NHIF Goals

The NHIF will concern itself with all aspects of the problem of head injury from prevention to late rehabilitation. Four of its major goals are:

STIMULATE PUBLIC AND PROFESSIONAL AWARENESS OF THE PROBLEM OF HEAD INJURY-THE SILENT EPIDEMIC

Identify causes and means of prevention.

Define the nature of disability after head injuries.

Set forth special needs in head injury rehabilitation.

Cite need for specific legislation to fund programs and services for the head injured.

EXPAND A CENTRAL CLEARINGHOUSE FOR INFORMATION AND RESOURCES FOR HEAD INJURY SURVIVORS AND THEIR FAMILES

Provide national and state resource directories

Distribute an NHIF newsletter.

Produce informational pamphlets on head injury.

Disseminate information on the legal rights of the head injured person.

3. DEVELOP A SUPPORT GROUP NETWORK FOR HEAD INJURY SURVIVORS AND THEIR FAMILIES

Assist families in organizing local support groups in all states.

Institute a "Hot line" for people in need.
Assist head injured individuals in organizing groups for socialization and problem solving.

4. ESTABLISH SPECIALIZED HEAD INJURY REHABILITATION PROGRAMS

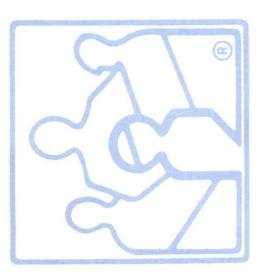
Encourage existing programs and develop new programs stressing cognitive retraining, behavior modification and vocational rehabilitation leading to independent living.

Design living facilities either transitional or permanent in association with rehabilitation programs.

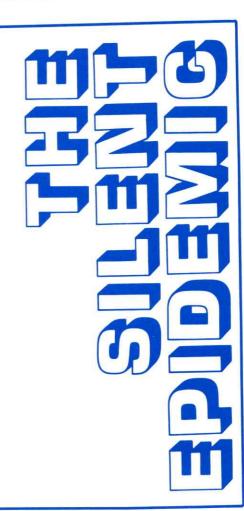


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TEMPENDED.



HELP FOR THE HEAD INJURED AND THEIR FAMILIES



MARYLAND HEAD INJURY FOUNDATION, INC.

7735 Old Georgetown Rd., Room 237 Bethesda, MD 20814 (301) 652-6443 1-800-221-MHIF



DEFINITION: TRAUMATIC HEAD INJURY

An insult to the brain caused by an external physical force; results in impairment of cognitive abilities or physical functioning (temporary or permanent).

INCIDENCE: ANNUAL

140,000 deaths from head injuries in U.S.

Kills more Americans under the age of 34 than all other causes combined.

50-70,000 individuals survive injuries but are left with impairments that preclude return to normal life.

Most victims are under 30 years of age. Maryland: 7,200 victims of head injury.

GOALS

Prevention

Stimulate public/professional awareness.

Provide clearinghouse of information.

Resource for educational material.

Represent head injured in State/Federal legislative processes.

Advocate funding for rehabilitation and transitional/permanent living.

Develop support groups throughout State. Sponsor membership meetings/social events for head injured and families.

Publish semi-annual newsletter

Support specialized programs for victims.

Provide speakers for groups.

Participate in community activities.

MEMBERSHIP

Open to head injured, families, professionals and friends.

Annual basic dues \$25. Corporate contributor program.

Corporate Contributor pro

MHIF:
Chapter of National Head Injury Foundation

ALL DONATIONS and MEMORIAL CARDS
ARE TAX-DEDUCTIBLE

11/87

Importance of Unbound Phenytoin Serum Levels in Head Trauma Patients

LARRY A. BAUER, PHARM.D.*†, W. A. DREW EDWARDS, M.S.*, E. PATCHEN DELLINGER, M.D.‡, VIDMANTAS A. RAISYS, Ph.D.†, and CYNTHIA BRENNAN, PHARM.D.*

Total (bound \pm unbound) and unbound phenytoin serum concentrations were measured in ten male comatose head trauma patients and ten male epileptic patients. Serum biochemistry and complete blood cell counts were normal for both groups, except albumin concentrations were below normal in the head trauma patients for nutritional reasons. Total phenytoin concentrations were 6.8 ± 1.8 mcg/ml for the head trauma patients and 14.5 ± 3.0 mcg/ml for the epileptic patients (p < 0.0002) even though phenytoin doses were similar. However, unbound phenytoin concentrations were within the therapeutic range of 1 to 2 mcg/ml for both groups and were not significantly different. Had only the total concentrations been measured, phenytoin doses might have been increased inappropriately in the head trauma patients. The reason head trauma patients had therapeutic unbound concentrations despite lower total concentrations was that the unbound per cent of phenytoin was higher in these patients $(21 \pm 3.2\%)$ than in the epileptic patients $(10 \pm 1.3\%, p < 0.0002)$.

Phenytoin is often administered to head trauma patients for the possible prevention of post-traumatic epilepsy (11). Early establishment of therapeutic concentrations (10-20 mcg/ml total concentration) appears to be of paramount importance in order for prophylaxis to occur (11). The drug concentration that is unbound to plasma proteins is generally considered the pharmacologically active portion (5, 8), and yet it is rarely directly measured due to technical difficulties in separating the unbound drug from the plasma. In most cases, total drug concentrations are assumed to reflect unbound drug concentrations. Phenytoin is highly protein bound (~ 90%) to albumin in normal patients (4, 10) so that slight alterations in protein binding may have a large influence on the unbound concentration. It has been proposed that monitoring unbound phenytoin concentrations (therapeutic range, 1-2 mcg/ml) may be optimal (5, 8). Because of feeding problems associated with comatose head trauma patients, albumin concentrations may be below normal, and phenytoin unbound concentrations altered in relation to total (bound + unbound) concentrations. The purpose of this study was to measure total and unbound phenytoin concentrations in head trauma patients.

METHODS

Ten comatose adult male head trauma patients in whom intravenous phenytoin had been administered for

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the prophylaxis of post-traumatic epilepsy comprised the study group. All had a normal serum biochemistry profile (electrolytes, glucose, BUN, alkaline phosphatase, total bilirubin, creatinine, SGOT, SGPT) and complete blood cell count. Serum albumin concentrations were low for nutritional reasons, although most were receiving hyperalimentation or nasogastric feedings (Table I).

Ten epileptic adult male outpatients who received oral phenytoin as sole therapy for their seizures were the control group. All had normal serum biochemistry profiles (including albumin) and complete blood cell counts. Mean (\pm SD) age and weight were 23.5 \pm 3.0 years and 74.1 \pm 6.2 kg, respectively. The average oral phenytoin dose was 370 \pm 67 mg/day and the mean albumin was 4.0 \pm 0.4 gm/dl. Neither the study nor the epileptic group received any drugs that are known to interact with phenytoin (anticoagulants, barbiturates, benzodiazepines, chloramphenicol, cimetidine, corticosteroids, disulfram, folic acid, isoniazid, phenylbutazone, sulfonamides, or other anticonvulsants).

Total and unbound phenytoin serum concentrations were determined from predose blood drawn 10 to 14 days after patients had been maintained on a constant dose. The concentration determinations were part of each patient's routine care. Total clearance was approximated by dividing the daily phenytoin acid (sodium phenytoin is 92% phenytoin acid) dose by the total phenytoin serum concentration. Unbound clearance was estimated by dividing the daily phenytoin acid dose by the unbound phenytoin concentration. These calculations assume 100% oral bioavailability (6, 7). Phenytoin serum con-

TABLE I Head trauma patient demographics

Patient No.	Age (yr)	Weight (kg)	Daily Pheny- toin dose (mg/ day)*	Albumin (gm/dl)	Type of Feeding†
1	27	80	300	2.7	NG
2	21	75	400	2.0	NG
3	23	90	400	2.2	NG
4	29	68	300	2.6	NG
5	22	72	500	2.3	NG
	22	70	300	2,6	NG
6 7	24	78	300	1.9	HA
	25	72	400	2.5	HA
8 9	22	83	400	2.7	HA
10	26	81	500	2.4	HA
Mean	24.1	76.9	380	2.4	4 11A/6 NG
SD	2.6	6.8	79	0.3	-

^{*} Doses were administered intravenously in equally divided doses every 12 hours.

centrations were determined using a homogenous enzyme immunoassay with a coefficient of variation less than 7% (EMIT-Syva). The unbound phenytoin was separated from serum samples using ultrafiltration (Free Level-Syva). Statistical comparisons between the study and control patients were made using the Mann-Whitney test.

RESULTS

Total phenytoin concentrations were lower in the head trauma patients (6.8 \pm 1.8 mcg/ml) than in the epileptic patients (14.5 \pm 3.0 mcg/ml; p < 0.0002) even though doses were similar (Fig. 1). Unbound phenytoin concentrations were similar in the two groups. Head trauma patients had a mean unbound concentration of 1.4 \pm 0.4 mcg/ml and epileptic patients had an average unbound concentration equal to 1.5 \pm 0.3 mcg/ml (NS, Fig. 2). The reason for similarity in unbound concentrations between the two groups is that the unbound percent ([Free Concentration \times 100]/Total Concentration) was larger in the head trauma patients (21 \pm 3.2%) than in the epileptic patients (10 \pm 1.3%; p < 0.0002).

The total drug clearance was 53.8 ± 13.0 L/day for the head trauma patients and 24.0 ± 5.3 L/day in the epileptic patients (p < 0.0004). Unbound drug clearance was similar for the epileptic patients (237.3 ± 58.7 L/day) and the head trauma patients (259.6 ± 69.5 L/day, NS). Since the steady-state serum concentration for total and unbound drug is determined by the quotient of the daily dose and the respective clearance term, total phenytoin concentrations were decreased in head trauma patients because total drug clearance was larger. However, since unbound drug clearance was similar for both groups, each had similar unbound phenytoin concentrations.

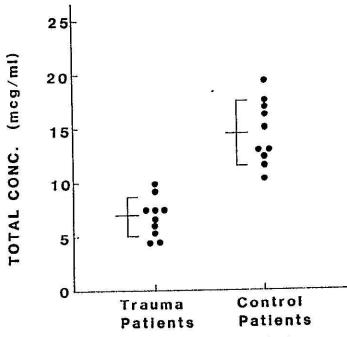


Fig. 1. Total phenytoin concentrations for the head trauma patients were lower (6.8 \pm 1.8 mcg/ml) than those observed in the control patients with epilepsy (14.5 \pm 3.0 mcg/ml; p<0.0002). This was despite the fact that similar doses were administered (trauma patients 380 \pm 79 mg/day, control patients 370 \pm 67 mg/day, NS).

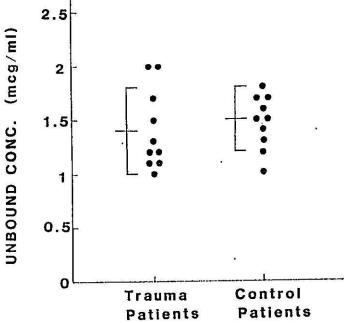


Fig. 2. Unbound phenytoin concentrations were similar in head trauma patients (1.4 \pm 0.4 mcg/ml) and control patients with epilepsy (1.5 \pm 0.3 mcg/ml, NS). Head trauma patients had a higher per cent unbound (21 \pm 3.2%) compared to the control patients (10 \pm 1.3%, p < 0.0002).

DISCUSSION

The unbound serum concentration of a drug is considered to be the pharmacologically available portion: only unbound drug can diffuse across biologic membranes to interact with drug receptors in the tissues and produce

[†]NG = nasogastric tube feedings, HA = hyperalimentation.

the desired pharmacologic effect (5, 8). A major assumption of measuring total drug concentrations is that the per cent unbound remains constant throughout the population. Only in this case does the total concentration reflect the unbound concentration. When the per cent unbound is altered, total concentrations can become very misleading.

In our head trauma patients, total phenytoin concentrations averaged 6.8 ± 1.8 mcg/ml. By monitoring these concentrations alone, doses would have been increased in order to achieve total concentrations between 10 and 20 mcg/ml. However, when unbound concentrations were measured they were found to be in the therapeutic range of 1 to 2 mcg/ml. Increasing the dose would not have been the correct thing to do for our head trauma patients.

Phenytoin is in a class of drugs whose total drug clearance is altered by the unbound per cent (8, 9). In general, as the unbound per cent increases for this group, total clearance increases and the steady-state total concentrations decline. This appears to be the case in the head trauma patients receiving phenytoin because total clearance (53.8 ± 13.0 L/day) was much larger for them than for the epileptic controls (24.0 \pm 5.3 L/day). Unbound clearance is influenced mainly by drug-metabolizing enzyme activity. Both groups were similar with regard to unbound clearance indicating that the intrinsic ability to metabolize phenytoin was similar between the two groups. Phenytoin obeys Michaelis-Menten metabolism and so clearance calculations are dose dependent (1). Because of this, the clearance terms calculated for each patient are dose specific and may change with dosage alterations.

Since phenytoin is highly bound to albumin, the higher unbound per cent in the head trauma patients was probably due to hypoalbuminemia (3). Our head trauma patients received intravenous phenytoin in order to avoid the nasogastric feeding-oral phenytoin absorption interaction (2).

Unbound phenytoin concentrations may be needed in head trauma patients with hypoalbuminemia. These patients appear to have higher unbound percentages in the serum, which can make monitoring total concentrations misleading. Unnecessary phenytoin dosage increases can be avoided by measuring unbound phenytoin concentrations in appropriate patients.

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Group Forming to Count 'The Silent Epidemic'

By KAREN M. HENSON Journal Staff Wither

Those in the know call it "The Silent Epidemic."

It strikes more than 100,000 people each year, and cuts across all racial, religious and socio-economic lines. The majority of its victims are in their late teens or early twenties, and a large percentage of area residents who know firsthand about the nightmare of head injuries will formally charter two local chapters of the National Head Injury Foundation.

The group has a number of specific goals, but they generally boil down to finding a better way to treat and rehabilitate those who suffer trau-

matic head injuries.

Proper treatment of the head injured is crucial. Of the 30,000 to 50,000 people who survive traumatic head injury each year, the majority are left with intellectual impairment that prevents them from returning to a normal life. Without proper rehabilitative therapy, those people can be doomed to life in a nursing home.

Until the advent of elaborate shock trauma units in area hospitals in the 1970s, treatment for head-injured victims was not an issue because the patients rarely survived their initial injuries, according to

Sue Lowe, an Olney resident who is vice president of the new Maryland Chapter of the NHIF.

Like many of those with severe head injuries, Lowe's son was involved in a serious car accident in 1981. He was rushed to the world-renowned shock trauma unit at University Hospital in Baltimore, where a crack trauma team saved his life.

Despite their success in keeping him alive, however, her son Joe remained in a coma for 13 months before dying last October.

"It was one year and 20 days," Lowe said. "You constantly watch your child shrink and shrivel until they die."

In addition to the pain of watching their son lie unresponsive for more than a year, Lowe said she and her husband were distressed by the lack of facilities in the area having coordinated programs for treating those with this type of massive injury.

After a month at University Hospital - where the bills ran close to \$100,000 — the Lowes were forced to put Joe into a Baltimore nursing home. While the home was able to provide the care needed to maintain Joe, it did not have any of the advanced facilities for treating a person with a massive head injury.

Treatment for severely head-injured patients is complex, elaborate and expensive, often requiring a whole gamut of physical and occupational therapy over a period of three to five years, according to Bev Whitlock, a county resident who is president of the local chapter of the NHIF. While a handful of facilities offering the necessary range of therapy exist in the country, the nearest one is located in Erie, Penn. - more than 300 miles away.

Whitlock, who is director of the county's Easter Seals Treatment Center and the mother of a severly brain-damaged child, notes that medical insurance companies often don't realize the extent of rehabilitation required for those with severe injuries. As a result, family members are forced to enter the maze of Medicare services, or try to come up with huge sums of money from their own pockets.

She also notes that recent studies are showing that even those who suffer relatively mild head injuries with only an hour or two of unconsciousness often have problems with memory and personality changes that

show up over time.

Another county woman whose daughter suffered a massive head injury in a car accident two years ago knows firsthand about trying to cope with massive medical bills. After two months in a coma, her daughter began the agonizingly slow process of pulling back into consciousness.

But when she finally left the hospital, her daughter could not walk without assistance, had lapses of memory and trouble speaking and had to be retrained in such basic

functions as using the toilet.

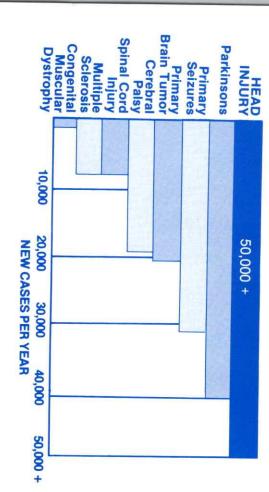
"It's like having a baby in a 20-year-old body," she said. The woman, who asked that her name not be used because of pending litigation in connection with her daughter's injuries, said she was lucky in that she had ties to the medical profession and could locate exactly the right services for her daughter. Others who don't have such ties face an unbelievable hard-

ship, she said. The new local chapters of the NHIF will try to provide help for those needing services by sharing the amassed experience of its members, and also will provide a kind of support group for the families of head

injured patients.

Another of the goals of the group is to push for the establishment of a coordinated treatment facility for head-injured patients in the Washington area. As Lowe points out, the Washington metropolitan area has a wealth of medical talent that could be tapped to provide the necessary expertise for such a facility.

ESTIMATED YEARLY INCIDENCE OF PERSONS LEFT WITH DISABILITY AFTER HEAD INJURY COMPARED TO OTHER IMPORTANT NEUROLOGIC DISEASES



Cerebrovascular disease is the commonest neurological dysfunction accounting for 450,000 cases yearly.

Compared to other neurological diseases the incidence of head injuries is much greater.

TRAUMA IS THE LEADING CAUSE OF DEATH IN THE UNITED STATES FOR PERSONS UNDER THE AGE OF 34, ACCORDING TO THE SURGEON GENERAL'S REPORT, HEALTH UNITED STATES, 1980.

The number of deaths each year, resulting from trauma of the head is estimated at over 140,000. The estimated prevalence of head injuries in the U.S. is 1,000,000 - 1,800,000.

Even more staggering is the fact that 50,000 - 70,000 people a year who survive with a serious head injury, are left with intellectual impairment of such a degree as to preclude their return to a normal life. These figures clearly reflect a problem of epidemic proportions.



50,000 - 70,000 people a year are permanently disabled! Most people who sustain head injuries are under the age of 30, and most are injured as a result of tragic motor vehicle or sports accidents. Accidents that physically disable and intellectually impair for a lifetime.

Until the establishment of NHIF in 1980, no single existing federal, state, or private agency concerned itself exclusively with the unique problems faced by the head injured and their families. Until NHIF, this "lost population" was silently and shamefully closeted away, and inappropriately placed in psychiatric institutions, schools for the retarded, or nursing homes.

Today, the National Head Injury Foundation proudly serves as the only advocacy organization working to improve the quality of life for those persons confronted by "The Silent Epidemic".

The NHIF and its State Associations are a membership organization composed of those families, friends, medical, and social service professionals concerned with the physical and emotional well-being of the head injured.

The NHIF is a non-profit agency supported by membership dues, fund raising events, contributions and grants.

Dedicated to the restoration and maintenance of the dignity of life for the victims of this "Silent Epidemic", the National Head Injury Foundation looks to our friends in public and private business and industry to help us in our cause.

For information on the NHIF and your State Association, write or call:

National Head Injury Foundation, Inc. P.O. Box 567
Framingham, Massachusetts 01701

(617) 879-7473

WHAT IS A TRAUMATIC HEAD INJURY?

Traumatic head injury is an insult to the brain, not of a degenerative or congenital nature but caused by an external physical force, that may produce a diminished or altered state of consciousness, which results in impairment of cognitive abilities or physical functioning. It can also result in the disturbance of behavioral or emotional functioning. These impairments may be either temporary or permanent and cause partial or total functional disability or psychosocial maladjustments.

PREVALENCE

Nationally, the number of deaths each year resulting from trauma to the head is estimated at over 140,000. Each year 50-70,000 individuals survive their injuries, but are left with perceptual and cognitive impairment of such a degree as to preclude their return to a normal life. The majority of people sustaining head injuries are under the age of 30.

In Maryland it is estimated that 7,200 people each year sustain head injury. Because of our excellent emergency medical services, more people survive, and with graver injuries, than would have survived just a few years ago.

These figures clearly reflect a problem of epidemic proportions — a "Silent Epidemic."

PRIORITIES

Stimulate public and professional awareness of the unique problems of the head injured.

Provide a central clearinghouse of information and resources.

Represent the interests of the head injured in State and Federal legislative processes.

Work toward increased public and private funding for rehabilitation and for transitional and permanent living arrangements.

Encourage development of support groups throughout the state.

Sponsor general membership meetings and social events for the head injured and their families.

Publish a newsletter twice a year

Participate in support groups.

Support specialized programs for the head injured stressing coordination of the following: cognitive retraining, speech therapy, physical therapy, occupational therapy, memory training, social/behavioral training, vocational and educational rehabilitation — leading to independent living

Donations for a memoriam or commemorative occasion are appreciated and tax deductible. Please write name of member(s) on check. Make check payable to: Maryland Head Injury Foundation, Inc.

MEMBERSHIP APPLICATION

Name	Phone_	(h)	(w)		
Address					
City	State	Zip			
Please check:					
Head injured person	Professional: Field				
Family of head injured	Friend				
If you want to serve on a committee w	hich one?				
Budget, Finance &	Legislative	Program Relat	n & Public ions		
By-Laws	Membership	Newsle	tter		
Type of membership (tax deductible)					
Individual and/or family \$25	Supporting \$50	Century Club	\$100		
Patron \$500	Sponsor \$1,000	.00 & up			



INJURED AND THEIR FAMILIES HELP FOR THE HEAD

Chapter of the National Head Injury Foundation, Inc.

FOUNDATION, INC. HEAD INJURY

MAKYLAND

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The statewide problem of head injury — funding and treatment availability — must be ad-

Head injured individuals and their families need no longer face this tragedy alone. MHIF, through

MHIF stands ready to act as catalyst and supporter of those who wish to work toward solutions

Injury Foundation, Inc. It is a non-profit, tax-exempt organization formed to provide support, informa-The Maryland Head Injury Foundation, Inc. (MHIF) is the Maryland Chapter of the National Head

Claire Fisher, R.N. - Millersville Jane Gerber, MSW - Baltimore Mary Krause, R.N.- Hanover Jerome S. Shipman - Potomac

dressed; we welcome your participation in this effort.

its board members, staft, and support groups, stands ready to help.

for this population of survivors, and to work with those who seek its prevention.

tion, education, and advocacy for head injured people and their families.

Jane Vickers, MSW - Baltimore Bernice Wolfson, MSW - Baltimore Deborah A. Yates, MS, CRC - Columbia

Maryland Head Injury Foundation, Inc.

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