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Research Submission

Childhood Maltreatment and Migraine (Part II). Emotional Abuse as a Risk Factor for Headache Chronification

Gretchen E. Tietjen, MD; Jan L. Brandes, MD; B. Lee Peterlin, DO; Arnolda Eloff, MD; Rima M. Dafer, MD, MPH; Michael R. Stein, MD; Ellen Drexler, MD; Vincent T. Martin, MD; Susan Hutchinson, MD; Sheena K. Aurora, MD; Ana Recober, MD; Nabeel A. Herial, MD, MPH; Christine Utley, MSN, CNP; Leah White, MPH; Sadik A. Khuder, MPH, PhD

Objectives.—To assess in a headache clinic population the relationship of childhood abuse and neglect with migraine characteristics, including type, frequency, disability, allodynia, and age of migraine onset.

Background.—Childhood maltreatment is highly prevalent and has been associated with recurrent headache. Maltreatment is associated with many of the same risk factors for migraine chronification, including depression and anxiety, female sex, substance abuse, and obesity.

Methods.—Electronic surveys were completed by patients seeking treatment in headache clinics at 11 centers across the United States and Canada. Physician-determined data for all participants included the primary headache diagnoses based on the International Classification of Headache Disorders-2 criteria, average monthly headache frequency, whether headaches transformed from episodic to chronic, and if headaches were continuous. Analysis includes all persons with migraine with aura, and migraine without aura. Questionnaire collected information on demographics, social history, age at onset of headaches, migraine-associated allodynic symptoms, headache-related disability (The Headache Impact Test-6), current depression (The Patient Health Questionnaire-9), and current anxiety (The Beck Anxiety Inventory). History and severity of childhood (<18 years) abuse (sexual, emotional, and physical) and neglect (emotional and physical) was gathered using the Childhood Trauma Questionnaire.

Results.—A total of 1348 migraineurs (88% women) were included (mean age 41 years). Diagnosis of migraine with aura was recorded in 40% and chronic headache (≥15 days/month) was reported by 34%. Transformation from episodic to chronic was reported by 26%. Prevalence of current depression was 28% and anxiety was 56%. Childhood maltreatment was reported as follows: physical abuse 21%, sexual abuse 25%, emotional abuse 38%, physical neglect 22%, and emotional neglect 38%. In univariate analyses, physical abuse and emotional abuse and neglect were significantly associated with chronic migraine and transformed migraine. Emotional abuse was also associated with continuous daily headache, severe headache-related disability, and migraine-associated allodynia. After adjusting for sociodemographic factors and current depression and anxiety, there remained an association between emotional abuse in childhood and both chronic (odds ratio [OR] = 1.77, 95% confidence

From the University of Toledo College of Medicine, Toledo, OH, USA (G.E. Tietjen, N.A. Herial, C. Utley, L White, and S.A. Khuder); Nashville Neuroscience Group, Nashville, TN, USA (J.L. Brandes); Drexel University College of Medicine, Philadelphia, PA, USA (B.L. Peterlin); University of Calgary, Calgary, AB, Canada (A. Eloff); Loyola University Medical Center, Maywood, IL, USA (R.M. Dafer); John Muir Medical Center, Walnut Creek, CA, USA (M.R. Stein); Maimonides Medical Center, Brooklyn, NY, USA (E. Drexler); University of Cincinnati, Cincinnati, OH (V.T. Martin); Orange County Migraine & Headache Center, Irvine, CA, USA (S. Hutchinson); Swedish Headache Center, Seattle, WA, USA (S.K. Aurora); University of Iowa, Iowa City, IA, USA (A. Recober).

Address all correspondence to G.E. Tietjen, Department of Neurology, 3000 Arlington Ave., MS 1195, Toledo, OH43614, USA.

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intervals [CI]: 1.19-2.62) and transformed migraine (OR = 1.89, 95% CI: 1.25-2.85). Childhood emotional abuse was also associated with younger median age of headache onset (16 years vs 19 years, *P* = .0002).

Conclusion.—Our findings suggest that physical abuse, emotional abuse, and emotional neglect may be risk factors for development of chronic headache, including transformed migraine. The association of maltreatment and headache frequency appears to be independent of depression and anxiety, which are related to both childhood abuse and chronic daily headache. The finding that emotional abuse was associated with an earlier age of migraine onset may have implications for the role of stress responses in migraine pathophysiology.

Key words: emotional abuse, headache, chronification

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Childhood maltreatment is highly prevalent and has been frequently associated with recurrent headache.[1-5] There is, however, a paucity of reports specific to migraine and its characteristics using either physician diagnosis or validated diagnostic instruments with the International Headache Society criteria.[6-8] In an earlier headache clinic-based study restricted to women with migraine, and another with men and women, increased frequency of migraine was associated with physical and sexual abuse, but the impact of childhood emotional abuse and neglect, both physical and emotional, was not considered.[7,8] Furthermore, the screening questionnaires used in those studies had not been validated.

The assessment of the relationship of migraine features and childhood maltreatment is complicated by the fact that many of the risk factors for development of chronic headache,[9,10] including female sex, lower socioeconomic status, substance abuse, obesity, depression, and anxiety are also associated with maltreatment history.[5,11-16] We found in analyses of this cohort that all types of childhood abuse and neglect are strongly associated with depression and anxiety, and that the relationship strengthens with increasing number of maltreatment types (Part I). Furthermore, depression and anxiety mediated the association of obesity with childhood maltreatment, migraine frequency, and migraine-related disability.[17] In our initial headache clinic study, which was restricted to female migraineurs, we examined the relationship of childhood maltreatment and migraine frequency, and it too appeared to be mediated by psychiatric disorders, specifically, depression.[7]

Our objectives in this paper were to assess in a large multicenter headache clinic population the relationships of different types of childhood abuse (physical, sexual, emotional) and neglect (physical and emotional) to migraine characteristics, including type, frequency, transformation, disability, allodynia, and age of migraine onset. We have controlled for potential confounders such as age, sex, race, education, household income, smoking status, caffeine use, substance abuse, and obesity. Because childhood maltreatment is also associated with depression and anxiety,[17,18] which in turn are associated with migraine,[19] the influence of these conditions on the relationship between maltreatment and migraine features was examined.

METHODS

Patient Selection.—This cross-sectional multicenter headache clinic study was conducted by the members of the Women's Issues Section research consortium of the American Headache Society. The recruitment occurred between February 2006 and June 2008 at 11 outpatient headache centers, after each center separately obtained approval from the Institutional Review Boards (IRB). Patient recruitment and data collection has been discussed in detail in Part I of this paper and in a published manuscript from this cohort.[20]

Data Collection.—The electronic survey collected detailed information on sociodemographics variables and current psychiatric symptoms, and childhood maltreatment (see Part I). Information was also collected regarding allodynia and headache-related disability. The treating physician determined the primary headache diagnoses based on the International Classification of Headache Disorders (ICHD)-2 criteria,[7] the average monthly headache frequency over the

prior 3 months, whether the headaches had transformed from episodic to chronic, and whether daily headaches were continuous.

Measures.—*Childhood Abuse and Neglect.*—In this study, maltreatment exposure occurring in childhood was assessed using the Childhood Trauma Questionnaire (CTQ).[21] This questionnaire is a 28-item self-reported quantitative measure that provides brief, reliable, and valid screening for history of childhood abuse and neglect. It measures 5 categories of childhood maltreatment that include physical, sexual, and emotional abuse, and physical, and emotional neglect. Details on the CTQ measure, maltreatment prevalence, correlation between the different categories of abuse and neglect, and the relationship with depression and anxiety in this study population are discussed in Part I.

Allodynia.—Information on migraine-associated allodynia was collected using the following question in the survey: "Do you experience pain or unpleasant sensation on your skin during a migraine attack with any of the following?" The list included "combing your hair," "shaving," "showering," "exposure to heat cold or heat," "resting head on pillow," and "wearing earrings or a necklace." Our questions were based on those used in published research on the topic[22] but our survey tool was designed prior to the publication of a validated tool encompassing severity.[23]

Headache-Related Disability.—The Headache Impact Test (HIT-6),[24] a 6-item scale that correlates well with headache severity has been determined to be reliable and valid in evaluating the impact of headache on health-related quality of life in patients seeking primary and headache subspecialty care. HIT-6 score ≥60 was considered as severe headache-related disability.

Depression.—The Patient Health Questionnaire (PHQ-9) is a self-reported diagnostic and severity measure for current depression (in the prior 2 weeks) using criteria from the Diagnostic and Statistical Manual of Mental Disorders (DSM) IV.[25]

Anxiety.—The Beck Anxiety Inventory (BAI) was used to assess the severity of patient anxiety.[26] The questionnaire consists of both physiological and cognitive components of anxiety addressed in the 21 items describing subjective, somatic, or panic-related symptoms.

Statistical Analysis.—All statistical analyses in this study were performed using SAS version 9.1 (SAS Institute, Inc., Cary, NC, USA) and fully described in Part I. The relationship between childhood abuse and neglect and migraine characteristics was examined using logistic regression analysis. Models were adjusted for age, gender, race, education, household income, smoking status, caffeine use, substance abuse, obesity, and current depression and anxiety. Adjusted odds ratios (ORs) and 95% confidence intervals (CI) were used to measure the strength of the relationships, and the significance of the ORs was examined using Wald's χ^2 test statistic.

RESULTS

A total of 1348 patients who received a diagnosis of migraine completed the surveys. The ICHD-2 diagnosis and some characteristics of the study population are presented in Table 1. Additional characteristics

Table 1.—Characteristics of the Study Population

	n (%)
International Headache Society Diagnosis (ICHD-II)	
Migraine (1.0)	1348 (100)
Migraine with aura (1.2)	543 (40)
Migraine without aura (1.1)	805 (60)
Gender	
Male : female	161 (12) : 1187 (88)
Age, years (mean ± SE)	41 ± 0.4
Age at onset of headache, years (mean ± SE)	19 ± 0.5
Headache frequency, days (mean ± SE)	14 ± 0.7
(≥15 days/month)	458 (34)
Transformed migraine	356 (26)
Continuous daily headache	238 (17)
Headache impact, score (mean ± SE)	58 ± 0.5
Severe (HIT-6 ≥ 60)	885 (66)
Migraine-associated allodynia (≥1 symptom)	817 (60)
Current Depression (PHQ-9 ≥ 10)	381 (28)
Current Anxiety (BAI ≥ 8)	761 (56)

BAI = The Beck Anxiety Inventory; HIT = The Headache Impact Test; ICHD = the International Classification of Headache Disorders; PHQ = The Patient Health Questionnaire.

are found in Table 1 of Part I. Diagnosis of migraine with aura was recorded in 40% of the participants, the rest having no aura. Majority of the participants were women (88%) and the average age of the participants in this study was 41 years. Thirty-four percent of all participants reported chronic migraine (frequency ≥15 days/month) and 26% reported a transformation from episodic to chronic. The majority of the study population had very severe headache-related disability based on the HIT-6 scores and at least 1 migraine-associated allodynic symptom. Prevalence of current depression was 28% (based on PHQ-9 score) and anxiety was 56% (based on BAI score).

Childhood maltreatment, either abuse or neglect, was reported by 58% of the study population (n = 781). Based on this cutoff score, physical abuse was reported by 21%, sexual abuse by 25%, emotional abuse by 38%, physical neglect by 22%, and emotional neglect by 38% of the study population. Table 2 shows the differences in the headache characteristics between migraineurs with and without a history of a particular category of childhood abuse or neglect. The proportion of respondents with migraine with aura in each maltreatment group ranged from 39% to 44% and was not significantly different among the groups. Migraineurs reporting emotional abuse were significantly younger at onset of headaches. Frequency of chronic migraine was higher in those reporting physical and emotional abuse, and physical and emotional neglect. Frequency of transformed migraine (episodic to chronic) was also higher in migraineurs with physical and emotional abuse, and emotional neglect. Of all the childhood trauma categories, only the migraineurs reporting emotional abuse had higher frequency of daily continuous headaches, severe headache-related disability, and symptoms of migraine-associated allodynia than the non-abused cohort.

Forty-two percent (n = 567) of the study population did not report any type of childhood abuse or neglect. Table 3 presents the results from logistic regression analyses comparing this group with those reporting the different categories of childhood trauma. All models were adjusted for age, gender, race, education and household income levels, smoking status, caffeine use, substance abuse, and obesity. Except for sexual abuse, all the other categories of childhood trauma were associated with chronic migraine and the strongest relationship was noted with emotional abuse. All 5 categories of childhood trauma were associated with transformed migraine. The strongest relationships were noted in migraineurs reporting emotional abuse, followed by physical abuse. Emotional abuse was also associated with severe headache-related disability, but this relationship was marginally significant. Of all the categories of childhood trauma, only physical abuse and emotional abuse were significantly associated with chronic and transformed migraine.

The associations of physical and emotional abuse with chronic migraine and transformation were further examined by controlling for current depression and anxiety. After adjusting for all previously referred variables and current depression and anxiety, only emotional abuse was associated with chronic migraine (OR = 1.77, 95% CI: 1.19-2.62, $P = .004$) and with transformation (OR = 1.89, 95% CI: 1.25-2.85, $P = .0027$). Emotional abuse in childhood was also associated with the headache onset age. Headaches started at a younger age in persons reporting childhood emotional abuse. In adjusted linear regression model, headache onset age was significantly associated with emotional abuse (F = 13.89, $P = .0002$).

DISCUSSION

In this study there are several novel findings. Our data suggest that childhood maltreatment, in particular emotional abuse, is a risk factor for chronic migraine, including transformed migraine and continuous daily headache. The association of emotional abuse with headache frequency and transformation appears to be independent of other factors, including depression and anxiety, which are related to both childhood abuse and chronic headache. We also found that emotional abuse was associated with severe headache-related disability, allodynia, as well as with an earlier age of migraine onset.

Migraine is a recurrent disorder with episodic manifestations. There is mounting evidence that migraine may be a progressive disorder, with reports suggesting that in at least 3% of migraineurs each

Table 2.—Childhood Abuse and Neglect and Association With Migraine Characteristics

	Physical abuse		Sexual abuse		Emotional abuse		Physical neglect		Emotional neglect	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
MA : MO, %	44 : 56	39 : 61	44 : 56	39 : 61	42 : 58	39 : 61	40 : 60	40 : 60	39 : 61	41 : 59
Headache onset age, years (mean ± SE)	19.2 ± 0.9	19.4 ± 0.4	18.6 ± 0.9	19.7 ± 0.5	17.9 ± 0.7*	20.4 ± 0.6	19.2 ± 0.9	19.5 ± 0.5	19.8 ± 0.9	19.1 ± 0.5
Chronic migraine	110 (40)***	348 (32)	111 (33)	347 (34)	209 (41)****	249 (30)	127 (44)***	331 (31)	197 (39)***	261 (31)
Transformed migraine	92 (33)*	264 (25)	90 (27)	266 (26)	170 (33)****	186 (22)	99 (34)	257 (24)	159 (31)***	197 (23)
Daily continuous headache	60 (21)	178 (16)	61 (18)	177 (17)	115 (22)*	123 (14)	71 (24)	167 (16)	104 (20)	134 (16)
Severe disability	200 (72)	685 (64)	244 (72)	641 (63)	367 (72)***	518 (62)	210 (72)	675 (64)	361 (71)	524 (62)
Migraine-associated allodynia	182 (65)	635 (59)	229 (68)	588 (58)	334 (66)***	483 (57)	195 (67)	622 (59)	325 (64)	492 (59)

*$P < .01$, **$P < .001$, ***$P < .05$, ****$P < .0001$.

Values reported are number (percentage) in each group of childhood trauma, unless indicated otherwise. Exposure to abuse and neglect is based on Childhood Trauma Questionnaire cutoff scores for low to extreme trauma compared to none or minimal trauma (physical abuse ≥8, sexual abuse ≥6, emotional abuse ≥9, physical neglect ≥8, emotional neglect ≥10).

MA = migraine with aura; MO = migraine without aura.

Table 3.—Adjusted Odds Ratios From Logistic Regression Models for Association With Childhood Trauma†

	Physical abuse	Sexual abuse	Emotional abuse	Physical neglect	Emotional neglect
Chronic migraine	1.79 (1.17-2.77)**‡	1.44 (0.90-2.29)	2.01 (1.36-2.97)***‡	1.69 (1.08-2.66)*	1.54 (1.03-2.31)*
Transformed migraine	2.14 (1.37-3.34)***‡	1.71 (1.07-2.75)*	2.23 (1.48-3.36)***‡	1.81 (1.13-2.88)*	1.76 (1.14-2.71)*
Daily continuous headache	1.32 (0.79-2.20)	1.19 (0.69-2.08)	1.45 (0.91-2.29)	1.31 (0.79-2.16)	1.12 (0.71-1.76)
Severe disability	1.45 (0.94-2.23)	1.47 (0.92-2.35)	1.54 (1.04-2.29)*	1.33 (0.82-2.16)	1.29 (0.86-1.95)
Migraine-associated allodynia	1.21 (0.79-1.84)	1.17 (0.75-1.82)	1.19 (0.81-1.75)	1.09 (0.69-1.73)	1.01 (0.69-1.48)

*$P < .05$, **$P < .01$, ***$P < .001$.
Values reported are adjusted odds ratios (95% confidence intervals) with the group reporting none/minimal childhood trauma for all categories of abuse and neglect (n = 567) as the referent.
†All models were adjusted for age, gender, race, education, household income, smoking status, caffeine use, substance abuse, and obesity.
‡Significant after Bonferroni correction for multiple hypotheses testing ($P < .01$).

year there is an evolution from an episodic to a chronic (>15 days/month) disorder.[27] Chronic daily headache (CDH), including transformed migraine, chronic migraine, and chronic tension-type headache, is believed to affect 3-5% of the general population,[27] with headache phenoptype depending, in part, on the time since headache disorder onset.[28] Risk factors for the development of chronic headache include female sex, lesser amount of education, obesity, and possibly a history of smoking, caffeine use, and medication overuse.[10,27] In our headache clinic population, as in other studies,[5,11-16] we found these factors to be associated with childhood maltreatment. In the case of obesity and smoking, the relationship to maltreatment was mediated through depression and anxiety. These common psychiatric disorders have, in turn, been demonstrated to be risk factors for migraine, for CDH,[10] and for pain in general. Biologically, the relationship of depression and pain may be enhanced both by similar underlying neurochemistry, as well as by psychosocial phenomenon.[29]

In our clinic cohort, depression and anxiety (both remote and current) were strongly associated with each type of childhood maltreatment. The association strengthened with an increasing number of maltreatment types, suggesting possible causality. Despite the strong association of maltreatment with depression and anxiety, we found that these 2 common psychiatric conditions were not the primary factors determining the relationship of childhood emotional abuse and chronic headache frequency. In a similar vein, findings from the National Comorbidity Survey suggested that the relationship between childhood abuse (physical and sexual) and pain is not dependent on depression.[29]

Another set of factors believed to influence the transition from episodic to a chronic headache includes those classified under "stressful life events," as has been demonstrated in several clinic- and population-based studies.[30-32] Stress is an important trigger of individual episodes of migraine, although the nature of this relationship is not well understood. Chronic stress purportedly affects both peripheral and central nociception, thereby leading to allodynia, hyperalgesia, and chronic head pain.[33] In this context, abuse, which has not been well studied in migraine, may be considered to be an important "stressful life event." A population-based study of adolescents in Taiwan, for instance, showed that both physical abuse and parental divorce were more common in the families of the adolescents with CDH than the control group.[31] Other types of abuse and neglect were not examined. A population-based study in adults focused primarily on events occurring in the year or 2 preceding the onset of CDH.[30] From among the 6 types of events measured, the strongest predictor of CDH was an ongoing "extremely stressful situation." Exposure to an "extremely stressful situation" was endorsed by just over half of the participants, with only 4%

admitting to an ongoing abusive relation, and the type of abuse was not specified. A recent clinic study of patients with orofacial pain demonstrated greater headache disability in those reporting "traumatic life events."[34] The events in that study included a history of physical, emotional or sexual abuse at any age and also childhood neglect. Unfortunately these were combined into one question, and the maltreatment type, and temporal relationship with headache onset or worsening can not be discerned. The findings from our cohort further highlight the potential importance of childhood abuse as an important stressful life event, although in some cases it first occurs years prior to headache onset. Research suggests that there is an interaction between early maltreatment and chronic stress that leads to hypothalamic-pituitary-adrenal (HPA) axis dysregulation[35] and increases the probability of developing a chronic pain condition.[36,37] It has been hypothesized that stressful times in early development initially cause hyperactivation of the HPA system, but with chronic stress over time there is a decrease in cortisol and adrenocorticotropin hormone (ACTH) release.[38] Hypocortisolism has been described in response to acute stress in healthy adults with a history of childhood maltreatment, as well as in persons with stress-related bodily disorders, including headache.[39]

Our data also underscore the importance of emotional abuse, a maltreatment type that is less well recognized and studied than either physical or sexual abuse.[40] More common and less blatant than contact forms of abuse, emotional abuse may reflect the underlying family environment. Studies suggest that emotional abuse may have more lasting consequences,[41,42] including psychiatric sequelae, than physical or sexual abuse.[43] Although it may occur independently,[44] emotional abuse is likely inherent in all abuse types,[40] and certain combinations may be particularly deleterious.[45] Most research on the effects of emotional abuse encompasses the psychological consequences, such as depression,[46] and not painful conditions.[47] Our finding that persons reporting emotional abuse had a significantly earlier age of migraine onset may have implications for its role in migraine pathophysiology.

The study began in 2006, cotemporaneous with publication of proposed revised criteria for chronic migraine (requiring that of the ≥15 days a month with headache, only ≥8 days/month be migraine), and medication overuse headache (not requiring reversion to episodic headache after discontinuation of offending medications).[48] Only 6% of the patients were documented by the physician investigators to have medication overuse headache (MOH), perhaps because they adhered to the earlier stricter definition (requiring reversion to episodic after discontinuation) or because there was no clear history of development or marked worsening during medication overuse. Our queries regarding substance abuse did not discern between use of prescription medications, illicit drugs, and alcohol. Physicians recorded whether patients met 1996 Silberstein-Lipton criteria for transformed migraine,[49] and also documented whether there was an actual evolution in frequency from episodic to chronic. The evaluation and diagnosis by headache specialists according to ICHD-2 criteria is a strength of our study. The sample size allowed us to control for multiple factors that may impact migraine characteristics. The geographic diversity and inclusion of both men and women allows generalization of findings within headache clinic populations. We acknowledge certain inherent biases in the design, including those of selection and recall. This study is limited by reliance on self-reports, and we could not ascertain whether abuse histories are valid. Research suggests that individuals are more likely to minimize adverse experiences rather than fabricate them.[50] In any case, the proportion of migraineurs reporting sexual and physical abuse are nearly identical in this and our earlier clinic-based survey.[7]

Our findings suggest that childhood maltreatment, particularly emotional abuse, may be risk factors for development of chronic headache, including transformed migraine. Although depression and anxiety are related to childhood maltreatment and to chronic frequency, the association of emotional abuse and chronic migraine/transformed migraine is independent of these psychiatric disorders. The finding that emotional abuse was associated with an earlier age of migraine onset suggests a possible role in migraine pathophysiology.

STATEMENT OF AUTHORSHIP

Category 1

(a) Conception and Design
Gretchen E. Tietjen, B.L. Peterlin, Vincent T. Martin, Rima M. Dafer, Nabeel A. Herial, Leah White

(b) Acquisition of Data
Gretchen E. Tietjen, Jan L. Brandes, B.L. Peterlin, Arnolda Eloff, Rima M. Dafer, Ana Recober, Michael R. Stein, Ellen Drexler, Vincent T. Martin, Susan Hutchinson, Sheena K. Aurora, Christine Utley

(c) Analysis and Interpretation of Data
Gretchen E. Tietjen, Nabeel A. Herial, Sadik A. Khuder

Category 2

(a) Drafting the Manuscript
Gretchen E. Tietjen, Nabeel A. Herial

(b) Revising It for Intellectual Content
Gretchen E. Tietjen, B.L. Peterlin, Rima M. Dafer, Vincent T. Martin, Susan Hutchinson, Christine Utley, Nabeel A. Herial, Sadik A. Khuder

Category 3

(a) Final Approval of the Completed Manuscript
Gretchen E. Tietjen; Jan L. Brandes; B. Lee Peterlin; Arnolda Eloff; Rima M. Dafer; Michael R. Stein; Ellen Drexler; Vincent T. Martin; Susan Hutchinson; Sheena K. Aurora; Ana Recober; Nabeel A. Herial; Christine Utley; Leah White; Sadik A. Khuder

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