Letters to the Editor

Discussion of "Sudden Infant Death Syndrome: Measurement of Total and Specific Serum Immunoglobulin E (IgE)"

Dear Sir:

I read with interest the significant paper "Sudden Infant Death Syndrome: Measurement of Total and Specific Serum Immunoglobulin E (IgE)" by Mirchandani et al (Vol. 29, No. 2, April 1984, pp. 425-429).

I wish to address myself to the reference made to our paper "The Sudden Infant Death Syndrome: A Possible Hypersensitivity Reaction Determined by Distribution of IgG in Lung Tissue" by Raven et al (Vol. 23, No. 1, Jan. 1978, pp. 116-128).

Briefly, by immunofluorescence techniques and use of specifically conjugated antihuman immunoglobulin, bound IgG was identified in the lung lesions of 33 SIDS victims, but not in the lungs of 10 matched controls. All were negative for IgA, IgM, and IgE. In four SIDS victims, positive for IgG, respiratory syncytial virus (RSV) was identified by indirect immuno-fluorescence staining of paraffin sections of lungs. Our study provided evidence of antigen-antibody damage caused by immune complex disease, compatible with hypersensitivity pneumonitis or allergic alveolitis.

In accordance with the accepted classification of systemic allergic reactions, Type I hypersensitivity refers to immunoglobulin E (IgE)-mediated immediate reaction seen in anaphylaxis and atopy. In the absence of IgE, our pathologic and immunologic studies are characteristic of Type III hypersensitivity associated with immunoglobulin G (IgG)-mediated-immune complex disease with antigen-antibody deposition in tissues, complement activation, and inflammation [*1,2*].

Our epidemiologic studies beginning with 1959, provided invaluable clinical markers [*3*]. It was clearly shown that the SIDS infant was not the healthy infant it was believed to be. In over 40% SIDS was associated with low birth weight, prematurity, fetal retardation, congenital defects, and failure to thrive—all inherent in adverse environmental factors operative through the mother and affecting the fetus during gestation. The half-life of maternal immunoglobulin (IgG) is three to six weeks, followed by a precipitous decline in the postneonatal period. The infant is most vulnerable for SIDS between two and four months of age. If this coincides with the cold months (October to April), during the seasonal endemic increase of viral (mainly RSV virus) infection in older children and adults, the repeated exposure hypersensitizes the immunocomprised infants who become victims to SIDS.

Preventive medicine and education is needed at all levels. Vaccination for RSV may be dangerous in the postneonatal period. Passive protection may be provided by immune gamma globulin during the high risk months. Breast feeding may be protective.

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References

[*1*] Raven, C., "SIDS—A New Perspective: Immunologic-Mediated Pulmonary Disease," *Journal of the American Medical Women's Association*, Vol. 35, No. 4, Nov. 1980, pp. 262-263.

[*2*] Raven, C., paper presented at the 8th International Convocation on Immunology, Witebsky Institute on Immunology, SUNY, Buffalo, June 1982.

[*3*] Raven, C., "SIDS: An Epidemiologic Study," *Journal of the American Medical Women's Association*, Vol. 29, No. 3, 1974, pp. 124-132.

Authors' Response

Dear Sir:

This is in response to the comments of Dr. Raven on our article "Sudden Infant Death Syndrome: Measurement of Total and Specific Serum Immunoglobulin E (IgE)" [*1*]. There are several problems in accepting her hypothesis that the lung pathology in SIDS infants is compatible with hypersensitivity pneumonitis or allergic alveolitis. This problem has been aptly addressed by Dr. Valdes-Dapena [*2*] and Dr. Mueller [*3*]. Morphological findings described by Dr. Raven [*4*] as being characteristic of SIDS infants are nowadays unacceptable to most pathologists. By her own admission, most of the cases included in her study show "more severe pulmonary pathology" and "the morphological findings were consistent with acute respiratory tract infection, acute intersitial pneumonitis, bronchiolitis, or segmental pneumonia." Sudden Infant Death Syndrome, by definition, is a sudden unexpected death by history, in which a thorough postmortem examination fails to demonstrate an adequate cause of death [*5*].

Clinical presentations of patients with acute hypersensitivity pneumonitis (Type III hypersensitivity) are fever, chills, dry cough, malaise, and profound dyspena 4 to 8 h after exposure of a previously sensitized individual to the antigen [*6*]. This has never been a clinical feature of infants dying of SIDS.

There are two possible explanations for the presence of IgG in the lungs of the infants studied by Dr. Raven. The first, as described by Valdes-Dapena [*2*], "it is not unusual to find antibody producing cells in the lungs of infants." It is not possible to explain adequately negative immunological findings in two normal control lungs on this hypothesis alone. The second, a more plausible explanation, is that the IgG represents attached immunoglobulins to monocytes-macrophages (found in lung sections) via Fc receptors. It is well-known that the monocytes and macrophages have receptors for the Fc portion of immunoglobulins and complement [*7,8*]. In a recent study of normal and leukemic monocytes, one of us has shown that the attached cytophilic antibody is frequently IgG, Kappa [*8*]. It is possible to remove these cytophilic or attached immunoglobulins from the cells by overnight incubation in serum free media. Thus, mere presence of immunoglobulins is not indicative of secreted immunoglobulins in response to antigenic stimulus. Elevated levels of serum immunoglobulins or specific antibodies to viral antigens have not been shown in SIDS infants [*9,10*].

In summary, with due respect to Dr. Raven's enthusiasm, there is neither morphological, immunological, nor microbiological support of her contention. It should also be mentioned that even though the material of Dr. Raven's study was from the Wayne County Medical Examiner's Office, none of the present staff of six board-certified forensic pathologists agree with her long-standing conviction that crib death is a result of viral interstitial pneumonia or a hypersensitivity reaction.

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References

[*1*] Mirchandani, H. G., Mirchandani, I. H., House, D., "Sudden Infant Death Syndrome: Measurement of Total and Specific Serum Immunoglobulin E (IgE)," *Journal of Forensic Sciences*, Vol. 29, No. 2, April 1984, pp. 425-429.

[*2*] Valdes-Dapena, M., "Can Crib Death be Prevented?" *Journal of Forensic Sciences*, Vol. 24, No. 3, July 1978, pp. 539-541.

[3] Mueller, K. H., "On: Pro and Con," *Journal of Forensic Sciences*, Vol. 23, No. 4, Oct. 1978, p. 663.
[4] Raven, C., Maverkis, N. H., Eveland, W. C., and Ackerman, W. W., "The Sudden Infant Death Syndrome. A Possible Hypersensitivity Reaction Determined by Distribution of IgG in Lungs," *Journal of Forensic Sciences*, Vol. 23, No. 1, Jan. 1978, pp. 116–128.
[5] Beckwith, J. B., "The Sudden Infant Death Syndrome," U.S. Government Publication (HSA) 78-5251, Department of Health Education and Welfare, Washington, DC.
[6] Caldwell, J. L. and Kaltreider, H. B., "Pulmonary and Cardiac Diseases," in *Basic and Clinical Immunology*, 2nd ed., H. H. Fudenberg, D. P. Stites, J. I. Caldwell, and J. V. Wells, Eds., Lange Medical Publications, CA, 1978, pp. 538–542.
[7] Huber, H., Polley, M. J., Linscott, W. D., and Miller-Eberhand, H. J., "Human Monocytes: Distinct Receptor Sites for the Third Component of Complement and for Immunoglobulin G," *Science*, Vol. 162, 1968, p. 1281.
[8] Mirchandani, I. H., Takbaczka, P., and Patutke, M., "Acute Monocytic Leukemia: A Surface Marker Study," *American Journal of Haematology*, Vol. 12, 1982, pp. 139–147.
[9] Valdes-Dapena, M., Eichman, M. F., and Ziskin, L., "Sudden and Unexpected Deaths in Infants—I. Gamma Globulin Levels in Serum," *The Journal of Pediatrics*, Vol. 63, No. 2, 1963, pp. 290–294.
[10] Clausen, C. R., Ray, G., Hebeseit, N., and Eggleston, P., "Studies of the Sudden Infant Death Syndrome in King County, Washington IV Immunologic Studies," *Pediatrics*, Vol. 52, No. 1, July 1973, pp. 45–51.

Discussion of "Determination of Carboxyhemoglobin in the Presence of Other Blood Hemoglobin Pigments by Visible Spectrophotometry"

Sir:

A very interesting article by Siek and Rieders appeared in the *Journal of Forensic Sciences* (Vol. 29, No. 1, Jan. 1984, pp. 39–54). In this article the determination of carboxyhemoglobin (HbCO) in blood is performed with the help of a mathematic system of three equations with three unknowns. This system is based on the absorption values of oxyhemoglobin of (HbO_2), HbCO, and reduced hemoglobin (Hb_r) at the three isosbestic points of their curves. The HbCO percentage is confirmed by the first derivative spectrum and by the evaluation of special features of the basic spectrum (that is, the λ_{max} at different CO%).

As it is shown by the authors at their examples, $\lambda = 548.2$ is not always an isosbestic point for the curves of HbO_2, HbCO, and Hb_r. It is obvious that this fact can cause inaccuracies of the method they suggested.

Another observation on the basic spectrum shows that a second peak, after reduction with $Na_2S_2O_4$, appears only when HbCO is more than 30% of the total hemoglobin.

Upon these observations we would like to make the following comments:

1. The curves around the isosbestic points are straight lines around which the slopes of both compounds are essentially even (in other words the second derivative is zero). A similar assumption is made by Sanderson et al [1].

We believe that zero points of the second derivative spectrum could show with greater accuracy the three isosbestic points where the measurements of absorption should be made. A correction of $\Delta\lambda$ as a result of scanning apparently will be needed.

2. The second peak which did not appear at the basic spectrum at HbCO concentrations lower than 30% will become more apparent at the second derivative spectrum which is extremely sensitive even to slight changes of the curvature of the basic spectrum.

We hold the opinion that the use of second derivative spectra can offer great advantages in the determination of HbCO in blood because of their accuracy, their sensitivity, and the great number of special features they offer.

At our laboratory we are working on these special features to establish a new method for the determination of HbCO in blood based on the undoubtful advantages of the second derivative spectra.

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Reference

[1] Sanderson et al, *Journal of Industrial Medicine*, Vol. 35, 1978, pp. 67-72.

Authors' Response

Dear Sir:

We are pleased to receive comment on our paper on the spectrophotometric determination of carboxyhemoglobin and largely agree with Athanaselis et al. Spectra covering a wavelength range, be it straight wavelength-absorption, first derivative, second derivative, or difference spectra, are preferable to point measurements.

While a defined peak for the reduced carboxyhemoglobin-hemoglobin first derivative scan is not pronounced until about 30% HbCO, the beginnings of a peak can be perceived as low as 5% HbCO. Our use of first derivative scans was for qualitative confirmation and not quantitative analysis. Our main quantitative tool was a delta-absorbance measurement, and our paper did show close agreement of delta-absorbance with the isosbestics points equations, with the classic Wolff technique, and with the position of the maximum nearest 576 nm.

The availability of high performance spectrophotometers will make many spectrophotometric approaches amenable to accurate HbCO determinations *in fresh clinical bloods.* The problem will remain in postmortem bloods that contain denatured globins, methemoglobin, and sulfhemoglobin. A second derivative method for forensic science purposes must be evaluated "on the front lines," so to speak, and not with fresh clinical bloods only.

It appears that spectrophotometric methodology for carboxyhemoglobin is making a strong comeback and we look forward to the second derivative method promised in the above letter.

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Discussion of "How Individual Are Personal Writing Habits?"

Sir:

I read with great interest the article by Ordway Hilton, "How Individual are Personal Writing Habits?" (Vol. 28, No. 3, July 1983, pp. 683-685). Mr. Hilton has raised a very interesting

question but his answers are limited. Document examiners ignored the aspect of determining personality from handwriting. Above all, the decision to write comes from brain. The hand obeys the command of brain, so we see writing on the paper. In other words, it is not only handwriting but brainwriting.

Mr. Hilton pointed out "Any two writings by different individuals usually contain some similarities, sometimes a great number, but the differences should distinguish between the writers." The basic question here is in what way the document examiner could utilize the personal habits to make the differences distinguish between writers? Is there any characteristic list of writing habits? Whether the document examiner can classify the writing habits which may belong to particular group or groups of individuals? Whether the relation of cause and effect can be established? Or is it some sort of professional secret? On the other hand, some answer of his question can be found when one considers the personality traits in handwriting analysis. Depending upon the writing specimen, it can be said that the writer may be sensitive to criticism, persistent, sarcastic, or deceptive, secretive, impulsive, and so on and so forth (Fig. 1). These personality traits could give a lead to the examiner to distinguish between the writers.

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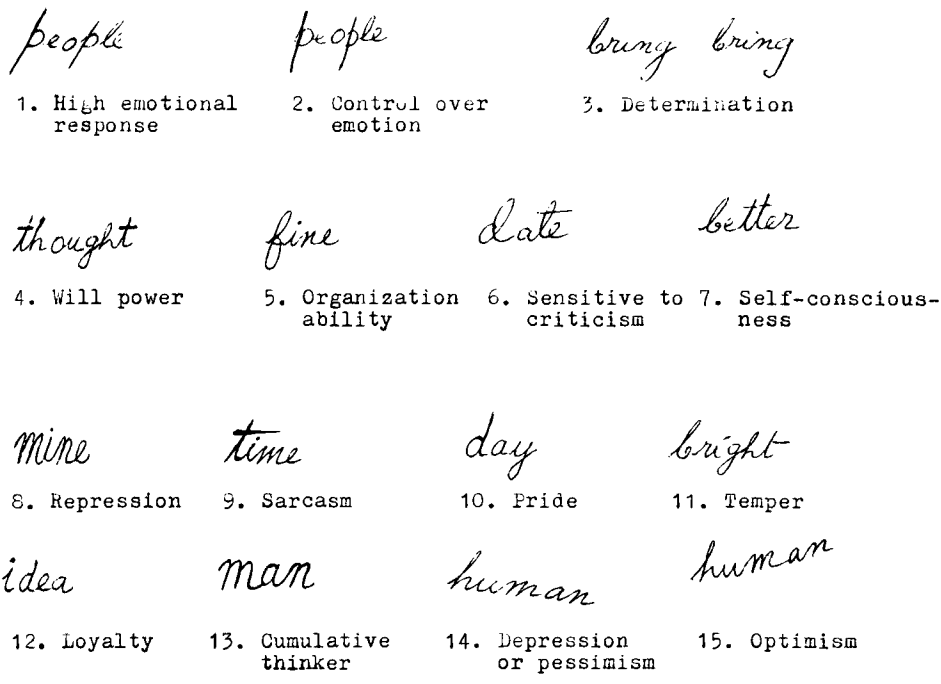

FIG. 1—*It is a general illustration. An opinion should not be formed from one word. The sequence of the occurrence of traits in the whole writing should be considered before passing an opinion.*
1. forward slant 2. vertical slant 3. down stroke letters, g *(loop or without loop) 4. weight of* t *bars 5. balanced stroke of* f *6. looped stems,* d,t *7. final or second letter stroke higher than the first,* t *8. close strokes,* m,n *9. arrow like* t *bars 10. tall stems,* d,t *11.* t *bar not touching the stem 12. small and rounded dot,* i *13. rounded tops,* m,n *14. downward droop or trend 15. upward slant.*

Authors' Response

Sir:

Dr. Nigoyi's letter shows a lack of understanding of the work of a questioned document examiner and how the identification of handwriting differs from graphological analysis. The identification of handwriting and graphological determinations of character traits are two very different disciplines that he choses to treat as one.

The production of handwriting involves a complex physical act. Between the brain and the moving hand and fingers is an extensive muscle and nerve system that must be trained to react in a coordinated way to produce the finished writing. Thus writing is more than simply "brain-writing" as Niyogi and some graphological writer term it. Writing can be changed by intensive practice, and it can deteriorate over a period of time by lack of proper attention to its production. Physical factors such as injury to the arm or hand can change a person's handwriting.

Niyogi's references to personality traits and his suggestion that document examiners should apply these to handwriting identification is an easy route to error in identification problems. Graphologists find similar personality traits in very different handwritings, that is those that can easily be distinguished by the identification processes. If one is inexperienced in identification of handwriting, overdependence on these traits in an identification problem can lead to serious error.

Differences in handwriting are found in the factors summarized in the paper under discussion and other factors not specifically mentioned. It was not the writer's intention to make an exhaustive list of writing characteristics and habits that have been treated in the basic literature of the field, but to point out that writing habits are seldom so unique that they are truly individual. Thus, identification rests on the consideration of all writing habits present and proper evaluation of the influence of variation. Differences in identification factors, despite simularities, are the means of distinguishing between two writers. Therefore, the questions raised in his last paragraph are beyond the scope of the original article.

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Discussion of "Procedures and Responsibilities in Forensic Toxicology—To What Extent Are They the Results of Laboratory Facilities?"

Sir:

In a letter to the editor of this *Journal*, Holmgren et al [*1*] discussed procedures and responsibilities in forensic toxicology. We would appreciate the opportunity to express our opinion on the same matter, since we were involved in the case they refer to. All essential medical and toxicological data dealing with the case of sudden child death associated with the ingestion of fluid dish detergent mentioned by Holmgren et al [*1*] have been reported previously [*2*]. Our comments are:

1. A sample of the stomach content was given to the manufacturer of the detergent with the understanding that their laboratory was best suited for the required analysis. As reported in our paper [*2*] they detected a specific marker—linear alkyl benzene sulphonate (LAS)—and calculated that about 1 mL of the detergent had been contained in the stomach shortly before death. They regarded this amount as toxicologically insignificant. However, as several hours had elapsed from the time of suspected consumption to the time of death we supposed that the amount contained in the stomach was just a fraction of the amount ingested. The Toxicology Department of National Institute of Forensic Chemistry in Linköping found much less (1/10)

of the detergent marker, but we decided to accept the former analysis, as it had been performed by experienced personnel. At that time we also requested from the Toxicology Department analysis for LAS in other body samples but we were refused.

2. One year after the death, the Toxicology Department reported that they found some differences between the alcohols (propanol, butanol, and so forth) (cf *1*) found in the stomach and the detergent bottle. These results were not easily interpreted, since the stomach content sample had been kept in a refrigerator for a whole year without preservatives. Thus we never withdrew our original postulate that the detergent was involved in the death of the child, but pointed out that the result from the Toxicology Department did not support our interpretation.

3. The case was discussed with several experts in the field of forensic pathology and toxicology both here in Stockholm and abroad. Moreover, it was presented at the meeting of Swedish Medico-Legal Association which was held in Stockholm, 5 Dec. 1980. Representatives from the National Institute of Forensic Chemistry were present but did not comment on the report at that time.

4. The later phases of this investigation were performed under conditions that were far from satisfactory from a scientific point of view. For example, *on behalf of the manufacturer* (cf *1*), a pediatric pathologist reexamined the microscopical sections (after the slides had been taken from our laboratory without our knowledge) and concluded that the cause of death was serous leptomeningitis and encephalitis. This diagnosis is neither compatible with the Toxicology Department's interpretation of the results nor could it be confirmed by us or by outstanding experts in forensic histology abroad. A more recent example is to accuse one of us as acting partially with regards to this case [*1*], without declaring the facts that oppose this judgement.

5. It should also be mentioned that Holmgren et al [*1*] wrote a letter dated 30 Sept. 1982 to the *Zeitschrift für Rechtmedizin* with the same type of comments on the chemical analysis as presented in their recent letter. Our objections were about the same as this time, and as far as we know the *Zeitschrift* did not publish the letter.

Everything taken into account, we sincerely wonder if this case is an adequate argument *for* centralization of all forensic toxicological examinations in one country to one laboratory.

And one more question: who carries the ultimate responsibility for the interpretation and evaluation of the cause of death—the forensic toxicologist or the medical examiner?

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References

[*1*] Holmgren, P., Jonsson, J., and Schubert, J., "Procedures and Responsibilities in Forensic Toxicology—To What Extent Are They the Results of Laboratory Facilities?" *Journal of Forensic Sciences*, Vol. 29, No. 1, Jan. 1984, pp. 16–18.

[*2*] Högberg, J. and Rajs, J., "Sudden Unexpected Child Death Associated with Ingestion of Fluid Dish Detergent," *Zeitschrift für Rechtsmedizin*, Vol. 89, 1982, pp. 51–55.

MEETING

The 9th Australian International Symposium on the Forensic Sciences will be held in Melbourne from 3-7 Feb. 1986 before the Police Surgeons Conference scheduled for the following week in Sydney. It will include sessions on all the forensic sciences fields. Send inquiries to:

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ACKNOWLEDGMENT

The authors (Christmore et al) of "Improved Recovery and Stability of Ethanol in Automated Headspace Analysis" in the Vol. 29, No. 4, Oct. 1984 issue of the *Journal* would like to acknowledge the contributions of Norman Weissman, Ph.D., and Philip C. Reynolds who independently called our attention to reports in the literature on the use of sodium dithionite as an inhibitor of oxyhemoglobin-catalyzed oxidation of ethanol.

ERRATUM

In the Vol. 30, No. 1, Jan. 1985 issue of the *Journal* on p. 8 Dr. Niyogi's name was misspelled inadvertently as Nigoyi. The correct spelling is Niyogi.