostoses. Seventy-four percent of participants reported taking some type of medication for their pain, with 17% taking a prescription narcotic, 26% taking non-narcotic prescription medication, and 57% taking over-the-counter pain medication. Appendix B lists the medications taken by participants. Fifteen percent of participants who reported pain had seen a pain specialist.

Chi-square testing was used to determine which variables were associated with pain, and four were found to be significantly associated: age, HME-related complications, surgery, and support group membership (Table 5). Significantly fewer individuals under the age of 11 years experienced pain ($P = 0.003$). To adjust for this age effect, all participants under the age of 11 were excluded so that further analysis could be performed on a more homogenous group. Chi-square testing was then repeated on all variables. Significantly more individuals with pain had HME-related complications ($P < 0.001$), specifically compression of tendons, muscles, or ligaments ($P < 0.001$) and compression of nerves ($P < 0.001$). A significant association was found for surgery and pain, with more individuals with pain having had surgery ($P < 0.001$). Membership in the MHE Coalition was the fourth significant variable found to be associated with pain ($P = 0.023$). Logistic regression was used to determine which factors were associated with pain outcome and to calculate risk ratios for these factors. All variables, including age, were used in this analysis. Only two factors were found: HME-related complications ($P < 0.001$) and surgery ($P = 0.001$). Individuals with HME-related complications were 5 (95% confidence interval [CI] 2.3–11.2) times more like to have pain, while those who had surgery were 3.8 (95% CI 1.7–8.6) times more likely to have pain. Logistic regression was also used to determine which factors were associated with surgical outcomes. Four factors were identified: HME-related complications ($P < 0.001$), interference with sleep ($P < 0.001$), age ($P = 0.008$), and age at first exostosis ($P < 0.001$). Participants with HME-related complications were 3.1 (95% CI 1.4–6.7) times more likely to have surgery. Participants who reported having more severe interference with sleep due to pain were 2.5 (95% CI 1.4–5.0) times more likely to have surgery, while older participants and participants with a younger age at first exostosis were 1.7 (95% CI 1.3–2.5) times and 2.1 (95% CI 1.3–3.2) times more likely to have surgery than other participants.

Two other important findings were observed (Table 6). Males and females did not differ with respect to pain, surgery, or HME-related complications. Female participants were just as likely to report having pain, surgery, or HME-related complications as male participants. Membership in the support group was associated with having surgery, HME-related complications, and pain, with significantly more individuals who were members of the support group having had surgery ($P = 0.044$), having HME-related complications ($P = 0.035$), and having pain ($P = 0.026$).

DISCUSSION

The goal of this study was to evaluate whether pain in HME is a significant problem, as previous natural history studies did not examine or identify pain as a significant outcome.[2,5] Our results suggest that pain is a significant problem, with 84% of the study population reporting that they experience pain and that pain has a negative impact on their lives. Similar pain rates were reported in MHE Coalition (85%) and Shriners Hospital (80%) participants, which indicates that pain is a pervasive problem for individuals who have HME. This is an important observation, as the participants from the MHE Coalition and the Shriners Hospital represent two different populations of individuals with HME. The finding of similar pain rates in both populations indicates that the pain outcome did not result from differential sampling.

An important new finding reported by 55% of participants is that they experience generalized pain. Previously, pain was associated only with the sites of exostoses and was considered to be secondary to compression of nerves or soft tissues; this study also found that 44% of participants reported isolated pain associated with an exostosis. Our results suggest that both localized pain and generalized pain are significant problems in HME. This raises the question of whether there is an underlying mechanism for generalized pain in HME.

TABLE 4. Pain Interference Ratings*

Interference Rating	Interference With General Activity	Interference With Sleep	Interference With Social Interactions	Interference With Mood
None (rating of 0)	38 (15.6%)	53 (21.7%)	75 (30.7%)	44 (18.1%)
Mild (rating of 1–3)	94 (38.5%)	78 (32.0%)	82 (33.6%)	87 (35.8%)
Moderate (rating of 4–6)	55 (22.5%)	56 (23.0%)	52 (21.3%)	53 (21.8%)
Severe (rating of 7–10)	57 (23.4%)	57 (23.4%)	35 (24.4%)	59 (24.2%)

*Data only for individuals with pain.

TABLE 5. Outcome by Presence or Absence of Pain

	Pain Group	No Pain Group	*P* Value
Age (years)	(n = 243)	(n = 46)	0.003
0–10	42 (17.3%)	20 (43.5%)	
11–20	53 (21.8%)	7 (15.2%)	
21–30	37 (15.2%)	4 (8.6%)	
31–40	47 (19.3%)	5 (10.9%)	
>40	64 (26.4%)	10 (21.8%)	
Surgery*	(n = 201)	(n = 26)	<0.001
Yes	185 (92.0%)	16 (61.5%)	
No	16 (8.0%)	10 (38.5%)	
HME-Related Complications*	(n = 201)	(n = 26)	<0.001
Yes	178 (88.6%)	12 (46.2%)	
No	23 (11.4%)	14 (53.8%)	
Compression of Tendons, Muscles, Ligaments*	(n = 201)	(n = 26)	<0.001
Yes	156 (77.6%)	9 (34.6%)	
No	45 (22.4%)	17 (65.4%)	
Compression of nerves*	(n = 201)	(n = 26)	<0.001
Yes	111 (55.2%)	3 (11.5%)	
No	90 (44.8%)	23 (88.5%)	
Coalition Member*	(n = 200)	(n = 26)	0.023
Yes	156 (78.0%)	15 (57.7%)	
No	44 (22.0%)	11 (42.3%)	

*Excluding participants under the age of 11 years.

Four variables were found to be associated with pain in HME in individuals: age, HME-related complications, surgery, and membership in the support group. Three of these factors (HME-related complications, surgery, and support group membership) may be related. It is possible that a person who has a more severe HME phenotype is more likely to have pain, and as a result of the complications or the pain is more likely to have surgery, and as a result of all of these factors (pain, complications, and surgery) is more likely to seek support from others similarly affected. This study cannot tease apart this relationship; nevertheless, these outcomes are important findings.

TABLE 6. Outcomes Based on Support Group Membership

	Members	Non-Members	*P* Value
Had Surgery	(n = 221)	(n = 71)	0.044
Yes	183 (82.8%)	51 (71.8%)	
No	38 (17.2%)	20 (28.2%)	
HME-Related Complications	(n = 221)	(n = 71)	0.035
Yes	171 (77.4%)	46 (64.8%)	
No	50 (22.6%)	25 (35.2%)	
Compression of Tendons, Muscles, Ligaments	(n =221)	(n = 71)	0.002
Yes	153 (69.2%)	35 (49.3%)	
No	68 (30.8%)	36 (50.7%)	
Other Complications*	(n = 221)	(n = 71)	0.026
Yes	85 (38.5%)	17 (23.9%)	
No	136 (61.5%)	54 (76.1%)	
Have Pain	(n = 221)	(n = 70)	0.026
Yes	192 (86.9%)	53 (75.7%)	
No	29 (13.1%)	17 (24.3%)	

*Complications such as pain when breathing, bone deformities, and spinal cord compression.

Logistic regression results showed that only HME-related complications and surgery had a significant role in pain outcome. Individuals with HME-related complications were five times more likely to report having pain. Since we did not assess the severity of the disease phenotype in this study, we cannot determine whether these individuals with HME-related complications have a more severe form of the disease. HME individuals reporting surgery were 3.8 times more likely to report having pain, and this result has important implications, as surgical intervention is a common treatment in HME. Two possible explanations may explain why surgery is associated with pain. First, while surgery may initially be undertaken to relieve pain, it could start a pain cycle in which the surgery itself leads to pain, which may lead to more surgery and then more pain. Alternatively, individuals who have surgery may be more severely affected with HME, and it is the more severe phenotype and not the surgery per se that causes pain. The finding that individuals with HME-related complications are 3.1 times more likely to have surgery supports this second possibility but does not rule out the first. The results suggest that individuals who have HME-related complications and/or surgery are at increased risk for pain. These findings also suggest that surgery should be avoided or kept to a minimum, as it is an important risk factor for pain in HME individuals. At the very least, this point must be considered before undertaking surgery and when considering repeated surgeries.

No significant differences were identified between males and females with respect to pain, surgery, or HME-related complications. This is in contrast to two HME studies that suggest that males have a more severe HME phenotype than females. Schmale et al found that the females in their study were more mildly affected than the males and concluded that their data supported the concept that the genes for HME are expressed more severely in males.[2] In support of this finding, Wicklund et al[5] found an excess of males undergoing surgical removal of exostoses; this suggested that males with HME are either more severely affected or that they seek medical attention more often than females with HME. However, the results from our study showed that there is no difference between males and females with respect to pain. Gender differences and phenotypic severity warrant additional study.

Malignant degeneration, a severe sequela of HME, is estimated to occur in 0.9% to 25% of HME individuals.[10,11] The higher estimates may relate to differential ascertainment in early study designs, as more recent studies estimate a 2% lifetime risk for malignant degeneration.[4,12] Malignant degeneration of an exostosis was reported by 4% of our study population, higher than more recent estimates. It is unknown why a higher frequency was found in this population, and thus this finding should be cautiously interpreted.

Assessment of pain is difficult, as it is subjective and requires sampling of a large sample set. One of the strengths of this study was the large number of individuals with HME who

participated. However, although we were sampling a large population, it is possible that individuals with pain were more likely to participate, especially in view of the fact that we cannot be certain whether those individuals who chose not to participate in the study did so because they do not have pain or due to other unrelated reasons. We found that equal numbers of participants in the MHE Coalition and the Shriners Hospital populations reported pain, suggesting that we were not sampling the pain-only group of HME individuals. While both the MHE Coalition and Shriners Hospital populations represent populations that have come to medical attention due to having HME-related problems or a family member with HME, not all of these individuals have pain, and thus we do not believe that the study was biased toward only individuals with pain. Lastly, pain is subjective and inherently difficult to characterize and describe in any population. To overcome this difficulty, different means of assessing pain were used, including numeric rating scales, a pain drawing, and multiple-choice questions. The questionnaire used in this study was developed for the study, and thus no validation data for the overall questionnaire are available. The results of the study should be interpreted with this in mind.

Information about pain in HME is important not only to those with HME but also to the physicians who provide treatment and care. This study shows that pain is a significant problem in HME and affects a large proportion of these individuals. Additional studies are needed to define the causes and characteristics of pain in HME. For example, it is important to determine the cause of generalized pain and whether pain is due to having a more severe HME phenotype or to personality or psychological factors unique to certain individuals and/or associated with HME. A prospective study of an HME cohort is also needed to better characterize pain in HME and to understand when individuals start to develop pain, if their pain experience changes over the course of their lifetime, and what the underlying pain process is.

In summary, this study suggests that pain has been underappreciated in HME and should be addressed when caring for individuals with this condition.

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APPENDIX A: HEREDITARY MULTIPLE EXOSTOSIS (HME) STUDY QUESTIONNAIRE

Date:
Date of Birth:
Part 1 - Demographics:

1) What is your sex?
[ ] Male [ ] Female

2) What is your ethnicity?
[ ] Caucasian, non-Hispanic [ ] Black, non-Hispanic [ ] Hispanic [ ] Asian/Oriental [ ] Other, please specify

3) What is your primary language?
[ ] English [ ] Spanish
[ ] Vietnamese [ ] Chinese
[ ] Other, please specify

4) What is your current marital status (not applicable for children)?
[ ] Single [ ] Married [ ] Divorced [ ] Widowed
[ ] Common Law

5) What is your highest level of education?
[ ] Lower than 8th grade [ ] Associate degree (2 yr)
[ ] Completed 10th grade [ ] Bachelor's degree
[ ] High School Diploma [ ] Master's degree or higher
[ ] Some College

6) How many people live in your home (including you)?
[ ] 1 [ ] 4
[ ] 2 [ ] 5
[ ] 3 [ ] More than 5

7) What best describes your approximate yearly household income before taxes (the income of all family members who are working and currently living at home with you)?

(To be answered by parent or guardian if you are under age 18)
[ ] Less than $10,000 [ ] $50,000–$74,999
[ ] $10,000–$24,999 [ ] $75,000–$100,000
[ ] $25,000–$49,999 [ ] More than $100,000

8) What type of health insurance are you covered by? Mark all that apply. (To be answered by parent or guardian if you are under age 18)
[ ] Health Maintenance Organization (HMO)
[ ] Preferred Provider Organization (PPO)
[ ] Private insurance
[ ] Medicaid
[ ] No insurance

Part 2 - HME and Medical History:

9) At what age was your first exostosis noticed (age in years)?

10) How old were you when you were diagnosed with hereditary multiple exostosis?

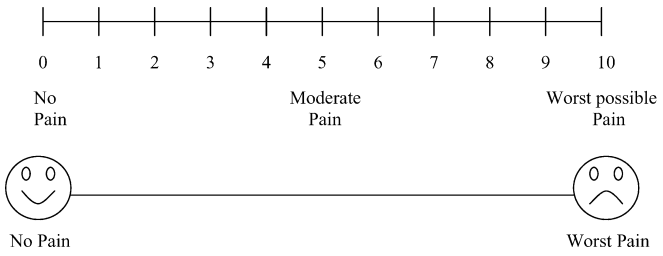
11) Have you had any HME-related surgeries (example: removal of exostosis, limb lengthening, stapling, limb straightening)?
[ ] Yes
[ ] No
b) If yes, how many surgeries?
c) At what age did you have the surgery, where was the surgery (example: knee, hip) and what type of procedure was it (example: exostosis removed, limb lengthening)? (If you need more space please use the extra sheet provided at the end of the questionnaire.)
Age: [ ] Location: Procedure:
Age: [ ] Location: Procedure:
Age: [ ] Location: Procedure:
Age: [ ] Location: Procedure:
Age: [ ] Location: Procedure:
Age: [ ] Location: Procedure:

12) Have you had any other medical problems due to the exostoses?
[ ] Yes
[ ] No
b) Compression or irritation of tendons, muscles, or ligaments?
[ ] Yes
[ ] No
If yes, please specify where on the body the compression is or was:
c) Compression of blood vessels?
[ ] Yes
[ ] No
If yes, please specify where on the body the compression is or was:
d) Compression of nerves?
[ ] Yes
[ ] No
If yes, please specify where on the body the compression is or was:
e) Have any exostoses undergone malignant changes (become cancerous)?
[ ] Yes
[ ] No
If yes, please specify the type of cancer (chondrosarcoma, osteosarcoma, other) and where on the body the cancer(s) is or was located:
f) Other complications (example: spinal cord compression, pain when breathing, etc.):
[ ] Yes
[ ] No
If yes, please specify

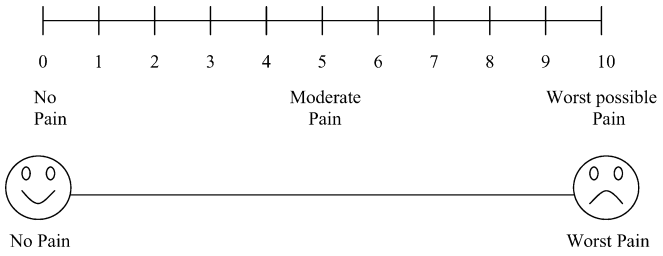
Part 3 - Pain:

13) In an average month (30 days) how often do you have pain?
[ ] Every day [ ] 10–14 days
[ ] 25–29 days [ ] 5–9 days
[ ] 20–24 days [ ] 1–4 days
[ ] 15–19 days [ ] Do not have pain

14) In an average month, how would you rate your **average** pain when you have pain? (Mark both scales)

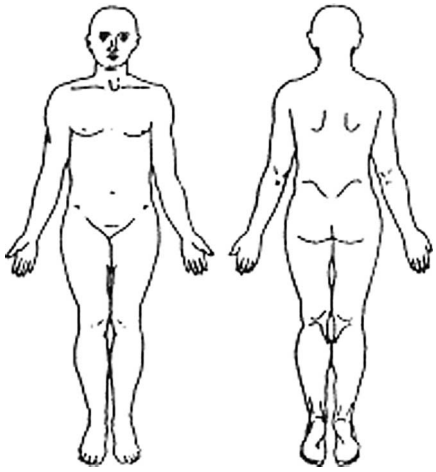


15) How would you rate your pain **right now**? (Mark both scales)



16) When do you have pain?
a) All the time (constantly throughout the day)?
[ ] Yes
[ ] No
b) On and off throughout the day (intermittently)?
[ ] Yes
[ ] No
c) At specific times or with specific activities during the day (example: when I wake up, when I walk)?
[ ] Yes
[ ] No
If yes please specify when during the day or what activities:
d) Other, please specify

17) Where do you have pain? (Please mark all parts of the body where you have pain)



18) Do you have pain where you have exostoses (bony outgrowths)?
[ ] Yes [ ] No

19) If you have had exostoses removed, do you have pain where the exostoses were?
[ ] Yes [ ] No

20) Do you have pain as a result of other HME-related surgeries (example: leg lengthening, stapling, etc.)?
[ ] Yes [ ] No
b) If yes, what caused the pain (example: nerve damage, etc.)?

21) Do you have pain in parts of your body where there are no obvious exostoses?
[ ] Yes [ ] No

22) How would you describe your pain over the past month? (Mark all that apply)
[ ] Aching [ ] Throbbing [ ] Shooting
[ ] Stabbing [ ] Gnawing [ ] Sharp [ ] Tender
[ ] Burning [ ] Exhausting [ ] Tiring
[ ] Penetrating [ ] Nagging [ ] Numb [ ] Miserable
[ ] Unbearable

23) In an average month, how many days or partial days of work or school do you miss due to pain?

24) Do you receive any special accommodations or assisted technology at work or school? (example: At work, do employers excuse you from tasks that would trigger pain, such as heavy lifting, carrying heavy objects, etc.? At school, do you have an Individual Education Plan (IEP) or 504 Accommodation Plan?)
[ ] Yes [ ] No

25) If yes, please explain: In an average week, how much does pain interfere with your general activity?

0	1	2	3	4	5	6	7	8	9	10
Does not interfere										Completely interferes

26) In an average week, how much does pain interfere with your sleep?

0	1	2	3	4	5	6	7	8	9	10
Does not interfere										Completely interferes

27) In an average week, how much does pain change how you interact with other people?

0	1	2	3	4	5	6	7	8	9	10
Does not change										Completely changes

28) In an average week, how much does pain affect your mood?

0	1	2	3	4	5	6	7	8	9	10
Does not affect										Completely affects

29) Have you experienced depression as a result of chronic pain?
[ ] Yes
[ ] No

30) What kinds of things make your pain feel worse (example: walking, lifting, playing)?

31) What kinds of things make your pain feel better (example: rest, medicine, heat)?

32) Do you have any other medical condition(s) that causes pain (example: Arthritis, Reflex Sympathetic Dystrophy Syndrome [RDS], etc.)?
[ ] Yes [ ] No
b) If yes, what is the condition(s)?

33) What do you think is the cause of your pain?
a) My pain is due to hereditary multiple exostosis.
[ ] Yes
[ ] No
b) My pain is due to treatment I have received (for example: surgery, medication).
[ ] Yes
[ ] No
c) My pain is due to another medical condition.
[ ] Yes
[ ] No
If yes, what condition?

34) Do you take any medication(s) for pain?
[ ] Yes
[ ] No
b) If yes, what medication(s), how often do you take them, and what dosage?

35) Are you receiving any other treatments for pain (ex: physical therapy, occupational therapy, chiropractic treatments, orthotics and/or braces, etc.)?
[ ] Yes
[ ] No
b) If yes, what treatments and how often?

36) Are you satisfied with the treatment you are receiving for your pain?
[ ] Yes
[ ] No

37) Have you ever seen a pain specialist?
[ ] Yes
[ ] No

38) Are you a member of the MHE Coalition?
[ ] Yes
[ ] No
b) If yes, how often do you participate in the support group (for example: e-mails, chats)?
[ ] Daily [ ] Weekly [ ] Monthly [ ] Every few months
[ ] Once a year [ ] Not active

Part 4 - Family History – If you do not have a family history of HME do not fill out this section. (If you need more room please use the extra sheet at the end of the questionnaire.)

Biological Parents

	Date of Birth Month/day/year	Alive or dead?	Age at death	Has HME?	Other major medical conditions?
Father	/ /	[ ] Alive [ ] Dead [ ] Unknown		[ ] Yes [ ] No	
Mother	/ /	[ ] Alive [ ] Dead [ ] Unknown		[ ] Yes [ ] No	

Full Siblings (brothers and sisters who have the same mother and father as you)

	Sex	Date of Birth Month/Day/Year	Alive or dead?	Age at death	Has HME?	Other major medical conditions?
Sibling 1	[ ] M [ ] F	/ /	[ ] Alive [ ] Dead [ ] Unknown		[ ] Yes [ ] No	
Sibling 2	[ ] M [ ] F	/ /	[ ] Alive [ ] Dead [ ] Unknown		[ ] Yes [ ] No	
Sibling 3	[ ] M [ ] F	/ /	[ ] Alive [ ] Dead [ ] Unknown		[ ] Yes [ ] No	
Sibling 4	[ ] M [ ] F	/ /	[ ] Alive [ ] Dead [ ] Unknown		[ ] Yes [ ] No	

Children

	Sex	Date of Birth Month/Day/Year	Alive or dead?	Age at death	Has HME?	Other major medical conditions?
Child 1	[ ] M [ ] F	/ /	[ ] Alive [ ] Dead [ ] Unknown		[ ] Yes [ ] No	
Child 2	[ ] M [ ] F	/ /	[ ] Alive [ ] Dead [ ] Unknown		[ ] Yes [ ] No	
Child 3	[ ] M [ ] F	/ /	[ ] Alive [ ] Dead [ ] Unknown		[ ] Yes [ ] No	
Child 4	[ ] M [ ] F	/ /	[ ] Alive [ ] Dead [ ] Unknown		[ ] Yes [ ] No	

Appendix B. Participant Medication List

Prescription Medications
- Amitriptyline
- Arthrotec
- Baclofen
- Bextra
- Celebrex
- Darvocet
- Dilaudid
- Etodolac
- Hydrocodone
- Lortab
- Loracet
- Methadone
- Naprosyn/Naproxen
- Neurontin
- Norco
- Oxycodone
- OxyContin
- Percocet
- Percodan
- Percogesic
- Piroxicam
- Trazodone
- Ultram
- Vicodin
- Vioxx

Over-the-Counter Medications
- Acetaminophen
- Advil
- Aleve
- Aspirin
- Ibuprofen
- Motrin
- Tylenol/Extra Strength
- Tylenol/Tylenol PM