HAWAII MEDICAL JOURNAL

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Contents

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Ipu Heke

Depicting a Hawaiian Gourd Drum.

Editorial

EGYPT-HAWAII CONNECTIONS

Norman Goldstein MD, FACP
Editor, Hawaii Medical Journal

Despite the fact that Egypt is halfway around the world from Hawaii, we have notable connections to one of the oldest civilizations.

Long before the days of modern communication and travel (the period between 3rd century BC and 3rd century AD) 10,000 mummies were buried near the Bahariya oasis, 260 miles southwest of Cairo. Robert Littman, Professor of Classics in the Department of Languages and Literature at the University of Hawaii and his fellow Egypt researcher, DeWolfe Miller, Professor of Epidemiology, noted that these mummies are unlike the residents of royal tombs in the famed pyramids. The Bahariya mummies come from all strata of society - rich, poor, and middle class - giving researchers an unprecedented opportunity to systematically examine a substantial cross section of society.[1]

To conduct this research, our two erudite U. H. professors assembled a team including Egyptologists, paleopathologists, epidemiologists, bio-archeologists, radiologists and physicians to work with Zabi Hawass, Chair of Egypt's Supreme Council of Antiquities who discovered the Bahariya mummies in 1996.

Littman received his BA and PhD at Columbia University and his M.Litt at University of Oxford, and lectures on the Egyptian Language, as well as Hebrew, Greek and Latin. In 2004, he was awarded the University of Hawaii Chancellor's Citation for Meritorious Teaching. So when Stanley B. Snodgrass told me of his memoir, Bugchasers of Egypt, who better could I ask to do a Book Review for the Hawaii Medical Journal? Littman actually took the book on a recent flight to Egypt. The book is about Stanley's service between 1946-1948 for the USNAMRU 3 (NAval Medical Research Unit). At the time, his unit was battling epidemics of relapsing fever and cholera, and used the first cholera vaccine.

Upon reading Stan's book, Gerry Michael, Emeritus Dean and Professor of Public Health at the University of Hawaii, wrote:

"Dear Colleague:
You are to be congratulated in having committed to writing a most useful and important segment of the long history of the contribution to Global Health by the United States Navy and its dedicated service personnel."

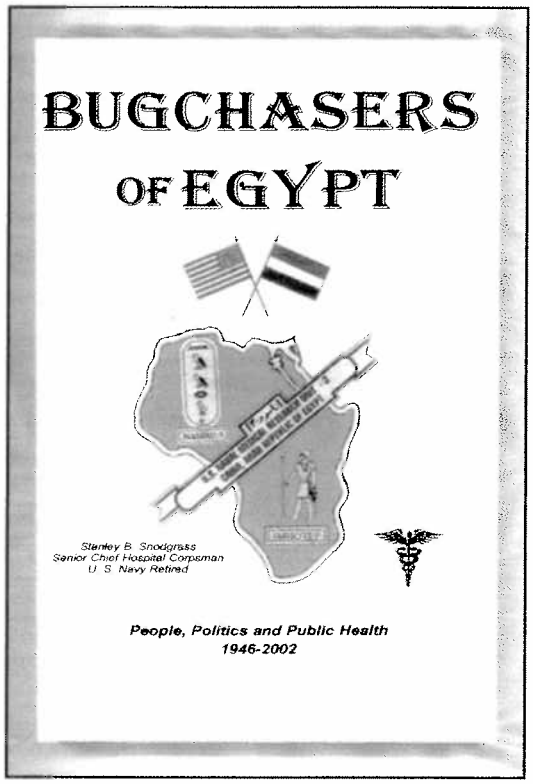
A copy of The Bugchasers of Egypt can be obtained by calling the author at 808-396-7407.

Mahalo to our Hawaiian Egyptologists, Stan Snodgrass, DeWolfe Miller, and Robert Littman.

Reference

1. Mālamalama 28;1, p 11. Jan '03

Book Review



Bugchasers of Egypt, Stanley B. Snodgrass, Xlibris Corporation [www.Xlibris.com] 2003; 348 pp.

Reviewed by:
Robert J. Littman PhD
University of Hawaii

This book contains memoirs relating the experiences of Stanley Snodgrass and various colleagues in fighting tropical diseases mainly in Egypt, as well as Africa and China. Snodgrass, after many years' hiatus, continued his career in public health in Honolulu, where he has now retired. The connecting thread of these memoirs is Namru 3. Namru is an acrostic for the US Naval Medical Research Unit. This organization originated in World War II to combat typhus, malaria and other epidemic and tropical diseases faced by soldiers and civilian populations. In 1946 Namru 3 was set up in Cairo, Egypt. It still functions today as the oldest and most versatile overseas infectious disease laboratory in the Department of Defense. It has been responsible since its foundation for helping control epidemics in Africa and preventing their spread to other parts of the world.

In 1946 Snodgrass was assigned to Namru 3. At the time he was not yet 21, a high school dropout with a wife pregnant with their first child. His only training was a five month course in the Navy School of Epidemiology. The Navy offered him a two year extension and a posting to Cairo. Young and adventurous, he grabbed the opportunity. As soon as he stepped through the door of the US Embassy in Cairo, where Namru 3 was then headquartered, he was dispatched to deal with an epidemic of relapsing fever in Imbaba. He soon helped fight a major cholera outbreak in 1947 which devastated Egypt, and saw the first use of cholera vaccine.

Snodgrass's memoirs of Namru 3 cover the period 1946-1948, and take up the first 7 chapters. This is followed by 12 chapters containing the memoirs of Namru 3 by Billy Cook, Warren Sanborn, and Raymond Warren, with connective narrative by Snodgrass. Among the topics covered are the 1947 outbreak of cholera, meningitis in Morocco, the formation of Namru 5 in Ethiopia, the expulsion of Namru from Egypt during the 1967 Six Day War between Egypt and Israel.

The memoirs are written in a breezy entertaining style. Anyone contemplating a career in epidemiology should read these accounts. For physicians whose practice keep them in the Western World, and who have never seen an epidemic of cholera, or Rift Valley Fever, it is an instructive look into how public health functions in the face of rampant disease and into the history of medicine. For the layman the book is a fascinating account of medical detection and practice in the Third World.

Ring vaccination versus mass vaccination in event of a smallpox attack

Chuen-Yen Lau MD, MPH, MS, Bryan Wahl MD, and Wendell K.S. Foo MD

Chuen-Yen Lau MD, MPH, MS

Bryan Wahl MD

Wendell K.S. Foo MD

Authors:
- School of Public Health, UCLA (C.Y.L.)
- University of Hawaii John A. Burns School of Medicine Class of 1999, Hospitalist, Alta Bates Medical Center, Berkeley, CA (B.W.)
- Assistant Clinical Professor Department of Surgery University of Hawaii John A. Burns School of Medicine (W.K.S.F.)

Correspondence to:
Wendell K.S. Foo MD
4224 Waialae Ave. Suite 5-311
Honolulu, HI 96816-5307
wendellfoo@hawaii.rr.com

Abstract

Since vaccination is critical in responding to smallpox exposure, vaccination strategies must be evaluated during bioterrorism preparedness. Information on historical factors, smallpox characteristics, public health capabilities and hypothetical attack scenarios was used to evaluate major vaccination strategies. In event of a smallpox attack, the optimal strategy is situational; mass vaccination may be best for dense island populations such as Oahu.

Introduction

Since the bombing of the World Trade Center on September 11, 2001 and the subsequent cases of anthrax, much concern has arisen regarding use of smallpox as a weapon of bioterror. Though smallpox officially exists in only two secure laboratories, one in the United States and one in Russia, other countries may harbor undocumented stores of the virus. It is feared that terrorists might use these illicit stores to generate biological weapons. Thus, plans for protecting the population in the event of a smallpox attack must be formulated.

Vaccination will play a central role in controlling the sequelae of a smallpox attack. The optimum strategy for immunization is unclear. Mass and ring vaccination are the two major tactics under consideration. In both, infected individuals would be isolated. However, mass vaccination would entail indiscriminate vaccination of the entire population while ring vaccination, also known as surveillance and containment, would involve targeted immunization of primary and secondary contacts. Which strategy would be most effective in preventing spread of smallpox, especially in island populations? What role does the risk of vaccination play in selecting a strategy? Given resource limitation, are both strategies equally feasible?

Methodology

Articles pertaining to smallpox vaccination policy were identified by searching PubMed. Keywords bioterror, bioterrorism, smallpox, vaccination and vaccine were used as the following string: (bioterror OR bioterrorism) AND (smallpox) AND (vaccine OR vaccination). All article types were considered. Language was limited to English. Information on historical factors, smallpox viral characteristics, public health capabilities and hypothetical attack scenarios was extracted from identified articles. Information was also obtained from the Centers for Disease Control website and textbooks. This information was used to evaluate major vaccination strategies.

Results

242 articles were identified using the delineated search strategy. Ring vaccination and mass vaccination were established as the major vaccination policies under consideration for responding to smallpox attacks. Based on titles and available abstracts, 32 articles were selected for use in further evaluation of vaccination strategies.

Pros and cons of each vaccination strategy are shown in Table 1. Discussion of these factors in light of historical experience and hypothetical scenarios follows below.

Discussion

Historical Lessons

History provides clues as to the effectiveness of both ring and mass vaccination. Though smallpox was declared eradicated in 1980, the struggle to reach that point was arduous. Smallpox had long been a deadly, feared disease, which killed in epidemic waves. During the late eighteenth century, Edward Jenner began promote vaccination with cowpox to prevent smallpox. His work eventually led to a vaccinia based smallpox vaccine. However, epidemics continued to decimate significant numbers of people.[1]

The first case of smallpox in Hawaii was diagnosed in 1853. It reportedly originated from a ship out of Boston. The subsequent epidemic afflicted 9,082 of Oahu's population of 19,126, with 5,748 deaths. Consequently, the legislature mandated mass vaccination for smallpox in 1854. Despite this measure, Hawaii

experienced three more smaller smallpox outbreaks in 1861, 1873, and 1882. These epidemics, with 282 additional deaths, were likely caused by failure to achieve a 100% vaccination rate.[2]

In 1967, the World Health Organization launched the Intensified Smallpox Eradication Program. The program initially also relied upon mass vaccination, which proved efficacious in Western countries. However, again, 100% vaccination rates were impossible to achieve and smallpox continued to plague developing nations, particularly those with dense populations. Meanwhile, events in Nigeria stimulated evolution of a new strategy. Though most of Nigeria's population had been vaccinated, a religious sect that had resisted vaccination developed an outbreak. Faced with limited resources and delivery delays, eradication campaign staff learned quickly to isolate infected individuals and vaccinate others to control disease spread. Within a few years, this method of surveillance and containment, known as ring vaccination, had successfully controlled several outbreaks in India and become a worldwide standard.[3,4]

With these two major vaccination strategies, smallpox was controlled over several decades. The last US case occurred in 1949.[5] Nonetheless, vaccine was still administered to all children, military recruits and tourists until 1972. Routine smallpox immunizations were subsequently discontinued in the US, as the risks of vaccine adverse reactions were felt to outweigh the risk of a future smallpox epidemic.[6] However, high-risk individuals continued to receive vaccine.[1] Worldwide, the last natural case occurred in Somalia in 1977. Successful smallpox management thus relied initially upon mass vaccination, and later ring vaccination strategies.

The Smallpox Threat

Though natural smallpox outbreaks are no longer a public health threat, officials fear that the virus may be employed as a weapon of bioterror. Given this scenario, selection of a vaccination strategy cannot be based solely upon historical factors. Smallpox was not traditionally considered a biological weapon; it didn't start from a point-source; and infectious characteristics were more predictable. At present, we do not know whether smallpox will be re-introduced to our now naïve population. If smallpox were re-introduced, would it be a mutated, more deadly form? Would it spread similarly to historical smallpox? And would it be suddenly introduced in one location or simultaneously in multiple locales? All of these issues influence decisions regarding a vaccine strategy.

Since the probability of a smallpox bioterrorist event is low, pre-event vaccination of the general population is not recommended. Only individuals likely to participate in an initial response to a smallpox event have been immunized.[7] Others will receive vaccination in response to a known exposure, rather than prophylactically.

Table 1.— Mass Vaccination Versus Ring Vaccination In the Event of a Smallpox Attack

MASS VACCINATION	RING VACCINATION
PROS:	PROS:
• Entire population is prepared	• Efficient use of resources
• Herd immunity	• Higher likelihood intended recipients are vaccinated
• Less intense surveillance required	• Effective up to 4 days post-exposure
• Public sense of security	• Incubation non-contagious; Prodrome sometimes contagious
• Special advantages to dense island populations such as on Oahu	• Likely effective for less populated Neighbor Islands, especially more geographically isolated communities such as Hana
CONS:	CONS:
• Resource requirements for administering vaccine	• Resource requirements for surveillance after attack
• Pockets of susceptibility may be overlooked	• Time required to trace primary / secondary contacts
• Everyone must consent	• Risk of overlooking high-risk individuals
• Adverse reactions / contraindications	• Public demand

Vaccination Strategies

Once a known smallpox event has occurred, agencies must be prepared to vaccinate at-risk individuals. This can be accomplished by either mass or ring vaccination. Each strategy has pros and cons.

Mass Vaccination

A mass vaccination response would ensure that the entire population is prepared for subsequent contact with infected individuals as well as for future attacks. Thus it would decrease the need for surveillance of contacts and reduce the extent of vigilance necessary. It would also provide herd immunity, reducing propagation of infection if contagious individuals did interact with the uninfected. Thus, this strategy would likely reduce the impact of future attacks. It might also give the public a sense of security, decreasing the probability of popular hysteria in response to perceived risk.

Nonetheless, mass vaccination has significant drawbacks. It requires tremendous resources. Not only would we need sufficient stocks of vaccine for an entire population, but also adequate trained personnel to administer it. The costs associated with such an undertaking would be staggering. Another problem with mass vaccination is its potential to inadvertently overlook certain groups of individuals, thus resulting in pockets of susceptibility. Along the same lines, at least 90% of individuals must submit to vaccination for this strategy to be effective. Mandatory vaccination may infringe on the individual's right to informed consent and to refuse medical care. Thus initiation of mass vaccination could be delayed by legal proceedings or formulation of guidelines.

Furthermore, the presently used vaccinia-based vaccine has side effects. Though rare, the risks associated with vaccination may outweigh potential benefits if the threat of smallpox exposure is low. Constitutional symptoms, eczema vaccinatum, myopericarditis, generalized vaccinia, progressive vaccinia and postvaccinial encephalitis are potential adverse reactions, but are more common among primary vaccinees than re-vaccinees.[8] In 450,293 healthy military vaccinees, one case of encephalitis and thirty-seven cases of acute myopericarditis developed after vac-

cination; there were no cases of eczema vaccinatum or progressive vaccinia.[9] However, adverse reactions may be more common in the general population. In a study on smallpox vaccine dilutions, fifteen of 148 vaccinees developed dermatologic reactions.[10]

Under normal circumstances, contraindications to smallpox (vaccinia) vaccine include dermatidities, immunodeficiency, immunosuppression, pregnancy, allergy to vaccine component, age under 18 years, concurrent illness, and breastfeeding. For pre-event prophylaxis, people with contraindications are not vaccinated because the risk of adverse reaction outweighs potential benefit. However, in the event of an actual attack, the benefits of vaccination outweigh the risks. Since there are no contraindications to post-exposure vaccination, the likelihood of adverse reactions increases. Mass vaccination could thus result in increased morbidity and mortality in people with pre-exposure contraindications.[11]

Ring Vaccination

Ring vaccination also has its pros and cons. On the positive side, ring vaccination strategy may utilize resources more efficiently. Because only primary and secondary contacts of infected individuals would be vaccinated, less vaccine and labor would be required to perform the actual immunizations. Focused surveillance with targeted vaccination would probably also increase the likelihood that intended recipients are vaccinated.

Were vaccination effective only if given prior to exposure, surveillance and containment might not be a prudent option. However vaccination is reportedly effective for four days post-exposure and can be supplemented with vaccinia immunoglobulin.[12] Although there are no FDA-approved antiviral medications indicated for smallpox at this time, the experimental compound hexadecyloxypropyl-cidofovir (HDP-cidofovir), has reportedly inhibited smallpox viral replication in early in vitro and mice studies.[13] Lastly, people are not infectious during the incubation period. Some become contagious when the prodromal symptoms begin, while others are non-contagious until the rash occurs. This course facilitates timely identification. Given these circumstances, at-risk individuals would still receive vaccination within a safe period. Thus surveillance and containment is a reasonable tactic.

On the other hand, there are drawbacks to ring vaccination. It requires rapid identification of exposed individuals, and thus more intense surveillance than mass vaccination once an attack is recognized. This sudden demand for labor and resources could become a serious problem in the event of multiple attacks within a brief period. Furthermore, ring vaccination would only protect primary and secondary contacts of known exposures. Given the possibility that some cases might not be detected in a timely manner, this could increase the risk of non-immunized individuals developing smallpox. Another problem is that members of the non-exposed general public would likely demand vaccination. Public opinion polls have suggested that approximately half of US adults would want to be vaccinated when the smallpox vaccine is available.[10] Such exigency would lead to deviations from protocol and confusion regarding vaccine administration.

Best of Both Worlds

Given the assumed characteristics of smallpox, the optimal method of vaccinating the general public would depend primarily upon the type of attack sustained. If an attack or few attacks were localized, ring vaccination would be a more reasonable strategy. It would facilitate efficient use of resources, appropriate protection and minimization of adverse reactions. However, in the event of multiple attacks or high risk of multiple subsequent attacks, mass vaccination would be more appropriate. Mass vaccination would provide protection to the large numbers at risk and reduce the need for intensive surveillance. This situation-based approach would maximize resource utilization while minimizing morbidity and mortality. Moreover, mass vaccination may be especially advantageous in dense island populations such as Oahu, to best avoid a reprisal of the devastating effect the virus had in Hawaii's smallpox- naïve population in the 19th century. In contrast, ring vaccination may be preferred on the less populous neighbor islands, especially in more geographically isolated communities such as Hana where surveillance may be conducted more readily and efficiently.

Mathematical models evaluating smallpox vaccination policy options are in agreement with this situational approach. Modeling takes into account several possible scenarios, characteristics of the virus, response logistics and varying probability of attack.[14,15] In general, models support a ring vaccination strategy so long as the probability of attack remains low. Once the probability of attack exceeds a particular threshold, which varies amongst models, mass vaccination may be more practical.

Regardless of vaccination strategy employed, education of the lay public must be addressed. The public should understand the mechanisms and implications of bioterror, specifically smallpox, before an event occurs. Studies have shown that the public is not knowledgeable about smallpox. In one survey, the majority of respondents believed there exists an effective treatment for smallpox, that there have been cases of smallpox within the past five years and that there is not enough vaccine for everybody in the US.[16] Such misconceptions could propagate in the community, contributing to inappropriate reactions, for example hysteria. Education would prepare the public to respond calmly and aptly.

Conclusion

In conclusion, mass vaccination and ring vaccination are the two major vaccination strategies that may be used in response to a smallpox bioterror event. Mass vaccination, which entails indiscriminate vaccination of the entire population, would be appropriate for multiple attacks, if risk of subsequent attacks is high, and in dense urban island populations such as Oahu. Ring vaccination, which entails surveillance with subsequent vaccination of high-risk individuals would be more appropriate for a localized smallpox attack and low risk for subsequent attack, such as on less populated, more geographically isolated communities on the Neighbor Islands. Thus, both ring and mass vaccination have a place in response to smallpox exposure. The choice between the two is situational.

Acknowledgements

The authors thank Dr. Robert Kim-Farley and Susan Foo, MAE for their invaluable feedback regarding this manuscript.

*See "**References**" p. 53*

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Descriptive Epidemiology of Congenital Hydrocephaly in Hawaii, 1986-2000

Mathias B. Forrester BS and and Ruth D. Merz MS

Mathias B. Forrester BS

Ruth D. Merz MS

Authors:
Hawaii Birth Defects Program, Honolulu, HI 96817

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Correspondence to:
Ruth D. Merz MS
Administrator, Hawaii Birth Defects Program
76 North King Street, #208
Honolulu, HI 96817-5157
Tel: 808-587-4120
Fax: 808-587-4130
E-Mail: hbdp@crch.hawaii.edu

Abstract

Using data from a birth defects registry, this study examined the epidemiology of hydrocephaly in Hawaii during 1986-2000. There were 294 cases of hydrocephaly, resulting in a rate of 10.4 per 10,000 live births. The hydrocephaly rate was lower with increased maternal age and female sex and higher with lower birth weight, lower gestational age, and multiple gestation pregnancy.

Introduction

Congenital hydrocephaly, enlargement of the cerebral ventricles and excessive accumulation of cerebrospinal fluid (CSF) in the cranium, is one of the most common congenital central nervous system (CNS) defects. Its prevalence in the United States has been reported to be 7-15 per 10,000 births.[1-4]

Congenital hydrocephaly is heterogenous in etiology, occurring secondary to other CNS defects (spina bifida, Arnold-Chiari malformation, holoprosencephaly, hydranencephaly, cysts, and tumors); chromosomal abnormalities (trisomies 13 and 18, 9(p), and triploidy); other syndromes (Walker-Wardburg, Meckel, Smith-Lemli-Opitz, and achondroplastic dwarfism); congenital infections (toxoplasmosis, syphilis, cytomegalovirus, rubella); and intraventricular hemorrhage.[5-7] However, in a number of cases the cause of congenital hydrocephaly is not known. A large percentage of infants with hydrocephaly have other birth defects as well.[6,8-10]

There have been few population-based studies exclusively examining the descriptive epidemiology of hydrocephaly,[6,8,11-14] only one of which was performed in the United States.[3] However, these and other investigations that included hydrocephaly among other birth defects have reported hydrocephaly risk to be influenced by sex,[3,4,6,12,14-17] plurality,[16,18-20] gestational age,[6] birth weight,[6,16,21] time period,[11-13,16] race/ethnicity,[22,23] and maternal age.[11]

The purpose of this investigation was to examine the relationship between congenital hydrocephaly and a variety of diagnostic and demographic factors in Hawaii during a recent fifteen-year period.

Methods

Data were provided by the Hawaii Birth Defects Program (HBDP), an active, statewide birth defects surveillance registry.[24] Inclusion criteria for the HBDP consists of all infants and fetuses of all pregnancy outcomes (live births, fetal deaths, elective terminations) regardless of gestational age where the pregnancy ended in Hawaii and one or more reportable birth defects had been diagnosed between conception and one year after delivery. Trained HBDP staff review records at all birth and pediatric tertiary care hospitals, facilities that perform elective terminations secondary to fetal anomaly, cytogenetic laboratories, and genetic counseling centers and all but one of the prenatal ultrasound facilities in the state to identify eligible infants and fetuses and to collect diagnostic, demographic, and health information.

This study included as cases all pregnancy outcomes with congenital hydrocephaly delivered in Hawaii during 1986-2000. Diagnoses of congenital hydrocephaly included the following terminology: hydrocephaly, ventriculomegaly, (cerebral) ventricular dilation/dilatation, enlarged (cerebral) ventricles. Measurements of ventricular size or CSF pressure were not used for case criteria because such information was not readily found in the medical records available to the HBDP. Cases of hydrocephaly associated with spina bifida (n=77) were excluded from this analysis to be consistent with the definition of hydrocephaly included in the National Birth Defects Prevention Network annual report[25] and to allow for comparison with some of the literature which also excluded cases of hydrocephaly associated with spina bifida or neural tube defects.[6,13,14] Cases of hydranencephaly (n=13) were also excluded from the analyses, as were all cases where the hydrocephaly diagnosis was listed as "possible" or "probable" (n=18). The HBDP does not collect cases of hydrocephaly secondary to intraventricular hemorrhage.

The total rate of hydrocephaly was calculated and the defect's distribution by pregnancy outcome determined. The proportion of cases with other major birth defects was identified and the distribution of other birth defects listed. The hydrocephaly rate by delivery year was computed and evaluated for secular trends. No attempt was made to adjust the year of delivery for elective terminations and fetal deaths should the

pregnancies have gone to term.

The hydrocephaly rate was calculated by maternal age, infant sex, plurality, gestational age (for live births alone), birth weight (for live births alone), residence at delivery, and maternal race/ethnicity. The rates among the various subgroups were then compared by calculating the rate ratio.

Residence at delivery was categorized as county and also whether the woman lived in metropolitan Honolulu (zip codes starting with 968) or the rest of Hawaii (zip codes starting with 967). Deliveries to non-Hawaii residents (n=11) were excluded from the analysis of residence. Maternal race/ethnicity was classified as white, Far East Asian (Japanese, Chinese, Korean), Pacific Islander (Hawaiian, Samoan, Guamanian), and Filipino. Maternal race/ethnicity listed as other (n=28) or unknown (n=11) was excluded from the analysis of race/ethnicity. Values were not always available for all of the variables, so the sums of the subgroups will not always equal the total number of cases.

Denominators were obtained from the Hawaii Department of Health Office of Health Status Monitoring as derived from birth certificates. Fetal death certificate information was not also used because the data were considered to be less complete. Ninety-five percent confidence intervals (CIs) were calculated by Poisson probability. Secular trends were analyzed by the Chi-square tests for trend.

Results

There were a total of 294 cases of congenital hydrocephaly identified in Hawaii among 1986-2000 deliveries. At the same time there were 281,866 total live births, so the resulting hydrocephaly rate was 10.4 per 10,000 live births (95% CI 9.3-11.7). Live births comprised 255 (86.7%) of the cases, while 21 (7.1%) were fetal deaths and 48 (16.3%) were elective terminations. If fetal deaths and elective terminations were excluded, the hydrocephaly rate was 9.1 per 10,000 live births (95% CI 8.0-10.2).

Of the total hydrocephaly cases, 86 (29.3%) were isolated and 208 (70.7%) had other major birth defects. A list of other birth defects diagnosed among hydrocephaly cases is provided in Table 1. The most common other structural birth defects were microcephaly, ventricular septal defect, and cleft lip with/without cleft palate. The results of a cytogenetic analysis was known for 135 (45.9%) of the cases. Chromosomal abnormalities were detected in 26 cases (8.8% of all of the cases or 19.3% of those cases with a cytogenetic analysis). The more common chromosomal abnormalities were trisomy 21, trisomy 18, trisomy 13, and Turner syndrome. An additional 26 (8.8%) of the cases had other syndromes, the most common of which were Sotos syndrome, Aicardi syndrome, amniotic band anomalad, and Pfeiffer syndrome.

Table 1.— Distribution of other major birth defects in congenital hydrocephaly cases, Hawaii, 1986-2000.

Diagnosis	Number	%
Anencephaly	2	0.7
Encephalocele	7	2.4
Holoprosencephaly	5	1.7
Microcephaly	25	8.5
Anophthalmia/Microphthalmia	8	2.7
Cataract	2	0.7
Glaucoma	1	0.3
Anotia/microtia	2	0.7
Truncus arteriosus	2	0.7
Transposition of great arteries	3	1.0
Tetralogy of Fallot	4	1.4
Single ventricle	1	0.3
Ventricular septal defect	22	7.5
Atrial septal defect	11	3.7
Endocardial cushion defect	1	0.3
Pulmonary valve atresia and stenosis	6	2.0
Aortic valve stenosis	2	0.7
Coarctation of aorta	3	1.0
Interrupted aortic arch	1	0.3
Choanal atresia or stenosis	4	1.4
Cleft palate	6	2.0
Cleft lip with/without cleft palate	17	5.8
Esophageal atresia and/or tracheoesophageal fistula	3	1.0
Pyloric stenosis	3	1.0
Small intestinal atresia/stenosis	3	1.0
Rectal and large intestinal atresia/stenosis	4	1.4
Malrotation of intestines	1	0.3
Hypospadias and epispadias	8	2.7
Renal agenesis/hypoplasia	1	0.3
Cystic kidney	7	2.4
Obstructive genitourinary defect	10	3.4
Congenital hip dislocation	4	1.4
Polydactyly	3	1.0
Syndactyly	11	3.7
Reduction deformity of upper limbs	4	1.4
Reduction deformity of lower limbs	1	0.3
Craniosynostosis	10	3.4
Diaphragmatic hernia	3	1.0
Omphalocele	3	1.0
Gastroschisis	1	0.3
Chromosomal abnormalities	26	8.8
Trisomy 21	6	2.0
Trisomy 13	2	0.7
Trisomy 18	6	2.0
Turner syndrome	2	0.7
Other syndromes	22	7.5
Aicardi syndrome	2	0.7
Amniotic band anomalad	2	0.7
Apert syndrome	1	0.3
Beare-Stevenson syndrome	1	0.3
Caudal regression syndrome	1	0.3
CHARGE association	1	0.3
Crouzon syndrome	1	0.3
Fryn syndrome	1	0.3
Neu-Laxova syndrome	1	0.3
Pallister-Killian syndrome	1	0.3
Pena-Shokeir syndrome	1	0.3
Pfeiffer syndrome	2	0.7
Prader-Willi syndrome	1	0.3
Sotos syndrome	3	1.0
Sturge-Weber syndrome	1	0.3
Waardenburg syndrome	1	0.3
Warburg syndrome	1	0.3
Total	**294**	

The list of birth defects is not intended to be comprehensive but to include those defects associated with infant mortality and morbidity, are easily diagnosed, or require health care intervention.

Table 2.— Rate per 10,000 live births of congenital hydrocephaly by various demographic and clinical factors, Hawaii, 1986-2000.

Demographic factor	Total live births	No.	Rate	Rate ratio	95% CI[a]
Maternal age (years)					
≤19	28,492	34	11.9	1.01	0.70-1.41
20-24	73,325	76	10.4	0.87	0.69-1.09
25-29	79,250	94	11.9	ref	
30-34	63,803	53	8.3	0.70	0.52-0.92
35-39	30,472	28	9.2	0.78	0.51-1.12
≥40	6,065	8	13.2	1.11	0.48-2.19
Maternal age (years) - chromosomal abnormalities excluded	28,492	33	11.6	1.01	0.69-1.42
≤19	73,325	69	9.4	0.82	0.64-1.04
20-24	79,250	91	11.5	ref	
25-29	63,803	47	7.4	0.64	0.47-0.85
30-34	30,472	24	7.9	0.69	0.44-1.02
35-39	6,065	3	4.9	0.43	0.09-1.26
≥40					
Race/Ethnicity	74,236	77	10.4	ref	
White	51,264	39	7.6	0.73	0.52-1.00
Far East Asian	78,396	88	11.2	1.08	0.87-1.33
Pacific islander	51,795	51	9.8	0.95	0.71-1.25
Filipino					
Geographic area	223,318	210	9.4	ref	
Honolulu	31,856	33	10.4	1.10	0.76-1.55
Hawaii County	27,548	29	10.5	1.12	0.75-1.61
Maui County	13,562	11	8.1	0.86	0.43-1.54
Kauai County					
Metropolitan Honolulu	84,949	69	8.1	0.74	0.58-0.94
Rest of Hawaii	195,843	215	11	ref	
Sex					
Male	144,835	157	10.8	ref	
Female	136,597	129	9.4	0.87	0.73-1.04
Birth weight (live births)					
<2,500 grams	19,752	101	51.1	11.12	9.06-13.51
≥2,500 grams	258,730	119	4.6	ref	
Gestational age (live births)					
<38 weeks	43,151	136	31.5	7.94	6.66-9.40
≥38 weeks	224,321	89	4.0	ref	
Plurality					
Singleton	274,512	275	10.0	ref	
Multiple birth	5,723	19	33.2	3.31	2.00-5.18

[a]CI, confidence interval.

The hydrocephaly rate varied widely over the time period, and no secular trend was identified (p=0.101). However, if the fifteen-year period is divided into three five-year periods (1986-1990, 1991-1995, 1996-2000), the hydrocephaly rate in 1991-1995 was higher than the rate in 1986-1990 (rate ratio 1.05, 95% CI 0.86-1.26). The hydrocephaly rate in 1996-2000 was lower than the rate in 1986-1990 (rate ratio 0.83, 95% CI 0.66-1.03) and significantly lower than the rate in 1991-1995 (rate ratio 0.79, 95% CI 0.63-0.98).

The hydrocephaly rate by various demographic and clinical factors is presented in Table 2. Hydrocephaly rates tended to be lower for the older maternal age groups, particularly when those cases with a known chromosomal abnormality are excluded. This is more clear when maternal age is grouped as less than 30 years and 30 years or greater. In these circumstances, the hydrocephaly rate is substantially lower among the older maternal age group for all cases (rate ratio 0.79, 95% CI 0.63-0.97) and for cases without known chromosomal abnormalities (rate ratio 0.69, 95% CI 0.54-0.87).

The rate of hydrocephaly varied among the four racial/ethnic groups, but the differences were not statistically significant. Hydrocephaly rates did not differ significantly by county of residence but were substantially lower in metropolitan Honolulu when compared with the rest of the state. Although the hydrocephaly rate was higher among males than females, the difference was not statistically significant. The rate of hydrocephaly was markedly higher among multiple births and live births with lower birth weight and gestational age.

Discussion

This population-based study examined the descriptive epidemiology of congenital hydrocephaly during a recent fifteen-year period. Although other population-based studies in the United States have examined hydrocephaly, in addition to a number of other birth defects, with respect to one or several potential risk factors, there is only one other known population-based investigation in this country that focused on hydrocephaly and a variety of demographic and clinical variables.[3]

The total hydrocephaly rate identified in this study (10.4 per 10,000 live births) is higher than that reported for New York (7.8),[1] California (7.6),[2] and Utah (7.0),[3] and lower than the rate for Alabama (15.2).[4] However, hydrocephaly rates appear to vary widely within the United States.[25] The differences in rates may reflect differences in case definition, ascertainment (active, passive), and types of pregnancy outcomes included (live births, fetal deaths, elective terminations).

Over 70% of the hydrocephaly cases in the current investigation had other major birth defects. This is higher than the 40%-55% rates reported in other studies,[6,8-10] although it is consistent with the 70%-80% rate presented in a review article.[5] The differences in rates between the present study and the literature may be due to differences in thoroughness of identification of additional birth defects or definition of additional birth defect. The chromosomal abnormality rate for hydrocephaly was higher than the 5% reported in another study[6] but consistent with the 8-10% mentioned in others.[8,12] The more common types of chromosomal abnormalities observed among the hydrocephaly cases (trisomies 21, 13, and 18) had been reported in the literature.[2,5,6]

The hydrocephaly rate varied widely over time, and no clear secular trend was identified. However, the rate in the last five-year period of the study was lower than in the previous time periods. While several previous investigations had reported a decline in hydrocephaly rates,[11,13] others reported an increase[12,16] or no change.[3,26] The recent decline in hydrocephaly rates in Hawaii is not believed to be due to decreased ascertainment of diagnosed cases because the ascer-

tainment procedures have not changed. There may have been a decline in the diagnosis of hydrocephaly, particularly of the more mild cases; however, there is no way to examine this potential explanation with the information available in the HBDP. A recent decline in the rate of neural tube defects has been tentatively linked to increased folic acid supplementation and fortification.[27] Several studies have suggested that multivitamin and folic acid use may reduce risk of hydrocephaly,[28-30] although the reduction observed in the studies was modest.

This study found that hydrocephaly rates were lower among older maternal age groups. This varies from several other investigations, which had reported either no association between maternal age and hydrocephaly risk[6,31] or increased risk with a maternal age of 37 years or greater.[11] The racial/ethnic variation in hydrocephaly rates observed in the present study were not statistically significant. Although several investigations had noted differences in hydrocephaly rates by race/ethnicity,[22,23] others had not.[4,6,17,32]

Hydrocephaly rates were significantly lower in metropolitan Honolulu than the rest of Hawaii. Another study reported no relationship between hydrocephaly and residence.[6] That hydrocephaly was slightly more common in males was consistent with the literature.[3,4,6,12,14-17]

The observation that hydrocephaly risk was elevated with lower gestation age and birth weight and with multiple gestation pregnancies had also been reported by other investigations.[6,16,18-21,33] Multiple gestation pregnancies generally have lower birth weights and shorter gestations; thus some of the association between hydrocephaly risk and plurality may reflect the relationship between hydrocephaly and these other factors. Hydrocephaly rates may be higher with lower birth weight and gestational age because if the hydrocephaly is prenatally diagnosed the physician may plan to deliver the infant early to minimize trauma during birth. Alternatively, the hydrocephaly may be a consequence of preterm delivery or both hydrocephaly and preterm delivery may be associated with another factor.

One limitation of the investigation is the relatively small number of cases, particularly when divided among subgroups. However, a number of statistically significant results were observed. Another restriction of this study was the classification of hydrocephaly. Due to the nature of the data available to the HBDP, classification of hydrocephaly could not be based on size of the cerebral ventricles or excessive accumulation of CSF. Cases were included if the data sources reported a diagnosis of hydrocephaly or described enlargement of the cerebral ventricles (ventriculomegaly, dilated cerebral ventricles, etc.). As a result, a portion of the cases included in the study may not be considered "true" cases of hydrocephaly. However, considering birth defects registries in the United States use similar data sources,[24] it is likely that hydrocephaly investigations based on data from other registries will have similar problems. Moreover, the results of this investigation were generally consistent with that of other studies, the majority of which did not indicate their inclusion criteria for hydrocephaly.

In conclusion, this population-based investigation in Hawaii found the hydrocephaly rate and relationship between the defect and maternal race/ethnicity, infant sex, birth weight, gestational age, and plurality to be consistent with the literature. However, the associations of hydrocephaly with maternal age and residence at delivery had not been previously reported.

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Normal Oxygen Saturation Values in Pediatric Patients

Monica K. Mau, Kelly S. Yamasato, and Loren G. Yamamoto MD, MPH, MBA

Monica K. Mau

Kelly S. Yamasato

Loren G. Yamamoto MD, MPH, MBA

Authors:
- Department of Pediatrics, University of Hawaii John A. Burns School of Medicine, Honolulu, HI 96822 (M.K.M., K.S.Y., L.G.Y)
- Emergency Department, Kapiolani Medical Center For Women And Children, Honolulu, HI 96826 (L.G.Y)

Correspondence to:
Loren G. Yamamoto MD, MPH, MBA
Department of Pediatrics
1319 Punahou Street, #733
Honolulu, HI 96826
Phone (808)983-8387
Fax (808)945-1570
Loreny@hawaii.edu

Abstract

Objectives: *To determine normal oxygen saturation (OSAT) values in infants and children measured by pulse oximetry.*

Methods: *Infants and children admitted to a children's hospital for elective surgery from 11/20/2000 to 3/30/2002 underwent surgical clearance screens consisting of illness symptoms, vital signs and OSAT in room air. Based on the presence of respiratory infection (RI) symptoms, a "normal" patient was defined as one without respiratory symptoms and who was not scheduled for surgery involving the airway, pulmonary or cardiovascular systems (APC).*

Results: *Of the 3600 forms collected, 2069 were completely filled out and for elective surgery. For all age groups combined, the percent of patients undergoing APC surgery or with RI symptoms for each OSAT were as follows (OSAT: %patients APC/RI): 100%: 13%, 99%-99.5%: 15%, 98%-98.5%: 14%, 97%-97.5%: 18%, 96%-96.5%: 38%, 95%-95.5%: 29%, and <95%: 0%.*

Conclusions: *Although OSAT of 95% and 96% are adequate (i.e., not requiring acute oxygen therapy), these values are associated with higher rates of APC/RI involvement and thus should be considered potentially abnormal. OSAT of 97% is on the border of normal. Normal OSATs can occur with APC/RI conditions, but an OSAT less than 97% is associated with a higher risk of an APC/RI condition.*

Introduction

Pulse oximetry has gained popularity as an inexpensive, noninvasive, and generally reliable means to assess oxygenation.[1] A suggested "fifth vital sign", pulse oximetry provides earlier detection of clinically occult hypoxemia by allowing continuous oxygen saturation (OSAT) measurements.[2] In a recent study, pulse oximetry was determined to be a simple, noninvasive screening test for congenital heart disease in asymptomatic newborns, further endorsing its utility as a test of overall health.[3] Data indicate that many physicians may not recognize moderate oxygen desaturation in some pediatric cases, and that pulse oximetry in these situations may provide important information that affects medical treatment.[4]

Despite its importance and widespread acceptance, the precise interpretation of pulse oximetry readings has not yet been clearly defined. "Normal" pediatric oxygen saturation values are inconsistent between sources. For example, normal arterial oxygen saturation values have been reported as 94-99%[5], 95-97%[6], and greater than 95%[7] by three different textbooks.

Considering the widespread reliance on pulse oximetry, as well as the lingering uncertainty over its precise interpretation, the purpose of this study is to more clearly define "normal" oxygen saturation values in pediatric patients (i.e., the oxygen saturation among normal children).

Methods

Infants and children admitted to a children's hospital for elective surgery from 11/20/2000 to 3/30/2002 underwent routine surgical clearance screening assessments consisting of illness symptoms (rash, fever, cough, wheezing, nasal congestion, vomiting, diarrhea, etc.), infectious disease exposure, nursing physical assessment, vital signs and OSAT in room air. These measurements were obtained in the emergency department by an emergency department nurse. The standard of nursing practice is to record reliable OSAT measurements which are steady, reproducible, with a steady perfusion bar or wave form signal. Copies of these clearance forms were saved as separate records in a "surgical clearance binder". These forms were reviewed by study investigators and the above information was recorded in a spreadsheet. The actual patient charts were not reviewed in most instances.

Most of these values should be indicative of OSAT values in healthy children because elective surgery is generally performed in children of stable health status. Of the 3600 forms collected, only those involving patients with elective surgical procedures were included (i.e., unscheduled, emergency surgical procedures were excluded), leaving 2127 forms. Forms with missing or illegible information were further researched through the hospital's computer system and medical records. Fifty-eight forms remained incomplete following this additional research, leaving a final total of 2069 forms included in the study.

A "normal" patient was defined as one without respiratory infection (RI) symptoms (nasal congestion, coughing, wheezing) on the clearance screening

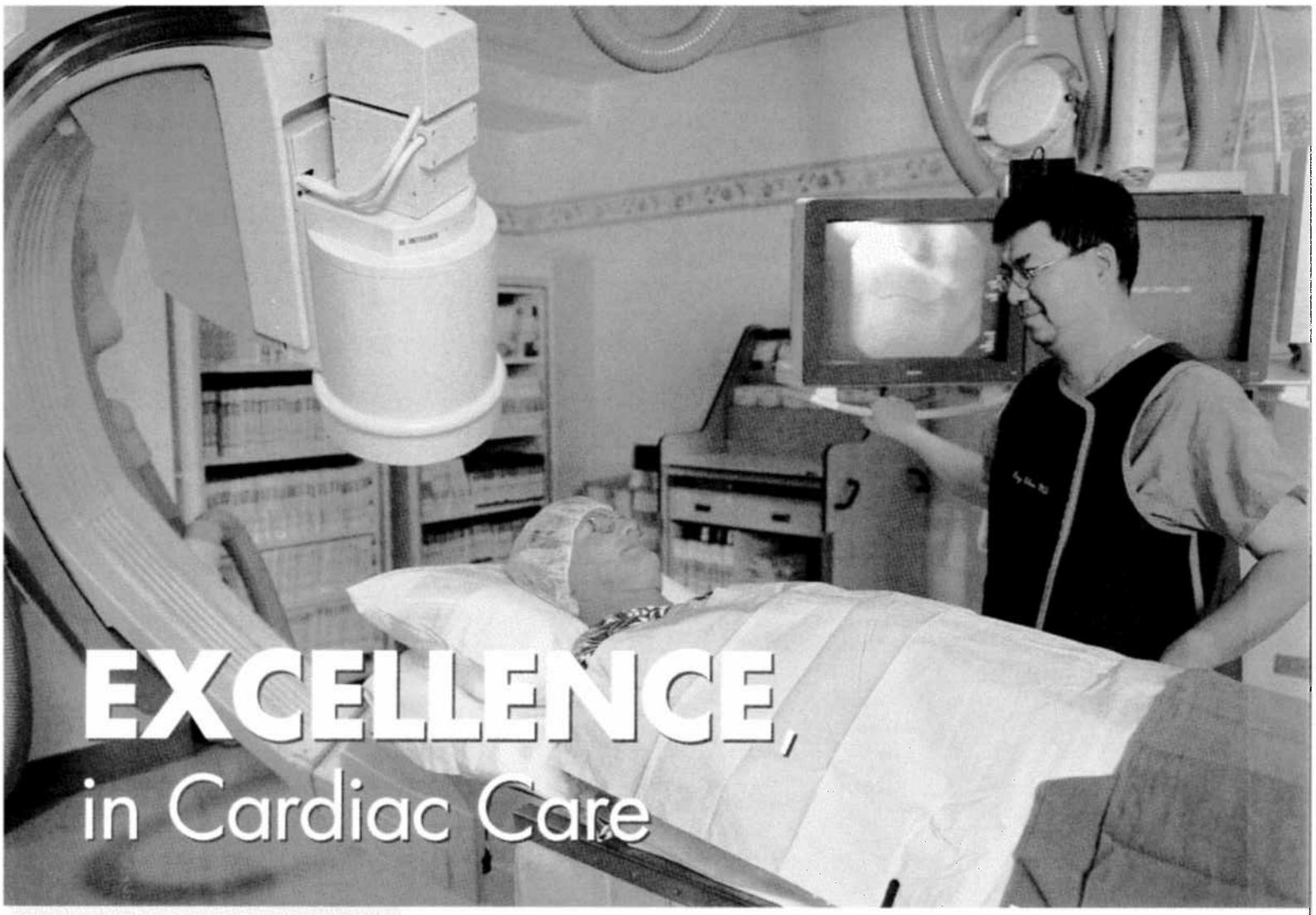

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Table 1.— Oxygen Saturation Values in Non APC/RI and APC/RI Children

	Oxygen Saturation (%)							
	100	99, 99.5	98, 98.5	97, 97.5	96, 96.5	95, 95.5	<95	total
< 1 yr (n=333)								
Non APC/RI	199	48	33	11	4	0	0	295
Patients with APC/RI	24 (11%)	6 (11%)	2 (6%)	4 (27%)	1 (20%)	1 (100%)	0	38 (11%)
1-5 yr (n=897)								
Non APC/RI	475	162	84	28	3	4	3	759
Patients with APC/RI	78 (14%)	30 (16%)	19 (18%)	6 (17%)	4 (57%)	1 (20%)	0	138 (15%)
6-19 yr (n=839)								
Non APC/RI	414	174	112	25	1	1	2	729
Patients with APC/RI	59 (14%)	32 (18%)	15 (13%)	4 (16%)	0	0	0	110 (15%)
All (n=2069)								
Non APC/RI	1088	384	229	64	8	5	5	1783
Patients with APC/RI	161 (13%)	68 (15%)	36 (14%)	14 (18%)	5 (38%)	2 (29%)	0	286 (14%)

assessment and who was not scheduled for surgery involving the airway, pulmonary or cardiovascular systems (APC). In some instances, the OSAT value recorded by nurses were two numbers such as "97%-98%". In such cases, this value was analyzed as the mean between these two numbers (e.g., 97.5%).

Patients were categorized as "normal" (defined above as non-APC/RI) and those with RI and/or APC findings. This categorization was then cross tabulated using various cutoff levels of oxygen saturation (eg., <98% versus >98%) to determine which cutoff value has the greatest degree of distinguishing the non-APC/RI patients from the APC/RI patients.

This study was approved by the hospital institutional review board.

Results

The distribution of oxygen saturation values among APC/RI and non-APC RI patients are shown in Table 1. All p values are doubled sided probabilities.

For patients under 12 months of age, APC/RI percentages were significantly higher in those with OSATs less than 98% (29% vs 10%, p=0.011). For patients in the 1 to 5 year age group, the APC/RI percentages in those with OSATs less than 97% and those greater than or equal to 97% were 33% vs 15% (p=0.052, not significant for a double sided hypothesis, but significant for a single sided hypothesis). For the combined patient group less than 6 years old, APC/RI percentages were significantly higher in those with OSATs <98% (24% vs 14%, p=0.014) and in those with OSATs <97% (33% vs 14%, p=0.012).

For patients 6-19 years old, only 4 out of 839 presented with oxygen saturations of <97%. As a whole (0-19 years), the APC/RI percentages were significantly higher in those with OSATs less than 98% (19% vs. 13%, p=0.048) and in those with OSATs less than 97% (28% vs. 14%, p=0.039).

Discussion

Ideally, a study to determine normal OSAT values should be done by measuring the oxygen saturation on a large group of healthy children and then measuring the oxygen saturation on a large group of children with respiratory infections and conditions involving the airway and cardiopulmonary systems. The OSAT values of the normal group should form a skewed distribution near 100%. The distribution would not be bell shaped because of the maximum limit value of 100%. Among the group of children with airway and cardiopulmonary conditions, the distribution of OSAT values will be broader (less of a peak) since many of them will have normal oxygen saturations and some of them will have abnormal values. At some cutoff oxygen saturation value, the frequency of this value among the normal group is very low, while it is moderately frequent in the airway and cardiopulmonary group. This value, most likely represents the borderline of what the expected oxygen saturation for a normal child should be.

The study methodology described attempts to use this concept with the limitation, that the patients are not chosen. Rather, this is a large cohort of patients undergoing elective surgery. Most of these children are normal, but some of them have documented respiratory symptoms and/or conditions involving the airway, pulmonary or cardiovascular system. This latter group of children (those with RI and/or APC conditions) defines the abnormal group. While this study design is not perfect, it does provide some data toward defining an abnormal OSAT value. Without this data and further data attempting to define the normal range, textbooks will continue to publish normal ranges based on a paucity of data.

The number of older children with low OSAT values (<97%) was very low. It is possible that older children are easier to assess by parents and physicians. Thus, it might be easier to determine that they might be having some respiratory compromise and are less likely to schedule elective surgery. Alternatively, they might be more tolerant of their elective surgical condition and thus, they are better able to wait for a more ideal surgical date when their respiratory status is optimal.

In the younger age groups, oxygen saturation values of 96% to 94% were more common than that found in the group of older children. It is unlikely to conjecture that this occurs because physicians believe that younger children tolerate hypoxemia during surgery better than older children. More likely explanations are that younger children are more difficult to assess, or that younger children have a greater need or priority for elective surgery procedures such that physicians would be more tolerant of respiratory symptoms to clear them for the surgical procedure that they need.

In children under 6 years of age, the percentage of APC/RI conditions is similar in OSAT levels from 98% to 100% suggesting that these values are "normal". At OSAT levels of less than 97%, the

APC/RI percentages increase significantly suggesting that these OSAT values are not normal. An OSAT value of 97% appears to be borderline. Although oxygen saturations of 95% and 96% are adequate (i.e. do not require acute oxygen therapy), our data indicate that these values are associated with higher APC/RI percentages and should be considered abnormal.

For children and adolescents ages 6-19, only 4 out of 839 patients presented with oxygen saturations of <97%. A similar type of statistical analysis to compare the APC/RI percentages in patients above and below certain values was not possible. However, the APC/RI percentages were similar to the rates in the younger children for all OSAT values from 100% to 97%, implying that these values in this age range are also normal.

A limitation of this study is the small number of patients who presented with OSATs less than 98% (103; 6% of total patients). Another limitation is the definition of "normal" and "abnormal". This study used the presence of an APC/RI condition to classify patients as those more likely to have a condition leading to hypoxemia, most often due to ventilation perfusion mismatch (VQM). Patients without respiratory infection symptoms and without airway, pulmonary, and cardiac problems are unlikely to be hypoxemic and are unlikely to have significant VQM. In our study, a patient could have had an APC condition and we would not have known about this. For example, if a patient with congenital heart disease arrives for a scheduled hernia repair, if they had no RI symptoms and the history of congenital heart disease was not written on the clearance form, study investigators reviewing the form would not have been able to classify the patient as one who has an APC condition. Thus, some non-APC/RI patients might have the potential for VQM, but this likelihood is much lower in the non-APC/RI group compared to the APC/RI group. In this study, non-APC/RI does NOT indicate that the patient is normal. However, this does serve as a useful control group which should have a substantially lower risk of VQM compared to the APC/RI group. If the percentage of APC/RI patients (i.e., abnormal patients) suddenly increases at a particular OSAT level, this suggests that this OSAT level is abnormal.

Although a future study could measure OSAT values during well child checks to further define this, office and clinic pediatric nurses are less experienced in identifying potentially hypoxemic patients compared to ED nurses who perform pulse oximetry measurements on ill patients more frequently. Additionally, since nearly all of these children would be normal, such a study would similarly suffer from a small number of patients with OSAT values of 97% or less.

The utilization of defining a normal OSAT value in clinical practice is to identify occult VQ mismatch. For example, an OSAT value of 95% with physical exam findings suggestive of an upper respiratory infection, should raise the suspicion of occult VQM. Since it is unlikely that a respiratory infection limited to the upper airways alone, would adversely affect oxygenation, common causes of VQM such as pneumonia and asthma should be considered. Unfortunately, OSAT can vary with other factors such as body position, medications, etc. OSAT measurements will often vary even in the absence of factors known to affect the OSAT. It is difficult to conclude that a difference of 1% could be clinical important. However, a normal range must somehow be defined with an understanding that there might be values of uncertainty at the fringe of this normal range.

In summary, although OSAT of 95% and 96% are adequate, these values are associated with higher APC/RI percentages and thus should be considered potentially abnormal. An OSAT of 97% is on the border of normal. Normal OSATs can occur with APC/RI conditions, but an OSAT less than 97% is associated with a higher risk of an APC/RI condition.

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Using the World Wide Web to Facilitate the Editing and Publishing of a Textbook for Faculty Professional Development

Loren G. Yamamoto MD, MPH, MBA

Loren G. Yamamoto MD, MPH, MBA

Author:
- Department of Pediatrics, University of Hawaii John A. Burns School of Medicine, Honolulu, HI 96822
- Emergency Department, Kapiolani Medical Center For Women And Children, Honolulu, HI 96826

Correspondence to:
Loren G. Yamamoto MD, MPH, MBA
Department of Pediatrics
1319 Punahou Street, #733
Honolulu, HI 96826
Phone (808)983-8387
Fax (808)945-1570
Loreny@hawaii.edu

Abstract

Objective: *The purpose of this report is to describe the editing and publication of a textbook to increase the opportunity for faculty to contribute textbook chapters, using the internet WWW to facilitate the editing process.*

Methodology: *An outline of 22 sections containing 214 chapters, was developed. Each section was assigned to an editor. Editors recruited authors for each of their section chapters. Chapters were submitted to the editors, then a chief editor completed the editing for the chapter.*

Results: *Chapters that were completed early, were posted on the WWW which permitted additional review by the authors facilitating communication with the editors. The additional lead time on the WWW permitted indexing and identification by internet search engines (e.g., Google), so that by the time the textbook was completed, most major search engines had already identified the on-line textbook. Page/type-setting was streamlined by the electronic transfer of the equivalent on-line chapter files to the publisher. 41 chapters were contributed by 18 senior faculty, 51 chapters were contributed by 29 assistant professors, 46 chapters were contributed by 23 non-faculty community physicians, 38 chapters were contributed by 27 residents, and 40 chapters were contributed by 37 medical students.*

Conclusion: *A textbook project such as this provides faculty with the opportunity to contribute to the medical literature enhancing their professional development. The WWW provides a new forum for publishing a textbook. It also provides a new communication option between editors and authors to better coordinate the content and editorial style of the chapters.*

Introduction

Professional development includes teaching, research and academic writing. Opportunities to teach are readily available. Research requires training and initiative. The opportunity to write for a textbook is largely limited to academic leaders in a specialty. Yet the skill of scholarly writing is an important aspect of professional development[1].

The World Wide Web (WWW) is a new publishing option as well as a new option to facilitate communication between textbook editors and chapter authors.

The purpose of this report is to describe a method utilizing the WWW to facilitate the development of a textbook project to increase the opportunity for faculty to contribute textbook chapters. While some textbooks are developed and published to fulfill an informational resource need, a textbook project such as this has the purpose of providing an opportunity for scholarly writing thereby promoting faculty professional development.

Methodology

The department of pediatrics at this university affiliated medical center initiated a general pediatrics textbook project to give its faculty the opportunity to contribute chapters for the textbook. Highly motivated individuals were selected as editors. An outline of 22 sections containing a total of 214 chapters) was developed. Each section was assigned to one of the editors. Editors recruited authors for each of the chapters within their sections. Chapters were submitted to the editors, then a chief editor completed the editing for the chapter. Chapters were posted on a web site used to post the completed portions of the textbook and to facilitate the editing process. The central theme was to encourage faculty to contribute one or more chapters to the textbook.

Results

This project began in June 2001 and the final textbook was submitted for publication in October 2003. The editorial group initially consisted of one chief editor and five associate editors. During the early phase of the project, three editors relinquished their duties and they were replaced by two new editors who expressed the interest to do the work necessary to carry the project forward.

In the process of submitting their chapters to an editor, each author experienced the process of submitting written material to an editor for review, followed by cycles of editing and revision. It was evident that the authors possessed varying levels of skills in processes such as their ability to present written material in an organized fashion, their ability to write questions to

check the reader's knowledge, and their ability to cite references properly.

During the project, chapters that were completed early, were posted on the internet World Wide Web (WWW). The web site title page described this as a textbook in development. This gave chapter authors a means of reviewing their own chapter and providing feedback between the editors to correct errors and to recommend changes in their chapter. This also gave internet search engines time to include the textbook's contents into their indexing data base, making it easier for search inquiries to locate the online textbook chapters once it was completed.

Page/type-setting was streamlined by the electronic transfer of the equivalent on-line chapter files to the publisher.

The final book contained approximately 650,000 words (including credits, table of contents and index), printed on 700 pages. Of the 214 chapters, 40 chapters were contributed by 17 senior faculty (associate professor or full professor), 48 chapters were contributed by 26 junior faculty (assistant professors), 46 chapters were contributed by 23 non-faculty physicians (most of these are private practice or military physicians who have medical school appointments but are not classified as regular faculty), 38 chapters were contributed by 27 residents, 40 chapters were contributed by 37 medical students, 1 chapter was contributed by a nurse practitioner, and 4 chapters were contributed by faculty physicians at other medical schools. Medical students and residents were given the opportunity to write some chapters under the direct supervision of the editors. Some chapters were written by two authors which accounts for the sum being greater than 214.

Finding a publisher was not difficult. "Vanity publishing" refers to the practice of paying a publisher to publish your book. Almost any book can be published via this means. By paying an up front fee to prepare the book for publication, most publishers can establish a print-on-demand arrangement, in which books are not printed until they are ordered. An ISBN (international standard book number) identifies all books, so that they can be catalogued by all bookstores. Although the book is not available on the shelf, a bookstore could still have it on catalog availability and they could order a single copy of the book if requested by a customer. Mail-order booksellers (Amazon.com, Borders.com, etc.) will display the book as if it is in their inventory and order it from the publisher if a customer orders the book.

Vanity publishing fees can range from $300 to $20,000 per book depending on the size of the book, the number of photographs/diagrams, and the publisher. The publisher we used, AuthorHouse (www.Authorhouse.com, Bloomington, IN) charged approximately $700 to publish this book of approximately 700 pages in paperback form. To reduce the publishing cost, this textbook was written to contain text only. No photographs or diagrams are included in the textbook. The retail price of this 700 page book was $18.75.

Discussion/Conclusion

The enthusiasm and energy level of the editors are important factors to complete a project such as this. It was disappointing to find that most authors were not very enthusiastic about contributing chapters. Several faculty members refused to participate. An opportunity to author a chapter in a textbook is an inviting opportunity. Yet many faculty members were not interested. It appears that in these instances, the barrier to professional development is lack of self-motivation. The actual contribution to such a project identifies the future potential of junior faculty. If a junior faculty member has difficulty writing a chapter on a general medical topic, it is likely that this same faculty member will have difficulty with the more difficult task of generating original research. The problem could be lack of time, lack of self-motivation, or lack of the technical skills required for academic writing. In contrast, while some senior faculty might choose to contribute chapters to a textbook project, their lack of contribution should be interpreted differently since their professional goals might be higher than merely contributing to somebody else's textbook.

As with any group of authors, there are those who meet all deadlines, there are those who have to be reminded (once or more), and there are those who need to be replaced with another author. For this type of project to succeed, at least one of the editors must have effective management skills, be experienced in medical publishing, and be committed to completion of the project.

The method of posting the chapters on a web site as soon as the initial editing was done was very successful. This provided an added benefit of releasing the chapter to the WWW public domain many months before the actual publication of the textbook. The textbook chapters were identified by internet search engines before the book was completed. The table of contents on the web site had to be frequently updated to indicate which chapters were available. It also put some indirect pressure on some of the slower chapter authors who could see that most of the chapters were completed and available on the WWW, while their particular chapter was still not available.

Using the WWW to facilitate the editing process provides the editor with total control over the appearance of the chapter since the authors were not able to upload new versions of the chapter to the web site server. All changes had to go through the editor. This method permitted the authors to rapidly view their chapter after editing, reducing the turnaround time between cycles of editing. In a more traditional editing arrangement, the chapter might go back and forth between the author and editor. Each exchange represents an opportunity for the author to reinsert something that the editor had previous removed or modified (i.e., overcome editorial control). Editorial control is important as an oversight for the accuracy of information, the proper citation of potentially controversial statements, the maintenance of a balanced point of view in potentially controversial subjects, and to maintain a consistent style and appearance of the chapters so that each chapter possesses some similarity (such that they all belong in the same book).

The opportunity for scholarly writing is more available to senior faculty and less available to junior faculty. Pololi, et al, described a program directed at 18 assistant professors who participated in a writing and faculty development program which consisted of 7 monthly 75 minute sessions utilizing mentors[1]. Other resource (including faculty time) expensive programs have also demonstrated success at improving aspects of faculty development, including scholarly writing[2]. Ongoing faculty development and sound mentoring relationships facilitate the academic advancement of clinical faculty[3]. This textbook project provided mentoring through the editorial process,

*See **"Using The WWW..."** p. 53*

Medical School Hotline

Leadership Training in Maternal and Child Health

Gigliola Baruffi MD
Professor, MCH, Public Health Sciences and Epidemiology
and
Jill McGrath Jones MA
Project Assisant

Accountability, evidence-based activities, and elimination of health disparities have become hallmarks of health services in public health and clinical medicine. To address these issues, a program of courses in Maternal and Child Health (MCH) Leadership has been developed at the University of Hawaii John A. Burns School of Medicine (JABSOM) Department of Public Health Sciences and Epidemiology (DPHS&E). This program aims to strengthen MCH professionals' competencies in data analysis and data-based program management; and address health problems of geographically isolated and culturally diverse populations. A significant contribution towards fulfilling a major goal of Healthy People 2010, which is the "elimination of health disparities", is the expansion of the availability of well prepared health workers who reside in geographically isolated areas, belonging to minority or underrepresented populations.

Women and children have a wide range of health needs[1,2] and often suffer disproportionately from health disparity prevalent among minority populations. The Census Bureau estimates that minority groups represent 77% of the population in Hawaii and that Native Hawaiians and Other Pacific Islanders in the state comprise the largest number among all the U.S. states (271,000)[3]. The University of Hawaii contributes to addressing minority health issues by training health professionals for the identified region.

The PH Certificate in MCH Leadership Program (see Note) intends to expand the MCH leadership in the region by recruiting and training MCH professionals in Hawaii and the U.S.-Associated Pacific Islands jurisdictions. The program focuses on health workers who reside and/or serve in isolated geographic areas, belong to minority or underrepresented populations, and work full-time. The curriculum concentrates on essential public health functions. The courses prepare students to be competent in five focus areas:

1. Analytical skills, including the ability to understand data and their relevance to program planning and policy development; and to communicate data as information.

2. Skills in needs assessment and priorities identification; program planning and proposal writing; program evaluation.

3. Skills in administration, management and policy development based on identified gaps; history of MCH programs and legislation; and advocacy skills.

4. Skills in community development, including the understanding of how communities function, the ability to identify, strengthen and support community leaders, and work successfully in a multicultural/multiethnic environment.

5. Skills to apply leadership concepts and principles in practice settings such as using a variety of communication techniques to advocate for MCH issues to the legislators, the press, and the community.

Competencies in focus areas are achieved by overlapping acquisition of progressively higher levels of knowledge and skills throughout the program. Learning objectives are presented in seemingly compartmentalized manner for the sake of clarity and course syllabus requirements. However, the objectives overlap and reinforce each other. The requirement is that courses be taken sequentially after having satisfactorily completed each objective before proceeding to the next.

The curriculum is implemented by the problem-based approach. Examples and illustrations are taken from existing MCH programs/projects in the State and the Pacific Islands jurisdictions. Material for exercises and hands-on practice include projects, interventions or issues identified from the student's agency or the community. Data are obtained from MCH service agencies, state vital statistics, the census, surveys and other local research

The program is geared toward working professionals and offers worker-friendly scheduling (evening and weekends classroom hours). Condensed, intensive classes are held in summer months. Currently, the PH Certificate in MCH Leadership is only available on the UH Manoa campus. Travel and tuition scholarships are available to students from U.S.-Associated Pacific Islands and neighbor Hawaiian Islands. In spite of these efforts, community meetings and discussions with health care professionals in the field have revealed that there is a need and desire for classes to be made available on site, on the neighbor islands, as well as in the Pacific Basin. Prospective students have expressed strong interest for continuing education and enhancement of MCH skills and competencies, but are unable to travel to the Manoa campus. To accommodate these students, a distance-learning element of the program is being developed. Options include ITV, HITS, Internet access and WebCT, and periodic live classes conducted by the faculty at the distance sites.

The PH Certificate in MCH Leadership training has enhanced the participants' abilities to adapt to change, to incorporate "lessons learned" from the experiences of their classmates, to generate new knowledge and innovative ways of understanding health and healthy behaviors. Participants have acquired skills in data analysis, presentation and interpretation, program planning and program evaluation. The curriculum's interactive approach has improved communication skills and confidence, provided students the ability to identify and articulate lacunae in health care and health care policies, and promoted self-assurance to initiate effective advocacy and change. Above all, students have gained the appreciation of incorporating the communities' cultural strengths in their work.

The graduate certificate in MCH leadership is also open to UH graduate students and other community professionals interested in MCH or wishing to upgrade their leadership skills. It offers the possibility for interested students, who meet admission requirements, to continue towards the MPH degree with specialization in Social and Behavioral Health Sciences. It also provides MPH students in epidemiology and social and behavioral health sciences the opportunity of a sub-specialization in maternal and child health, an important public health field.

Since January, 2002 the MCH certificate program has trained 25 health professionals. Thirteen of them have completed the Certificate and 12 are at different stages of the program. The development of leadership skills remains as the main theme for all who occupy positions of influence in a health system and are called upon to promote community participation in health endeavors.

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NOTE: The Public Health Certificate in MCH Leadership is supported by the Federal Maternal and Child Health Bureau (MCHB), Health Resources and Services Administration (HRSA). It is located in Department of Public Health Sciences and Epidemiology (DPHS&E), John A. Burns School of Medicine (JABSOM), at the University of Hawaii at Manoa.

The Two Faces of Telomerase

Richard Allsopp PhD
Assistant Professor
Institute for Biogenesis Research
University of Hawaii

Telomeres are genetic elements that cap and protect the ends of all chromosomes in eukaryotic cells, and are therefore, essential for chromosome stability. Telomerase, a ribonucleoprotein enzyme complex, is a specialized reverse transcriptase that functions to complete the replication of telomeres in dividing cells. Telomerase is composed of an essential RNA component (TR), which serves as a template during telomere replication, and an essential catalytic component called telomerase reverse transcriptase (TERT)(Figure 1). Most somatic cells in humans lack telomerase, and consequently telomeres shorten to some degree during aging in nearly all tissues comprised of mitotically active cells. On the other hand, telomerase is activated during pathogenesis of most cancers, allowing completion of telomere replication in these cells. Thus enhanced expression of telomerase in somatic cells has been proposed as an anti-aging therapy, whereas inhibition of telomerase in cancer cells has been proposed as a therapy for cancer treatment. Here I review the pros and cons of telomerase with regard to these potential therapeutic applications.

The physiological role of telomerase

The main function of telomerase is to complete telomere replication in the germ line (see figure). This has been proven in mice strains

Figure 1. The 'good' and 'bad' features of telomerase.

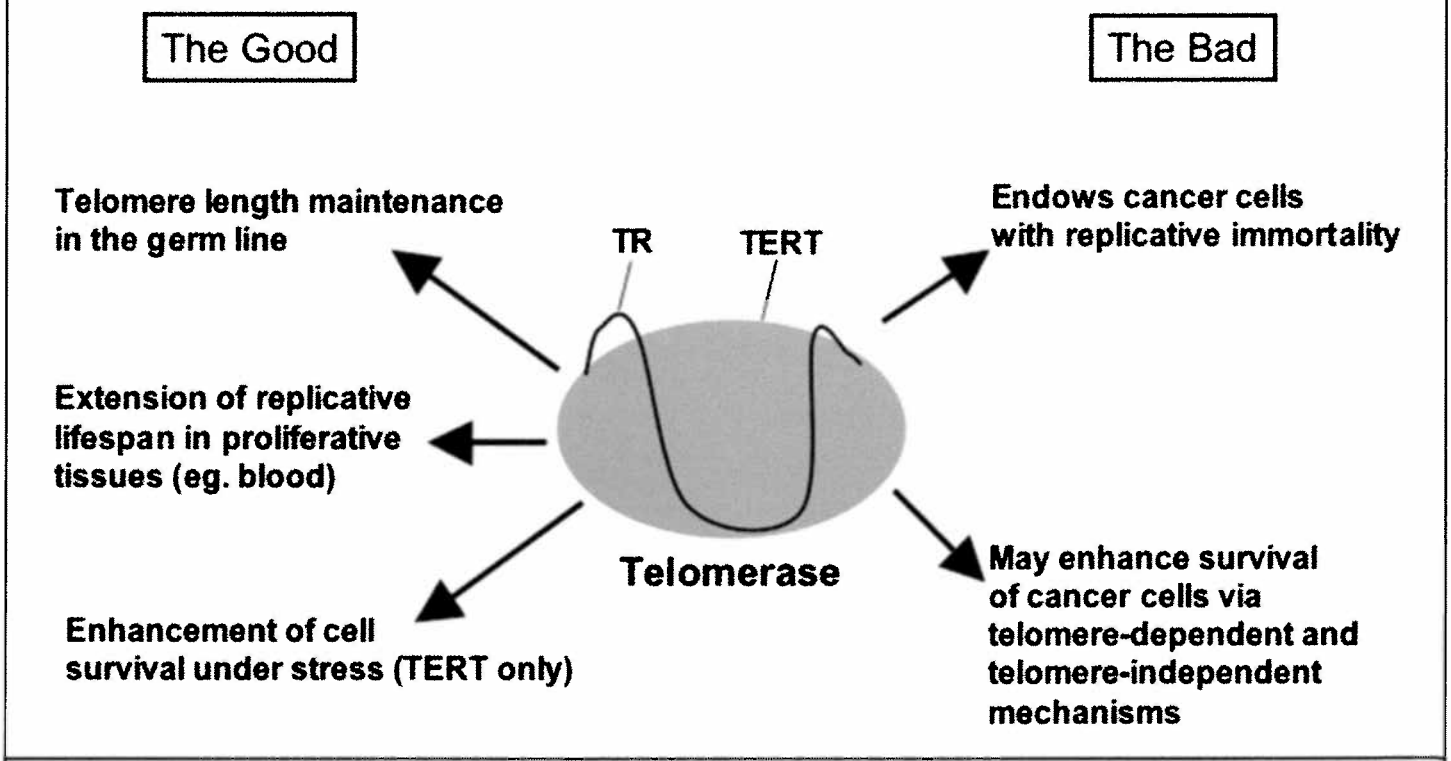

Figure 1.— The 'good' and 'bad' features of telomerase.

in which either the *TR* gene or *TERT* gene has been knocked out. Propagation of either the TR-/- [1] or TERT-/- [2] mice strain leads to continuous telomere erosion with each successive generation until, after three to five generations, depending on the strain, the loss of a telomere from one or more chromosomal ends becomes prevalent. The consequence is telomere dysfunction and cell cycle arrest at the cellular level, and an accelerated aging phenotype including sterility at the organismal level.

Telomerase also functions to slow the rate of telomere shortening in tissues with a relatively high turnover rate. This is primarily supported by analysis of telomere shortening during replicative aging of hematopoietic stem cells (HSC) from wild-type and telomerase deficient mice. Telomeres do shorten during replicative aging of the hematopoietic system, including HSC, in wild-type mice (and humans), despite the presence of telomerase activity at readily detectable levels in these cells. However, hematopoietic cells, including HSC, from early generation TR-/- or TERT-/- mice have been shown to have a roughly two-fold increase in the rate of telomere shortening and a markedly reduced replicative capacity relative to wild-type mice[3,4].

Finally, evidence is now emerging that suggests TERT may have a telomere-independent function in promoting cell survival in response to stress. For example, a transgenic model system has been developed to allow over-expression of TERT in basal keratinocytes[5]. These TERT transgenic mice exhibit enhanced wound healing capacity relative to wild-type mice. This is unlikely to be a result of telomere length maintenance in proliferating cells at the site of the wound since inbred mice have unusually long telomeres.

Telomerase and cancer

In humans, interestingly, telomerase was first detected in cancer cells (HeLa cells), not normal somatic cells[6]. Indeed, with the advent of the highly sensitive PCR-based TRAP assay for detection of telomerase activity, high throughput analysis of thousands of different tumor samples has demonstrated that >90% of human cancers express telomerase[7]. As in germ line cells, the activation of telomerase in cancer cells allows these cells to acquire replicative immortality. This was first shown during transformation of human embryonic kidney cells with SV40 large T antigen, where the rare emergence of immortal transformed colonies was shown to coincide with the activation of telomerase and telomere length maintenance[8]. We now know that one of the primary mechanisms for telomerase activation in cancer cells is the transcriptional activation of the *TERT* gene. In humans, most cells express moderate to low levels of TR, but no detectable levels of TERT. Furthermore, telomerase can be fully activated and telomeres elongated in various normal human somatic cells in vitro simply by the ectopic expression of TERT[9]. Two important conclusions may be drawn from this data. First, telomerase may be a very attractive candidate for cancer therapy. Preliminary studies have shown that inactivation of telomerase in vitro and in animal models leads to replicative arrest and/or death of tumor cells and loss of tumorigenicity in vivo[10]. Second, new targets for cancer therapy may emerge from a better understanding of the regulation of TERT expression.

More recently, data has emerged to suggest that telomere-independent functions of TERT may promote cancer development as well. This is evidenced by studies utilizing transgenic mice in which TERT over-expression in keratinocytes or blood cells leads to the predisposition or development of skin cancer[5] or lymphomas (Allsopp and Weissman, unpublished observations) respectively.

Telomerase: Fountain of youth or catalyst of death?

Clearly, telomerase plays an important role in the survival of most types of cancer, and thus extreme caution is warranted in the use of telomerase, or more specifically, TERT, as a therapy to rejuvenate old cells. On the other hand, there is no direct evidence to date to suggest that telomerase activation per se (ie. ectopic expression of TERT) predisposes human cells to a cancer phenotype. Transgenic studies in mice very often cannot be directly extrapolated to humans due to fundamental differences in biology. In particular, it is well established that mice cells are more easily transformed than human cells. Furthermore, there are significant differences in telomere and telomerase biology between mice and humans. The transient expression of TERT, under the control of a tightly regulated inducible promoter, in certain human cell types may very well turn out to be a safe and efficient way to re-set the replicative clock.

Also, as mentioned above, telomerase and proteins that regulate telomerase are likely to be useful targets for cancer therapy. However, the role of telomerase in the germ line and proliferative tissues should not be ignored in any telomerase-based cancer therapies, despite the normal phenotype of early generation telomerase knockout mice. Mice telomeres are, on average, four times longer than human telomeres, so the development of critically short telomeres upon inhibition of telomerase will be much quicker in humans than mice. Accurate targeting of any telomerase-based drugs to treat cancer will be important. In the end, it appears that we may be able to have our cake and eat it too with telomerase, as long as we are careful.

For more information on the Cancer Research Center of Hawaii, please visit our website at www.crch.org.

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"Before we can play doctors, Eddie, we need a lot of old magazines for our waiting room."

"References..." from p. 36

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an actual experience in scholarly writing which is not ordinarily available to junior faculty, and a tangible academic achievement in completing a chapter (a successful endeavor), to promote faculty development utilizing fewer resources than other programs described in the literature. The use of the WWW greatly facilitated the editing process, reducing the amount of work for each editor. Secretarial support staff was not required for the editing process.

The WWW version of this book could standalone as an electronic book. It is an electronic publication with no cost if one has access to a server and web site domain. Electronic journals and electronic books can be published and circulated through the WWW. The online documents can be continuously updated, as opposed to a paper book which requires an enormous effort and a substantial expense to publish a new edition. Despite the ubiquity and acceptance of electronic online reference materials, having a book in hand is an academic/professional accomplishment. The cost of on demand publishing has declined substantially, making both paper and electronic publishing more feasible for individuals and smaller department programs.

In conclusion, the WWW can be used to facilitate the editing process of organizing a textbook. It is also a new medium for academic publishing, which can be used to facilitate the professional and academic development of faculty.

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The Weathervane Russell T. Stodd MD

In The Old Days It Was Self Abuse. Now It's Game Boy.
A study of 10,000 workers at four Japanese companies, average age 43 years, claimed a link was found in the development of glaucoma in heavy computer users. The researchers reporting in the Journal of Epidemiology and Community Health found the risk to be particularly strong in myopic males. The report noted that a third of the workers were found to be glaucoma suspects. While glaucoma is typically found in the elderly population, these workers were young, healthy males spending a lot of time staring at a video display screen.

Sometimes Even A Blind Pig Finds A Truffle.
It seems an unlikely source for a creative idea, but the Department of Health and Human Services (DHHS) has instituted a pilot program called "early offers" for malpractice complaints in federally funded community health centers and also in the Indian Health Service. When a person has suffered an injury and files a malpractice complaint, HHS will investigate. If it is found that the patient deserves a monetary settlement, the patient will be sent a letter explaining the program, and given 90 days to submit an offer to a third party administrator. HHS also has 90 days to provide a settlement offer. If the dollar amounts match or if the patient expects less than offered, the case is settled. If there is no agreement, the patient can proceed with a law suit as if nothing had transpired. Wow! Here is a plan with no lawyers, no court costs, no depositions, no prolonged delays, and just a simple, rapid disposition of a potentially thorny problem. Summarily, the entire award goes directly to the patient. The trial lawyers club is sure to mount a campaign to kill this plan.

The Purest Form Of Charity Is Not Tax Deductible.
You can donate cash, a car or some other valuable to your church or favorite charity and get a deduction on your income tax. But suppose instead you give a precious body part such as a kidney to a sibling, or other family member, or a friend, or even a stranger who needs an organ for survival. To date, there is no federal tax deduction for organ donations. Two states, Wisconsin and Georgia, allow deductions for lost wages, travel and lodging expense up to $10,000 for those who generously serve up a body part for transplant. According to the United Network for Organ Sharing, 17 people die each day for lack of a vital organ, and 87,000 are waiting and hoping for organ transplants. In 1993, 16% of transplants came from live donors, but that number had increased to 27% in 2003. Bio-ethics experts question the use of the tax code to encourage such donations, since that would give state imprimatur to the action (Would that be so bad?). No one suggests that donors should receive payment, but surely some mechanism can be devised to reward such altruism.

Why Is Grandma Throwing Up?
The Center for Disease Control and Prevention (CDC) put out some interesting statistics on reproduction in American women. Fewer women under age thirty are giving birth, while deliveries in ages 30 and beyond are increasing. Teen birth rates fell 3% in 2003, marking a trend that has continued for 12 consecutive years. On the opposite end of the reproductive spectrum, the delivery rate for women 40 to 45 increased 5%. Meanwhile, the caesarian section rate is growing by big numbers. Nine years ago, 18% of deliveries were by caesarian, but in the intervening years it has increased half again to 27.6% in 2003. The precise reason for the increase is not known, but speculation centers around older women giving birth, and physicians' concerns about the risk of vaginal delivery. Moreover, VBAC (vaginal delivery after c-section) complications have resulted in some huge malpractice awards, a factor which always lingers in the obstetrician's mind.

Everything Has A Limit, Except The Attorney's Bounty.
Skeptics who doubt the value of a $250,000 cap on non-economic damages in controlling malpractice premiums can look to Texas. The Texas Medical Liability Trust, a physician-owned company formed in 1979 which provides policies for more than half of Texas physicians, cut premiums by 12% after voters passed a constitutional amendment patterned after California's MICRA statute. Now they have projected a further reduction of 5% beginning in January 2005. If the Senate of the United States will pass a similar bill, that ugly malpractice cloud won't disappear, but it will be far less ominous, and it would move the issue off state legislative agendas. Then our local law makers can get on to other important things, such as finding a parking place in Honolulu.

Try To Keep Your Road Kill Under Ten Pounds.
On an overall basis for motor vehicle deaths, the number of motorists killed by collision with animals is minuscule. Still, the statistics are interesting, because the number increased by 27% for 2003 over the previous year. What is strange is the propensity for motorcycle deaths. While the total number of fatalities was 201, 60 (30%) of those were motorcycle deaths, far out of proportion for the number of bikers on the road. The ratio is 41 car-truck registrations for each motorcycle. Two thirds of the biker fatalities were not wearing helmets, and of the auto deaths, 60% were not wearing seat belts. For autos and light trucks, the main risk was not in striking the animal (usually a deer), but in loss of control and rolling over, or striking an object off the road. In 14 cases, death occurred because a deer struck by a car, crashed through the windshield of a car going the opposite direction.

The Drug Advertising People Are In Need Of Brain Dialysis.
Another thing that was better done in the those golden halcyon days gone by, was drug marketing. Fifteen years ago, pharmaceutical companies depended almost entirely upon a staff of representatives to call on doctors to market their products. In 1989 the pharmaceutical lobbyists pressured the Food and Drug Administration to loosen the requirement for a "brief summary" of indications, side effects, effectiveness, etc. Subsequently, direct-to-consumer (DTC) advertising took off exponentially. In 1989, drug producers spent $12 million on DTC, but by 2001 the figure had grown to $2.38 billion. Now when an ad appears on television, it is difficult to know if the mini-drama is selling beer, perfume, a cruise or sex. Pfizer was warned to discontinue a Viagra add showing a balding man accompanied by an attractive woman, advising that the drug would bring back that "wild thing" which they both remember. The scene never tells explicitly what the drug is supposed to do, but there can hardly be any doubt. Of course, the last line is always, "ask your doctor....." It's easy to despise the drug marketers in this new millennium.

They Are Empowered By The Department Of Homeland Stupidity.
While conducting a classroom search for a missing item at Holme Elementary School in Philadelphia, a ten year old girl was found to have a pair of scissors in her book bag. School officials acknowledged that she had not threatened anyone, but called the police, claiming a violation of state law for "weapons" on campus. The girl was removed from class, handcuffed(!), and taken to the police station where she was released without being charged with a crime. The child was frightened and cried profusely. She also noted that scissors are routinely used in classrooms. Still, the moron school officials suspended her for 5 days while awaiting a hearing.

What A Deal! A Trip To Disneyland And Botox For Your Wrinkles.
Two ambulatory surgery centers in southern California are under federal indictment for fraud. These creative people are accused of targeting people with generous insurance plans and flying them to California. They provide hotels, travel expense, and a cut of the proceeds for heavily overpriced and unnecessary procedures such as sweat gland removal, pain management, adult circumcision and colonoscopy. Patients also frequently get a cosmetic procedure as a bonus. Additional participants in the scam are recruiters and physicians.

ADDENDA

- Pirates believed that wearing an ear ring in a pierced ear improved their eyesight.
- 94% of physicians between the ages of 60 to 64 hire a tax pro to do their annual IRS return.
- The skin you peel after a bad sunburn is called blype.
- A hungry fly came into the bar and settled down next to an attractive woman. " Hey, lady, I like that stool you're sitting on."

Aloha and keep the faith —rts■

Contents of this column do not necessarily reflect the opinion or position of the Hawaii Ophthalmological Society and the Hawaii Medical Association. Editorial comment is strictly that of the writer.

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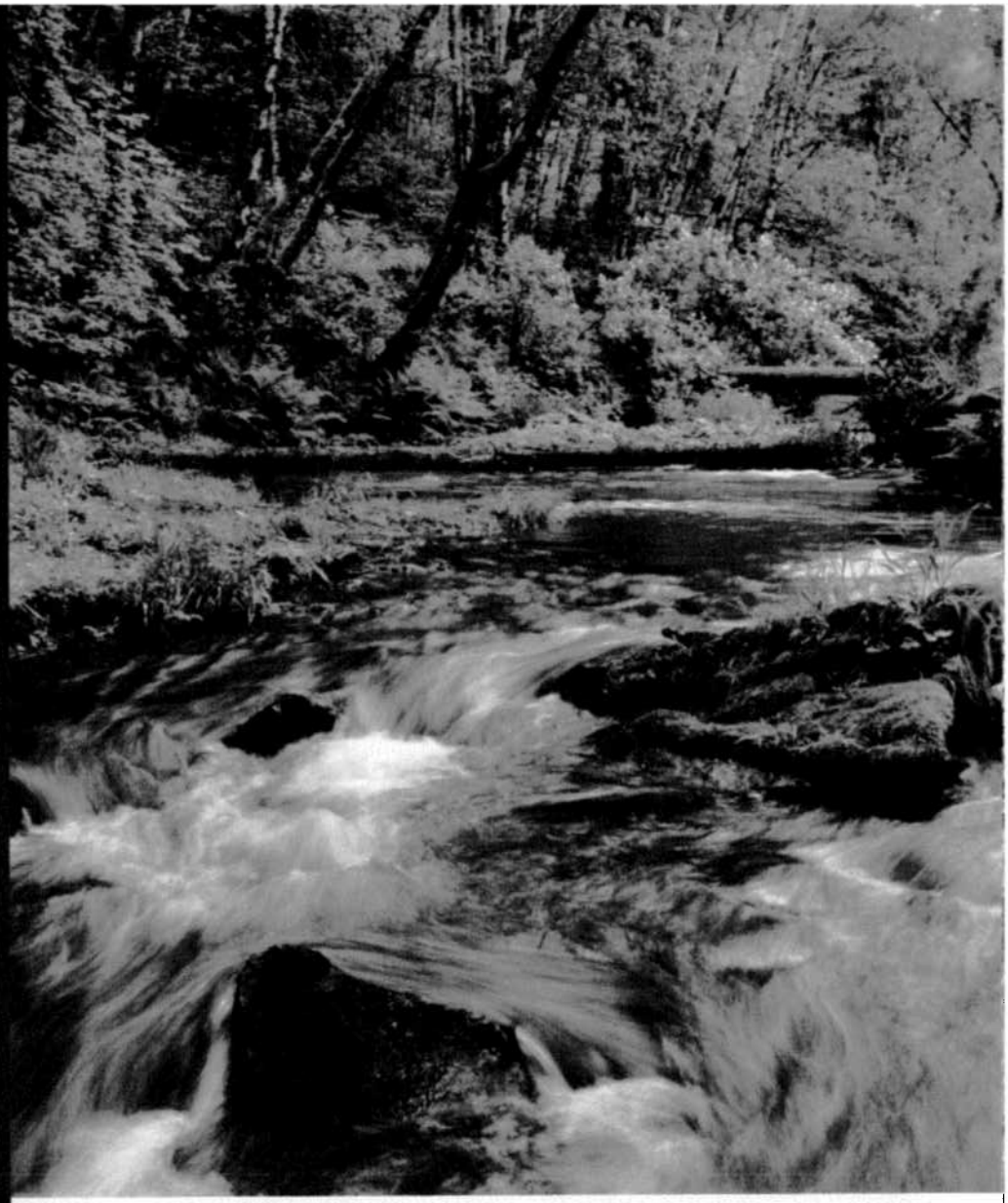

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