Letters to the Editor

Abnormal Electrophoretic Pattern of Glycosylated Hemoglobin in Sickle Cell Disorders

To the Editor: Sickling disorders constitute one of the most important genetic abnormalities worldwide. A point mutation results in the insertion of valine instead of glutamic acid in the sixth position of the β chain of hemoglobin (Hb; β_6 glu →val).[1]

Hb glycosylation involves the nonenzymatic addition of glucose to the terminal valine of β chain of Hb. Glycosylated Hb (HbA_{1c}) is currently used to reflect the mean daily blood glucose concentration over the preceding two months.[2,3]

The objective of our study was to find out the impact of sickle cell (SC) disorders (SC disease and trait) on the concentration of glycosylated Hb. The background is the involvement of the β chain of Hb in sickling by both the process of glycosylation and the sickling mutation.

Seventeen cases were selected from the Hematology Clinic of Al Noor Specialist Hospital, Makkah Al Mukarramah, Saudi Arabia (age range from 11 to 45 years; 6 males, 11 females; 10 Saudis and 7 non-Saudis). None of the cases had been transfused within the preceding six months and all proved to be normoglycemic. The patients had all been tested during regular outpatient follow-ups (i.e., none of them was in crisis). The clinical assessment, complete blood counts (CBC), sickling test,[4] and the electrophoretic patterns (Tables 1 and 2) confirmed that 14 were suffering from SC anemia (SS), while three had asymptomatic SC trait (AS).

Blood samples were withdrawn on EDTA tubes. CBC, blood glucose and Hb electrophoresis were performed. Hb gel electrophoresis was performed on alkaline (pH 8.6) and acidic (pH 6.0) media on the Beckman paragon electrophoresis system (Beckman instruments, Brea, C A). Glycated Hb electrophoresis was assayed as well on Beckman gel electrophoresis (pH 5.2). The expected range for HbA_{1c} is from 3.3% to 5.6%. Percentages of different Hb bands were quantified by scanning the gels with Beckman APPRAISE densitometer at 600 nm for Hb electrophoresis and 415 nm for glycosylated Hb.

The relative percentages of Hbs S, F, A, and A_2 (in alkaline and acidic pH), as well as that of glycosylated Hb in patients with SC disease are compiled in Table 1. Eleven out of 14 cases with SC disease (78.6%) exhibited high values of glycosylated Hb well above the upper normal of 5.6%. The three cases of SC trait, on the other hand, showed normal levels of glycosylated Hb (Table 2).

The levels of glycosylated Hb were reported to be influenced by—among other factors—the red cell life span being lower in various hemolytic anemias.[5] Paradoxically, we demonstrated in this study significantly high percentages of glyco-Hb in the majority (78.6%) of cases with SC anemia (Table 1), although all were normoglycemic. This phenomenon was not elicited in SC trait individuals (Table 2). It is not known whether this increased level of glycosylated Hb encountered in nondiabetic sicklers genuinely reflects an enhancement of the process of Hb glycosylation. Diabetes mellitus in general is rarely encountered in sicklers, mainly because of their relatively shorter life expectancy.[1] It is, however, tempting to assume that the proximity of sickling mutation to the NH_2 terminal of β chain in Hb S may promote the process of glycosylation.

Cox et al.[6] previously reported that elevated Hb F levels (>2%) caused spurious increases in glycated Hb concentrations as determined by electrophoresis. This was apparently not always true in our series. Cases with levels of Hb F <2% (e.g., cases 4 and 10 in Table 1) still have high levels of glycosylated Hb. Furthermore, the correlation was even very poor between the levels of Hb F

TABLE 1. *Electrophoretic patterns of Hb (alkaline and acidic pH) and glycosylated Hb in patients with sickle cell disease.*

		Alkaline Hb %			Acidic Hb %			
SI no.	A_2	S	F	A	S	F	A	Glycosylated Hb%
1	0	92.0	8.0	0	96.8	3.2	0	7.3↑
2	2.6	90.2	7.2	0	96.2	3.8	0	4.7
3	4.1	95.9	0	0	100	0	0	4.1
4	3.9	96.1	0	0	100	0	0	10.0↑
5	3.3	86.3	10.4	0	92.4	7.6	0	11.2↑
6	2.8	87.4	9.8	0	96.1	3.9	0	7.5↑
7	3.3	85.1	11.7	0	93.3	6.7	0	9.4↑
8	3.1	96.0	0	0	97.8	2.2	0	10.2↑
9	1.8	94.8	3.4	0	95.8	4.2	0	11.2↑
10	4.4	95.6	0	0	98.3	1.7	0	6.0↑
11	2.3	93.9	3.8	0	95.7	4.3	0	15.6↑
12	2.7	97.3	0	0	NT	NT	NT	6.0↑
13	2.6	97.4	0	0	NT	NT	NT	11.7↑
14	2.9	97.1	0	0	NT	NT	NT	3.0
Range	0-4.4	85.1-97.4	0-11.7	0	92.4-100	0-7.6	0	3.0-15.6
Mean	2.8	93.3	3.9	0	96.6	3.4	0	8.4

NT=not tested.

TABLE 2. *Electrophoretic patterns of Hb (alkaline and acidic pH) and glycosylated Hb in sickle cell trait individuals.*

Alkaline Hb %	Acidic Hb %

SI no.	A_2	S	F	A	S	F	A	Glycosylated Hb%
1	2.8	37	0	60	49	2.8	48.2	2.5
2	3.1	30.2	0	66.7	36	0	64	1.2
3	2.6	30.0	0	67.4	34.7	3.8	61.6	3.6
Mean	2.8	32.4	0	64.7	40	2.2	57.9	2.4

NT=not tested.

(in acidic pH) and glycosylated Hb (r=0.5995282).

On the other hand, measurement of HbA_{1c} by high performance liquid chromatography (HPLC) or electrophoresis was found to be unsuitable in certain homozygous hemoglobinopathies, including SC anemia, but not in the heterozygous states.[7] Some authors[8] using glyco-Hb columns reported different results. It is therefore recommended to use immunoassays rather than electrophoresis in monitoring glycosylated Hb in such cases.[7] Fructosamine determination might also offer a better guide to the glycemic status in sicklers. This is our next interest.

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Prevalence and Etiology of Childhood Sensorineural Hearing Loss (SNHL) in Riyadh

To the Editors: I read with great fascination the scientifically designed research work on SNHL by Drs. El Sayed and Zakzouk.[1] The research work was unique and original, and also provided basic and crucial information about this sizable problem. The authors did not find similar literature in the Middle East to refer to, which emphasizes the need for similar work to be done in this area. Having read the paper in depth, I wish to raise a few points. 1) The response rate for the participants in the study was not mentioned. This would have given an indication about the representation of the target population in Riyadh. 2) Out of a total of 6421 children, 1256 were chosen for further evaluation. Those children were chosen according to certain risk factors obtained on the basis of history and examination. This method assumes that history and clinical examination are reliable tools for discovering hearing impairment, but this reliability is questioned in the literature.[2-5] I think that involving a sample of those proved negative by history and examination would be relevant. It would assure reliability, and possibly increase the number of those who need further evaluation. 3) The paper recommended immunization against meningitis to prevent SNHL. I do not believe that providing meningitis vaccine to all children to prevent SNHL may be justified.

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Reply

To the Editor: We would like to thank Dr. Al-Ansari for his letter relating to our article, and would also like to make the following comments.

The response rates for participation in this study were almost equal in the six socioeconomic strata. Moreover, the

sampling method used in the study ensured control over the sample size in each age group.

In spite of extensive research, there is probably no ideal screening method that enables perfect identification of all degrees of hearing impairment in infancy and childhood. The ideal method must be reliable, noninvasive, cost effective, and with a high degree of sensitivity and specificity. Mass universal screening of hearing was found to be inadequately productive and unnecessarily expensive.[1] High-risk registration screening programs have been recommended by the Joint Committee on Infant Hearing, formed in 1969 and comprising representatives from the American Speech and Hearing Association, the American Academy of Ophthalmology and Otolaryngology, and the American Academy of Pediatrics.[1] The list was expanded in the 1990 position statement.[2] Many researchers have used the high-risk registration in studying the prevalence of hearing impairment.[3-5]

We did not recommend immunization to *all* children against meningitis to prevent sensorineural hearing loss (SNHL). We stated that since early diagnosis and treatment of meningitis are not effective in reducing postmeningitic SNHL, prevention of meningitis is the only way to reduce such complication. One way of preventing meningitis is certainly by immunization. Therefore, it is not unreasonable to assume that immunization can help in reducing postmeningitic deafness. We did not discuss any recommendation regarding when and to whom immunization should be provided.

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Tracheal Stenosis

To the Editor: Tracheal stenosis is a challenging problem for the surgeon as well as for the patient. The widespread use of endotracheal intubation during the last 25 years has resulted in more frequent laryngotracheal stenosis, which requires complex procedures.

Over a 15-year period (1981-1996), we treated 189 patients with benign tracheal stenosis: 161 of these were postintubation, 19 posttraumatic and 9 idiopathic stenosis. The patients consisted of 181 males and 8 females, with ages ranging from 12 to 51 years. All patients underwent surgery, except one who refused the operative treatment. After a full investigation which included bronchoscopy (fiberoptic and rigid), indirect laryngoscopy, tracheal tomography, or CT scan, patients underwent a one-stage surgical treatment through cervical approach, tracheal mobilization, resection of the affected section of the trachea (2 to 8 rings), and primary end-to-end tension-free anastomosis. Laryngotracheal resection was performed in 166 patients and cricotracheal segmental resection in 22 patients. At the end of surgery we inserted a thin chest suture in all the patients to maintain neck flexion up to 10 days. All the patients were extubated at the end of surgery. We did not use infrahyoid release or intrathoracic perihilar mobilization technique.

One hundred and thirty patients achieved good or excellent results in respiration or voice, 18 needed reconstruction, and 34 needed regular dilatation. In some patients, the surgery was complicated by granuloma formation at the anastomotic site, which was removed by coagulation. In six cases we used laser therapy for anastomotic stricture, which gave a good result.

One 63-year-old patient who refused surgery was treated by insertion of silicone tracheal stent, which doubled the airway diameter. The stent was well tolerated clinically, and the patient noted relief of dyspnea at once.

The most important element in the surgery of tracheal stenosis is recurrence prevention. This can be achieved by the tracheal mobilization technique (limited to suprahyoid release and peritracheal dissection), primary end-to-end tension-free anastomosis, and insertion of chin-to-chest suture for up to 10 days.

The incidence of post-tracheostomy stenosis can be reduced by careful placement of the stoma, avoidance of large apertures, elimination of heavy and prying ventilatory connecting equipment, and meticulous care of the tracheostomy. Cricothyroidostomy must be avoided. Cuff stenosis can be avoided by using low-pressure cuffs.

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Antibiotics: A Need for Regional Surveillance and a Control Program

To the Editors: The September 1996 issue of your journal contained two interesting papers on antimicrobial agents and bacterial resistance.[1,2]

The article of Kambal et al.[1] presented information about the current status in Saudi Arabia of *Haemophilus influenzae* susceptibility to antimicrobial agents, and compared findings to studies reported from other parts of Saudi Arabia, Kuwait, USA, South Africa, Thailand and some European countries. The presentation of comparative findings draws attention to the need for monitoring local and regional development in antimicrobial bacterial resistance. In this context, we would like to share some relevant information that was published on the antimicrobial susceptibility pattern of bacterial isolates, including *H. influenzae*, from Lebanon.[3] The *H. influenzae* isolates from both Saudi Arabia and Lebanon showed almost similar and high susceptibility to ampicillin, cephalothin and chloramphenicol. However, there was a marked difference pertaining to the susceptibility of isolates to erythromycin: 91% susceptibility in Lebanon compared to 57% in Saudi Arabia. Generally, the overall antimicrobial resistance rate against several bacterial species in Lebanon seems to fall between figures reported from the Arabian Gulf countries (higher), and those from medical centers in Europe and the USA (lower).

The editorial by Drs. Tabbara and Frayha[2] highlighted a significant concern about the global rise of bacterial resistance against old and new antimicrobial agents, with its subsequent limitation of options in treating bacteria, many of which can potentially cause severe infections. The major contributing factor to this resistance is the indiscriminate use of antibotics. Suggested solutions emphasize education in antibiotic use.[3,4] In addition, the region is in need of a dynamic body or forum that coordinates and emphasizes collaborative scientific efforts to establish a regional surveillance program to monitor, and hopefully control this potentially threatening situation of bacterial resistance to antibiotics, and its grave consequences to our patients and the community. Medical professionals and institutions in Saudi Arabia are the prime candidates to spearhead this endeavor.

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Survey of Medical Research Publications

To the Editor: With reference to the article entitled "Profile of Medical Research Publications from the GCC Countries, 1990-1994,"[1] a survey was conducted on the number of scientific publications written by the faculty members at the College of Medicine, Abha, over an eight-year period between 1988 and 1995. The survey showed that there were 139 publications during this period, and that they mostly covered local health problems of significant clinical interest to the region.

The *Medline-on-Silver-Platter* system and the database of King Abdulaziz City for Science and Technology (KACST) were used as the sources. The database of KACST was accessed through the King Saud University Gulfnet terminals available at the College. The search parameters were Abha and Saudi Arabia. Publications cited in the 1996 *Medline* disc were not counted in the search because they were not yet complete. The results of the search were fed into a desktop computer. Another search using the Reference Manager software version 7.02 was used to extract the required publications. Final sorting of references was done manually to exclude duplicate articles, and other articles published elsewhere.

The number of publications cited in the *Medline* database for the eight-year period (1988-1995) was 114, while those cited by the KACST database was 25, consisting mainly of publications in local journals. The largest number of articles were published in 1992 and 1995 (39 and 33 respectively). The number of publications, though relatively modest, nevertheless represents an impressive source of information about the region from a junior college which began graduating doctors in 1987. It should also be mentioned that the actual number of publications is much larger than what has been cited from these two sources. A large amount of research work has been published in journals that are not listed by either the Medline System or by the KACST database.

The significance of such research work is being reflected in the improving health services offered by the

College, and in its contribution to the pool of knowledge in basic medical sciences.

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Secondary Cardiac Hemochromatosis in Saudi Patients

To the Editor: We read with interest the report by Drs. Madani and Bormanis[1] entitled "Severe hereditary hemachromatotic cardiomyopathy responsive to small-volume venesection combined with deferoxamine." It raised certain points that applied to one of our patients who had a secondary cardiac hemochromatosis. He was a 21-year-old male, β-thalassemia major who presented at the hospital with symptoms and signs of congestive cardiac failure. His laboratory investigations showed diabetes mellitus, liver and testicular invovement with serum ferritin of 4600 μg/L. His echocardiogram showed biventricular enlargement, functional tricuspid and mitral regurgitation, and ejection fraction of 30%. A biopsy of the right heart proved the diagnosis. Although the patient had been on subcutaneous deferoxamine during his frequent blood transfusions, it was probably inadequate due to the small size of the heart chamber.

The patient was subjected to intensive intravenous deferoxamine therapy via infuse-a-port with captopril and Lasix therapy, with the resultant improvement. By four months, his ejection fraction became 45% with decrease in the degree of valve regurgitation, as assessed by echo. The response is well prescribed,[2,3] but would this be sustained as reported?[4] This will be answered during the long follow-up of this patient with late presentation. Early recognition of this potentially reversible disease is of vital importance. However, it is also important to assure adequate chelating of iron by blood test.

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Soda Lime Canister Hazard: Heed the Warning Label!

To the Editor: Recently our anesthetics department experienced a potentially near-catastrophic mishap. Anesthetic maintenance personnel left a clear plastic cellophane wrapper on a carbon dioxide (CO_2) soda lime canister (Puritan Bennett Corp. Lenexa, KS, USA, prepackaged, non-hygroscopic soda lime USP/NF granule: 4 to 8 US mesh 2.5-5.0 mm). High airway pressures (60-70 cm H_2O), associated with markedly reduced tidal volumes and end-tidal pCO_2, resulted in severely reduced lung compliance and subsequent failure to adequately ventilate the patient. The pre-packaged soda lime CO_2 canister refill is normally labelled with a bright orange-colored warning "REMOVE WRAPPER BEFORE USE" (Figure 1). This alert should have been readily apparent to anyone maintaining the soda lime CO_2 canisters. Despite a previously related case report on Baralyme CO_2 packaging hazards admonishing manufacturing modifications to: 1) omit paper seals, 2) to enlarge and construct seals of bright contrasting color, this anesthetic mishap could not be prevented. Unfortunately, the anesthetist was unaware that the soda lime CO2 canister had been changed between cases. By chance, a circulating anesthetic consultant

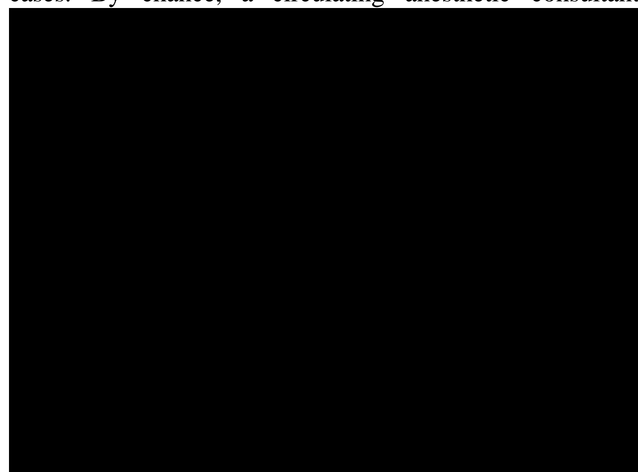

FIGURE 1. A soda lime CO_2 canister.

recognized the problem immediately, having personally experienced a similar problem during his residency training. It is clear that human error can be blamed for this near mishap, but the incident underscores the gravity of heeding warnings on all labels and relating even minor equipment changes, no matter how trivial, to allied anesthetic personnel. Ultimately, it is only through painstaking examination of the anesthesia machine and breathing circuit prior to each anesthetic induction that such mishaps can be prevented.

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