CHEMICAL MANUFACTURERS ASSOCIATION

December 16, 1981

MEMORANDUM

TO: Vinyl Chloride Program Panel

FROM: Carol R. Stack

Please note that the December Program Panel meeting has been rescheduled for January 27, 1982 at 9:00 A.M. in the Lobby Conference Room.

Environmental Health Assoicates (EHA) is preparing an alternative proposal for the epidemiology study update. EHA expects to submit the proposal to CMA by the end of the year. Copies will be distributed to Panel members for review prior to the January 27 meeting.

If you are unable to attend this meeting, please let me know as soon as possible.

Tentative Agenda

1.0 Reassessment of epidemiology study update; status of contract negotiation

2.0 Review of alternative proposal from Environmental Health Associates

3.0 Status Report - University of Louisville study

CRS/seh

CMA 007945

CMA
Notice of Meeting
of the
Vinyl Chloride Program Panel

Date: December 16, 1981

Time: 9:00 A.M.

Place: CMA Offices
2501 M Street, N.W.
Washington, D.C. 20037

☐ I will attend the meeting.

☐ I will not be able to attend the meeting.

_____
(Name)

_____
(Company)

Please return this form to Dr. Carol Stack at the address shown above.

November 23, 1981

Dear Vinyl Chloride Program Panel Member,

A meeting of the Vinyl Chloride Panel is scheduled for December 16, 1981 at 9:00A.M. in CMA headquarters, Board Conference Room B. This is an important meeting that I urge you to attend.

For the past several months, CMA staff have attempted to negotiate a contract with Environmental Health Associates (EHA) to conduct an update of a vinyl chloride epidemiology study. To date we have been unsuccessful in writing a contract that will satisfy EHA's requirements and, from CMA's viewpoint, protect the needs and financial interest of those companies supporting the study.

This past summer we thought an agreement was reached and CMA executed the contract. EHA responded with an amendment to the contract that we did not find acceptable and the situation is stalemated once again. At this point, CMA needs input from Panel members regarding the extent to which EHA's terms are acceptable, or unacceptable, to the sponsoring companies.

The contract and amendment are enclosed for your review. A memorandum written by Mr. Pat Joyce, CMA legal counsel, on the status of the negotiations is also included.

I look forward to meeting with you on December 16. Would you please indicate your attendance on the attached form and return it to me as soon as possible.

Sincerely yours,

Carol R. Stack

Carol R. Stack, Ph.D.
Administrator
Vinyl Chloride Program

Enclosures

/seh

CMA INTEROFFICE MEMO

TO: Carol Stack
Program Administrator Vinyl Chloride

FROM: Patrick C. Joyce
Staff Attorney

DATE: November 10, 1981

RE: Vinyl Chloride Contract with Environmental Health Associates

Based on our conversation of October 30, 1981, with Dick Davis of EHA and his lawyer, it is my recommendation that we communicate with the chairman of the Vinyl Chloride Panel on the status of our contract negotiations.

In August 1981, we believed there was agreement in principle with EHA on the terms of the contract to perform the update on the vinyl chloride study. On October 15, 1981, EHA proposed new and significant changes in the terms of the contract. The conversation Dr. Stack and I had with EHA on October 30, 1981, was intended to resolve my difficultities with those proposed changes. It was unsuccessful.

EHA insists that EHA be permitted to terminate the epidemiological study at some unknown time in the future if in the exclusive judgment of EHA the study should not be completed.

EHA has also taken the position that it cannot make a realistic estimate of the cost to complete this study. Therefore, EHA objects to our efforts to establish a maximum dollar amount for the completion of the study. EHA will not agree to a maximum cost even if CMA agrees to permit cost overruns beyond an estimated price.

EHA insists that CMA reimburse the contractor for the costs, as soon as they are incurred. Such a reimbursement arrangement is inconsistent with the conventional practice of reserving a significant percentage of the total contract price until the final report is presented and accepted by th program panel.

Obviously, EHA desires to have the type contract whereby CMA would be obligated to pay for all the costs, labor, and expenses incurred by EHA in the performance of this contract. However, under such circumstances there would be no means by which CMA could properly budget for this long term contract or exercise any meaningful control over cost overruns.

Accordingly, the standard practice at CMA is to award only fixed price contracts. Much leeway can be provided in fixed price contracts to provide for acceptable cost overruns without providing "blank checks" for the contractors.

It is my understanding that the vinyl chloride program panel is favorably impressed with the qualifications of EHA. It is also my understanding that the vinyl chloride panel found the estimate from EHA with some cost overruns acceptable. Since EHA has now withdrawn its estimate, I believe it advisable that the panel reconsider the value of EHA's services.

CMA can legally award a contract on a cost plus expense basis for EHA; however, the panel should be fully aware that many months from now CMA would have little control over EHA's cost overruns. Therefore, there are good policy reasons for not acceding to EHA's demands.

Other alternatives to a cost plus contract are available if EHA is sincerely interested in performing this study. As you know, EHA has requested a series of contracts so that the payments could be staggered. The difficulty with this approach is that it, like EHA's current proposal, could result in the expenditure of over $100,000 without any substantive workproduct being completed other than an improved data base. EHA would not be obligated to render any professional opinions.

If I can be of further service to the Panel or Dr. Torkelson, please advise.

AMENDMENT TO AGREEMENT

ENVIRONMENTAL HEALTH ASSOCIATES, INC. (hereinafter "the Contractor") and CHEMICAL MANUFACTURERS ASSOCIATION, INC. (hereinafter "CMA"), hereby amend their Agreement for the Update of the Epidemiological Study of Vinyl Chloride Workers (CMA Reference No. VC 9.0 Epi-EHA) by amending and restating Paragraphs 24 and 25 thereof to read as follows:

24. The Contractor's Estimated Cost for this project is $205,207 which consists of $11,495 for Tasks 1 through 5 of Phase I (which have been completed at the initiation of this Agreement); $63,567 for Tasks 6 through 8 of Phase I; and $130,145 for Tasks 1 through 6 of Phase II. The aforementioned Estimated Costs are itemized by tasks in Exhibit A and a Ceiling Cost is indicated for each task.

The Scope of Work set forth in Contractor's proposal will be performed within the total Ceiling Cost of $263,230. However, if the Contractor determines that its projected actual costs for the entire project, calculated at the labor rates set forth in the proposal, will exceed the total Ceiling Costs for the project by more than 30%, CMA agrees to review the Contractor's itemized projected cost overruns. CMA shall not unreasonably and without good cause refuse to compensate the Contractor for that portion of those previously unforeseen expenses which are more than 30% in excess of the ceiling costs.

In the unlikely event of a dispute over cost overruns, the Contractor shall not delay completion of the Scope of Work pending resolution of the negotiations, provided that CMA agrees to reimburse Contractor for any costs incurred in continuing performance of this Agreement pending such resolution.

In the event that (i) the Contractor is unable to complete the Scope of Work because of circumstances beyond its control (including, without limitation, a material lack of available data or a material delay or failure to perform on the part of CMA or a study plant) or (ii) CMA determines for any reason that it will not compensate the Contractor for that portion of its costs which are more than 30% in excess of the Ceiling Costs; then the Contractor may terminate the Agreement in the manner provided in Paragraph 28.

For performance of this Agreement by the Contractor, CMA shall make payments to the Contractor as follows:

Initial Payment	a)	Upon execution of this Agreement by both parties $55,000.
Interim Payments	b)	Upon receipt of each quarterly report described in Paragraph 16, quarterly payments in the amount stated in Attachment A (Payment Schedule) (adjusted as provided below) until such time as the total amount paid by CMA (including the initial payment) shall reach the lessor of (i) 85% of the Contractor's total costs, or (ii) $223,000.
Final Payment	c)	Upon receipt of the Final Report by CMA as defined in Paragraph 26 accompanied by a detailed accounting of materials and services purchased, and time expended for the total project, a sum in the amount of $15,207, subject to adjustments as provided herein.

Interim payments called for by the Payment Schedule shall be adjusted upward by an amount equal to the difference (if any) between (i) 85% of the Contractor's total costs through the quarter to which the interim payment relates and (ii) the total of all payments previously made by CMA and the scheduled interim payment for such quarter.

If the actual costs at the completion of the project are less than the Estimated Costs of $205,207, the Contractor shall deduct the difference between the actual costs and $205,207, and credit CMA for that difference in the final invoice.

25. Within 60 days of the completion date defined in the Work, the Contractor will provide to CMA one unbound original and 25 copies of its draft final report. This draft final report will describe all work performed, record essential data and discuss results and conclusions in a manner customary in similar reports.

The Contractor's scientific conclusions and professional judgments arising out of performance of the Work shall be the responsibility of the Contractor and shall not be subject to CMA control. However, CMA shall have the right to review such judgments and conclusions prior to preparation of the final report for the purpose of proposing clarifications, and making format and editing comments, but not for the purpose of substituting CMA's opinion for that of the Contractor.

DATED: October 15, 1981.

ENVIRONMENTAL HEALTH ASSOCIATES, INC.

By Richard L. Davis
Vice President and Treasurer

CHEMICAL MANUFACTURERS ASSOCIATION, INC.

By _____
Vice President and Treasurer

Agreement

between

CHEMICAL MANUFACTURERS ASSOCIATION

and

Environmental Health Associates, Inc.

CMA Reference Number: VC 9.0-Epi-EHA

1. The parties to this Agreement are Environmental Health Associates, Inc. (hereinafter the Contractor) and th Chemical Manufacturers Association, Inc. (hereinafter CMA).

2. CMA will be represented during this Agreement by Carol R. Stack, Ph.D. the Program Administrator. All communications with CMA shall be directed to the Program Administrator. Changes in this Agreement must be authorized in writing by the Program Administrator and any increase in cost must be authorized in writing by CMA's Treasurer.

3. The Contractor will employ Dr. Donald Whorton to personally direct and supervise the performance of this Agreement. If any change in key personnel occurs, the Contractor must promptly notify CMA, in which event the Agreement is subject to renegotiation or termination at CMA's option.

4. The Contractor agrees to perform in the manner described in the Scope of Work "A Proposal for the Update of the Epidemiological Study of Vinyl Chloride Workers" March 1981, which is attached and expressly made part of this Agreement.

5. This Agreement and the attached Scope of Work represent a contract between the parties. There are no promises, terms, conditions, or obligations other than those contained herein; and this Agreement shall supersede all previous communications, representations or agreements, either verbal or written, between the parties hereto.

6. If it is deemed necessary to make changes in the approved Scope of Work after this Agreement is made effective, such changes and reasons for the changes are to be documented by the Contractor in the final report. Oral authorization by CMA for changes in the Scope of Work is permitted but a memorandum of the change must be sent by the Contractor within five working days.

7. The Contractor shall maintain the highest standard of professional conduct and apply its best efforts in the performance of this Agreement in conformity with generally accepted standards for the type of Work specified.

8. The Contractor shall be an independent contractor throughout the term of this Agreement. The Contractor will employ the staff, control the personnel, provide the facilities, and have exclusive control over its employees and the expenditure of funds provided by CMA in this Agreement.

9. The Contractor shall agree to protect, defend, indemnify, and hold CMA harmless from any and all judgements, orders, decrees, awards, costs, expenses, attorney's fees, settlements and claims on account of damage to property or personal injury, including death, which may be sustained by the Contractor, its employees, CMA, CMA's employees or third parties (except for damage or injury caused by the negligence of CMA) where such damage or injury occurs in connection with the performance of this Agreement.

10. The Contractor, by executing this Agreement, shall certify that it has comprehensive liability insurance covering the performance of this Agreement.

11. CMA and the Contractor agree to full disclosure of scientific information developed through this Agreement. However, the Contractor shall not release such information ~~before publication by CMA~~ without prior CMA knowledge and review. This provision is not intended to inhibit private scientific exchange and consultation with the personnel or organizations participating in support of the project.

12. If patentable discoveries should ensue, these shall be declared in the public domain without any retention of proprietary interest by any party to this Agreement.

13. The Contractor shall use its best efforts to comply with all Government regulations in existence or promulgated during the term of the Agreement which are relevant to the performance of this Agreement. If compliance will result in additional unforeseeable expense to the Contractor, the Agreement may be renegotiated or terminated at either party's option.

14. The Contractor shall enter into a reasonable confidential business information agreement with any participant in this Work who requests such an agreement.

15. In the event that the Contractor's facilities become the subject of a Governmental inspection where confidential records or data pertaining to this Agreement are requested, the Contractor shall immediately notify CMA. The Contractor shall inform the Government of the confidential nature of the material. CMA shall have the right to participate in the Contractor's response to th inspection notice. The Contractor shall provide CMA copies of any data provided to the Government relevant to this Agreement or scientific research conducted for CMA.

(a) The Contractor shall notify CMA of any private or Governmental request for information on matters relating to either an ongoing or completed Agreement with CMA.

(b) In the event the Contractor receives any legal instrument requiring production of data, work papers, computer printouts or other material related to corporate data obtained by the Contractor in the course of this Agreement, the Contractor shall promptly notify CMA. In such an event the following provisions apply.

(1) The Contractor shall give CMA the opportunity to quash, modify or otherwise respond to any compulsory process.

(2) The Contractor shall cooperate fully with any effort by CMA to narrow the scope of any such compulsory process, to obtain a protective order limiting use of disclosure of the information sought therein, or in any other way to obtain continued protection of the confidentiality of CMA members' data.

(3) The Contractor shall be entitled to be represented by counsel of its choice. CMA will share reasonable expenses in connection with any joint actions taken by CMA (or by others acting for CMA) with the Contractor in response to any such compulsory process.

16. The Contractor will furnish written quarterly progress reports and invoices to CMA. Progress reports will include procedures and findings during the reporting period and will include a status report giving the timetable for completion of the Work. The timetable shall indicate any delays in the completion of the technical tasks which may affect the timely completion of the Work.

17. In the event of significant adverse findings during the course of the study, the Contractor agrees to notify promptly the designated representative of CMA by

telephone with a follow-up letter within five working days.

18. It shall be the responsibility of CMA and the participating companies to provide data, material, and expertise which are required of them in the Work. Any delay arising out of the failure of CMA or its participating companies to complete their respective tasks shall be the sole responsibility of CMA and its participating companies, provided that the Contractor shall have, in writing and in a timely fashion, identified such responsibilities and the effect of such delays in its periodic progress reports.

19. If the Contractor should be prevented from performing the Work on account of flood, riot, legal prohibition, strikes, Acts of God, epidemics, explosions, acts of war or other catastrophes beyond the control of the Contractor, premature termination of the Agreement may be permitted by CMA upon five working days' notice to either party. The Contractor shall take all necessary steps to remedy any delays resulting from such catastrophic occurrences and notify CMA promptly of such events. Records shall be stored in facilities secur from fire or theft.

20. The Contractor agrees, if requested by CMA, to appear as a witness before or prepare a written statement for a court, regulatory agency or other organization regarding any matters connected with this Agreement. The Contractor's fees for such testimony shall be negotiated in the event of such a request by CMA; the Contractor's fees, however, shall not exceed the fees the Contractor usually charges for professional consultations.

21. The Contractor agrees to use reasonable care in handling any property of CMA entrusted to the Contractor's care or purchased by the contractor with CMA funds. The final report and any supporting documentation originating with the Contractor will be retained by the Contractor. Upon completion of the Work, the Contractor shall store these notebooks, data, photographs, etc., in a safe, secure manner. CMA shall have free access to such material. The Contractor shall not dispose of any materials relating to the study without the prior written approval of CMA. Such materials will be retained in confidenc unless otherwise authorized by CMA in writing for a period of 5 years.

22. Personnel designated by CMA will have reasonable access to the Contractor's personnel, facilities, records, samples, and data relevant to the Work. CMA may designate one or more consultants who may observe or audit the conduct of Work. The Contractor shall cooperate fully

with such observations and audits. CMA shall compensate EHA for professional services expended beyond 48 hours ~~if~~ an audit is conducted after submission of the Final Report.

23. The Contractor shall obtain CMA's written approval before subcontracting or assigning any portion of the Work. No such approval shall relieve the Contractor from any of its obligations pursuant to this Agreement. The Contractor agrees to bind each of the approved subcontractors to the provisions of this Agreement.

24. The Contractor's Estimated Cost for this project is $205,207 which consists of $11,495 for Task 1 through 5 of Phase I (which have been completed at the initiation of this Agreement); $63,567 for Tasks 6 through 8 of Phase I; and $130,145 for Tasks 1 through 6 of Phase II. The aforementioned Estimated Costs are itemized by tasks in Exhibit A and a Ceiling Cost is indicated for each task.

The Scope of Work set forth in Contractor's proposal will be performed within the total Ceiling Cost of $263,230. However, if the Contractor determines that its projected actual costs for the entire project, calculated at the labor rates set forth in the proposal, will exceed the total Ceiling Costs for the project by more than 30%, CMA agrees to review the Contractor's itemized projected cost overruns. CMA shall not unreasonably and without good cause refuse to compensate the Contractor for that portion of those previously unforeseen expenses which are more than 30% in excess of the ceiling costs.

In the unlikely event of a dispute over cost overruns the Contractor shall not delay completion of the Scope of Work pending resolution of the negotiations.

For performance of this Agreement by the Contractor, CMA shall make payments to the Contractor as follows:

Initial Payment a) Upon execution of this Agreement by both parties $55,000.

Interim Payments b) Upon receipt of each quarterly report described in paragraph 18, quarterly payments in the amount stated in Attachment A (Payment Schedule) until such time as the total amount paid by CMA shall reach $190,000 including the initial payment.

Final Payment

c) Upon receipt of the Final Report by CMA as defined in paragraph 26 accompanied by a detailed accounting of materials and services purchased, and time expended for the total project, a sum in the amount of $15,207, subject to adjustments as provided herein.

In the event that costs exceed the Estimated Cost, CMA will make payment of the excess up to the total ceiling costs upon submission and approval of the Final Report. If the actual costs at the completion of the project are less than the Estimated Costs of $205,207, the Contractor shall deduct the difference between th actual costs and $205,207, and credit CMA for that difference in the final invoice.

25. Within 60 days of the completion date defined in the Work, the Contractor will provide to CMA one unbound original and 25 copies of its draft final report. This draft final report will describe all work performed, record essential data and discuss results and conclusions to the satisfaction of CMA.

The Contractor's scientific conclusions and professional judgments arising out of performance of the Work shall be the responsibility of the Contractor and shall not be subject to CMA control. However, CMA shall have the right to review such judgments and conclusions prior to their submission for the purpose of clarifications, and format and editing comments, but not for the purpose of substituting CMA's opinion for that of the Contractor.

26. The final report will be due at CMA within four weeks of the Contractor's receipt of CMA comments on the draft final report. The Contractor shall provide CMA with one unbound original and 40 copies of the Final Report.

27. The Contractor shall not, without the prior written approval of CMA, use the name of CMA in connection with any advertising, promotional literature, or other public disclosures. In scientific articles published with CMA's consent, the Contractor shall give credit to CMA and company personnel as appropriate.

28. CMA may terminate the Agreement with 30 days written notice to the Contractor. In such event, the Contractor will present to CMA a detailed accounting of costs to date of termination, including reasonable and necessary expenses incurred in terminating the project in an appropriate manner as well as providing for the proper storage of the raw data for a period of time agreed to at termination. In the course of such termination, the

Contractor shall make every effort to submit to CMA all data and information relevant to the Work accumulated to the date of termination.

29. All correspondence, reports, and manuscripts sent to CMA concerning this Agreement will contain the CMA Reference Number VC 9.0-Epi-EHA and shall be in English.

30. The Agreement becomes effective when Execution is complete.

ACCEPTED FOR:	ACCEPTED FOR: Chemical Manufacturers Association, Inc.
_____ Signed	Gary C. Herrman
_____ Name Typed	Gary C. Herrman Vice President and Treasurer
_____ Title	10/8/81 Date
_____ Date	

EXHIBIT A

	Estimated Cost	Ceiling Cost
Phase I		
Tasks 1 - 5	$11,495	$11,495
Task 6	40,347	52,450
Task 7	10,308	13,400
Task 8	12,912	16,785
Total Phase I	$75,062	$94,130
Phase II		
Task 1	$ 8,406	$ 10,900
Task 2	31,078	40,400
Task 3	18,985	24,700
Task 4	16,174	21,000
Task 5	13,649	17,700
Task 6	41,853	54,400
Total Phase II	$130,145	$169,100
Total Project	$205,207	$263,230

PAYMENT SCHEDULE		ESTIMATED COST SCHEDULE
Initial	$ 55,000	$11,495
End 1st Qrt.	20,000	33,697
End 2nd Qrt.	20,000	29,870
End 3rd Qrt.	20,000	5,043
End 4th Qrt.	25,000	16,597
End 5th Qrt.	25,000	60,887
End 6th Qrt.	25,000	33,667
Final	15,207	13,951
Total	$205,207	$205,207

cc
Clark Cooper MD
M.N. Johnson MD
Carol Stack PhD
Fran Lichtenberg
Ralph Cook MD

Mutation Research, 98 (1982) 97–100
Elsevier Biomedical Press

ICPEMC

INTERNATIONAL COMMISSION FOR PROTECTION AGAINST ENVIRONMENTAL MUTAGENS AND CARCINOGENS

ICPEMC Working Paper TG1/2*/79

Mutagenicity and teratogenicity of vinyl chloride monomer (VCM)

Epidemiological evidence

Johannes Clemmesen

Stockholmsgade 43, 2100 Copenhagen, Denmark

(Received 16 September 1981)
(Accepted 21 September 1981)

The rarity and special character of angiosarcoma hepatis and its association with exposure to vinyl chloride monomer (VCM) has occasionally led to the error that a case of this tumor is tantamount to such exposure. Apart from the possibility that a number of such cases may in the past have been taken for cholangiocarcinomas, the experience of a British team of histopathologists going over cases from Britain during 1963–1973 has revealed some over-estimate of the frequency of this lesion, with the additional experience that only 1 of the *agreed* 14 cases could be confidently associated with exposure to vinyl chloride (Baxter et al., 1977). It follows that exception must be taken to the conclusion that single cases of angiosarcoma hepatis from the surroundings of polyvinyl factories may be taken as evidence of an escape directly from the plants or otherwise.

It would, however, be important if mutagenic or teratogenic effects of VCM be demonstrable either in the surroundings of factories or in the domestic environment of workers employed in PVC-producing facilities, and this possibility is the subject of the following review.

* It has been agreed to publish this document as a working paper for Task Group 1 of the International Commission for Protection against Environmental Mutagens and Carcinogens (ICPEMC). The views expressed are those of the author and do not necessarily represent those of the Commission. They are published to stimulate discussion and comments, which will be welcomed by the author.
All correspondence and reprint requests should be addressed to the secretary of ICPEMC: Paul H.M. Lohman, Ph. D., Medical Biological Laboratory TNO, P.O. Box 45, 2280 AA Rijswijk (The Netherlands). Tel. 15-138777, telex 38034 pmtno nl (ICPEMC document 158-1981-15.5).

An investigation of a possible increased occurrence of birth defects in the surroundings of PVC plants or among the children of workers has been attempted by Infante (1976) and Infante et al. (1976). The studies were based on data from 4 Ohio communities, of which 3, Ashtabula, Painesville and Avon Lake, had at least 1 polymerization facility in operation, Ashtabula since 1954, Avon Lake since 1946, and Painesville since 1946, with a 2nd plant opened in 1967. The 4th community, North Ridgeville, was near to Avon Lake and was without PVC production. Population numbers ranged from 24000 in Ashtabula to 12000 in Avon Lake. Between the census years 1960 and 1970 the population of Avon Lake increased by 30%, whereas the populations of Ashtabula and Painesville remained about the same.

According to birth-certificate data for 1970–1973, it appeared that while the rate of malformations for the entire State per 1000 live births was 10.14, the rates in the index communities were : Ashtabula, 17.37; Painesville, 18.10; and Avon Lake, 30.33. For these 3 cities with PVC production facilities the differences between observed and expected numbers of malformations in each city were significant at the $P < 0.01$ level according to the χ^2 test. Nevertheless, the highest rates for malformations were found in North Ridgeville, 27.26; and in Geneva, 12 miles from Ashtabula, 25.40, both cities without PVC plants (Infante, 1976.)

Infante, furthermore, found an excess of CNS defects among still-births and live births from the index cities, with the exception of Avon Lake. Most of the excess, however, was attributable primarily to Painesville and secondarily to North Ridgeville. It was therefore obvious that the findings did not link PVC production with the said anomalies.

Edmonds et al. (1975), observing that the increase reported was not uniform and appeared more prominent in the Painesville area, analyzed data collected through the Center for Disease Control's hospital-based Birth Defects Monitoring Programme (BDMP). For 2 hospitals located in cities with polymerization plants, Pottstown in Pennsylvania and Painesville in Ohio, they compared CNS-malformation rates for white infants born during 1970–1974 with the rates for white infants in each State. No increase was seen in the Pennsylvania hospital, but an increase, primarily in anencephaly and spina bifida, was noted in the Painesville hospital amounting to 22 cases, or twice the expected.

After inspection of the birth-defect registry for Ohio, 1 more case could be included in the study, bringing the total to 15. Interviews with parents revealed that none of them had worked at either of the 2 PVC plants in Painesville. However, 2 of the fathers of controls had worked at 1 of the plants. A significantly larger proportion of control mothers than case mothers worked (including housewives) within a 10-mile radius of the PVC plant, which was probably a chance occurrence (95% confidence level).

It was concluded that, although the follow-up confirmed a moderate increase in CNS malformations in Painesville, Ohio, no association had been found with vinyl chloride exposure.

A further study (Edmonds, 1976) of data from hospitals in Pottstown, Pennsylvania, and in Painesville, Ohio, revealed no difference between the cases and the controls in possible ex
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controls in possible exposure to VCM. Residential histories showed no difference between the cases and controls when compared at various distances from the PVC plants.

In Kanawha County the author found a difference in the pattern of residents for cases and controls living within 3 miles, but the available data suggested no association with VCM.

In a personal communication, Selikoff reported that he had estimated fetal deaths among wives of workers exposed to VCM at 7–14 per 100 pregnancies, although without the use of controls. Referring to this statement, Infante et al. (1976a) attempted a comparison of pregnancy outcome among wives of VCM workers before and after exposure, compared with wives of PVC workers and a similar number of rubber-factory workers matched as a group to the VCM workers by age. A total of 95 VCM-polymerization workers and 158 rubber and PVC-fabrication workers was interviewed in October 1974.

Interviews were conducted with workers, not with their wives. Questions about pregnancy outcome were contained in a much larger interview questionnaire, which was the initial item of a cross-sectional health survey including physical examination. No data were obtained on maternal age, but, on the basis of paternal age, fetal death rates for the primary VCM exposure group were age-adjusted to the control group separately before and after the husband's exposure.

It should be mentioned that Paddle (1976) asked for tabulation of the raw data before analysis finding that age adjustments appeared to have influenced figures misleadingly.

From these data published without delay by Infante et al., (1976b), in combination with those of the first publication, the following observations stand out. Before exposure, the mean paternal age at conception for study pregnancies was 26.4 years and for controls 23.0, with crude fetal death rates of 10.1 and 6.9%, respectively.

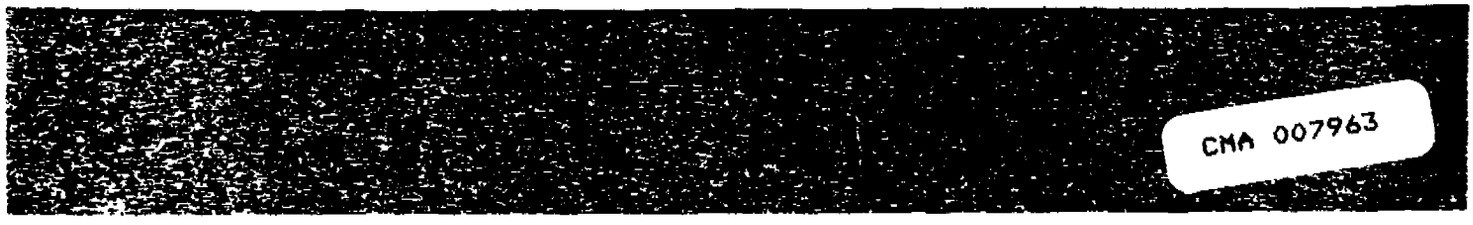
Because fetal loss is known to increase with increasing parental age, the fetal death rates for the primary VCM exposure group were age-adjusted to the control group. This reduced the rate for the study group, before exposure, from 10.1 to 6.1%.

Contrarily, the raw rate, after exposure, of 16.5% for the study group versus 8.8% for controls was only slightly influenced by age adjustment, showing 15.8% for the study group, so that Paddle's objection was fully justified.

The asymmetry in age, before exposure, between study group and controls, is paralleled with an asymmetry in numbers of families which, before the husband's exposure, numbered 70 for study families against 62 after exposure, versus 95 and 159, respectively, for control families.

Further objections were raised by Downs et al. (1977) in a critical review prepared for the plastics industry. They pointed out that matching by age should have been based on age prior before employment not on age at the interview, and that age adjustment to the controls' standard, made separately before and after exposure, does not justify comparison of these 2 values. The use of Mantel-Haenszels test, which requires independence of the 2 rates being compared, is also found incorrect.

Therefore, when the evidence is weighted, it seems that there is no demonstration so far of an effect of VCM as alleged by Infante et al.



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NEUROLOGICAL CHANGES IN VINYL CHLORIDE-EXPOSED WORKERS

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Vinyl chloride (VC) toxicity for the human organism is not still fully clear. The occupational exposure to VC is linked with the development of liver hemangiosarcomas, or with other malignant processes of varying locality. Some authors diagnose changes in terms of scleroderma, universally are described roentgenologically detected lesions of interphalangeal joints and zonal osteolysis. They are described in association with Raynaud's syndrome (12, 10, 1, 4, 5 and others). Lange with his colleagues (12) describes angiologically detectable constriction of digital arteries, stenosis or partial occlusion of phalangeal blood vessels. Described are also various types of dysesthesia in fingers, particularly cold and numbness sensations. Also Byczkowska (3) reports frequent occurrence of finger paresthesia, whitening of fingers, but also of palms and soles, and other symptoms of peripheral vasomotor disorders.

Neurological manifestations are described only sporadically. Spirtas and colleagues (16) emphasize particularly the narcotic action of VC at higher peak exposure concentrations. This manifests itself by vertigo, nausea and headache pains. Mentioned are also hand paresthesiae (princkling, formication). Langauer-Lewowicka (11) analyzes also the clinical symptoms in her group of 200 examinees who showed most frequently signs of cerebellar symptomatology. She recorded frequent occurrence of headaches and sleep disorders, but also trigeminal neuralgia.

Because of a lack of more detailed neurological studies among the VC-exposed persons, we conducted field investigations among the occupationally exposed workers in a plant where there was six years before put into operation a workshop with a considerable VC hazard.

MATERIAL AND METHODS

The group of examinees consisted of 293 workers (263 males and 30 females), age 18—58 years, mean age 32.8 years. Of these 76 % were below 40. The average time of exposure was 2.8 years (range from 2 months to 8 years). After consultations with plant physician and plant toxicologist the group was divided into two subgroups according to the level of exposure. The subgroup of high-risk workers, in which the tentatively established maximum allowable concentration of 10 mg . m^{-3} had been frequently and sometimes highly exceeded, involved polymerization workers and some maintenance workers (a total of 109 persons). The subgroup of lower-risk category of workers included those engaged in drying and bagging operations, but even here they were sometimes exposed to high peak exposure concentrations during cleaning and sampling operations, and those from the other plant workshops — combustion, compressors, cracking, chlorination, regeneration — where the exposure risk was relatively low (a total of 184 persons).

All the workers were examined neurologically, some of them repeatedly. A more detailed analysis of subjective complaints was performed on the basis of EOD and N5 questionnaire surveys. Electroencephalographic examination with photostimulation was made in 232 persons (255 recordings). The group of controls consisted of 48 persons without exposure to toxic substances.

RESULTS

An overview of subjective complaints is presented in Table 1. Headaches occur frequently, but they are less frequent than in the control group. The incidence of gastrointestinal disorders and other neurovegetative disorders (palpitations, retrosternal pressure sensations) are significantly higher than in controls. Psychic disturbances were observed only in those exposed.

Table 1. Overview of subjective complaints in workers occupationally exposed to vinyl chloride, in a comparison with controls

Complaints	VC — exposed		Controls	
	number	%	number	%
Headache	46	15.7	9	19.6
Sleep disorders	16	5.5	2	4.4
GIT disorders	20	6.9	1	2.2
Vertigo	3	1.0	1	2.2
Psychic disturbation	13	4.5	0	0.0
Dysesthesia	9	3.1	1	2.2
Palpitations	14	4.8	0	0.0
Total number of examinees	293	100.0	46	100.0

Significant differences were observed between the two subgroups of exposed workers divided according to the level of exposure (Table 2). The subgroup of more exposed workers showed a higher incidence of headaches and

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Table 2. Overview of subjective complaints in workers occupationally exposed to vinyl chloride, relation to the level of exposure

Complaints	Total		More exposed		Less exposed	
	number	%	number	%	number	%
Headache	46	15.7	19	17.4	27	14.7
Sleep disorders	16	5.5	7	6.4	9	4.9
GIT disorders	20	6.9	11	10.1	9	4.9
Vertigo	3	1.0	2	1.8	1	0.5
Psychic disturbation	13	4.5	6	5.5	7	3.8
Dysesthesia	9	3.1	7	6.4	2	1.1
Palpitations	14	4.8	5	4.6	9	4.9
Total number of examinees	293	100.0	109	100.0	184	100.0

gastrointestinal disorders, and furthermore, of dysesthesia of extremities. There was observed also a certain correlation with the length of exposure (Table 3). In persons with the exposure time longer than 4 years, the incidence of headaches was double the incidence in the group with a shorter time of exposed for more than 4 years. Sleep disorders, gastrointestinal complaints, vertigo and psychic disturbances were also more frequent in those with a longer time of ex-

Table 3. Overview of subjective complaints in workers occupationally exposed to vinyl chloride, relation to the length of exposure

Complaints	Total		Exposure longer than 4 years		Exposure shorter than 4 years	
	number	%	number	%	number	%
Headache	46	15.7	24	23.8	22	11.0
Sleep disorders	16	5.5	8	7.9	8	4.2
GIT disorders	20	6.9	9	8.9	11	5.7
Vertigo	3	1.0	3	3.0	0	0.0
Psychic disturbation	13	4.5	8	7.9	5	2.6
Dysesthesia	9	3.1	8	7.9	1	0.5
Palpitations	14	4.8	4	4.0	10	5.2
Total number of examinees	293	100.0	101	100.0	192	100.0

posed workers is characterized in Table 4. The group of more exposed workers showed a significantly lower per cent of normal findings and a higher per cent of more severe findings than the group of less exposed workers.

Graph 1 presents incidence of the most frequent, objectively diagnosed syndromes detected in exposed and control groups. The most frequent was the lesion of peripheral neurons, either motor or sensory, or both of them [16.8 % : : 8.7 %]. Diagnosed were impairments of muscle tonus or trophicity, reduction or loss of tendon and bone reflexes, abnormal sensitivity. Compared to controls,

Table 4. Severity of objectively diagnosed changes in workers occupationally exposed to vinyl chloride in relation to the level of exposure

Severity of changes	Total		More exposed		Less exposed	
	number	%	number	%	number	%
Normal	165	57.0	50	46.0	115	62.5
Light changes	112	38.0	49	45.0	63	34.2
Manifest changes	16	5.0	10	9.0	6	3.3
Total number of examinees	293	100.0	109	100.0	184	100.0

the group of exposed workers showed also more frequently the symptomatology of peripheral neurovegetative disorders (12 % : 4.4 %), specifically acrohypothermy, acrohyperhidrosis or whitening of fingers, associated with dysesthesia.

Graph 1: Objectively diagnosed changes in VC-exposed workers in a comparison to controls. X-axis — objectively diagnosed changes: A — peripheral neuron lesions, B — peripheral neurovegetative symptomatology, C — cerebellar symptomatology, D — vestibular symptomatology, F — extrapyramidal symptomatology, G — disperse central symptomatology. Blank column — group of controls, hatched column — group of VC-exposed. Y-axis — % of examinees

Graph 2 shows objectively diagnosed symptoms in relation to the level of exposure. A marked difference is in the incidence of peripheral neuron lesions: more exposed workers are affected more than twice as often (25.6 % : 11.8 %). Celebellar and vestibular syndrome is also more frequent (10 % : 7.6 % and 6.4 % : 3.3 %, respectively). There are also certain indications of a correlation with the length of exposure, see Graph 3: those with more than 4 years of exposure have more frequently peripheral neuron lesions (22.8 % : 13.6 %) and cerebellar impairments (13.9 % : 5.7 %). Frequency of the vestibulocerebellar syndrome is also higher (5 % : 0.5 %) in these persons.

The results of EEG examinations of exposed and 81 non-exposed control workers are compared in Table 5. The per cent of abnormal EEG recordings in the group of exposed workers is higher than in the control group; the EEG abnormities detected in the controls were always least severe. Abnormities

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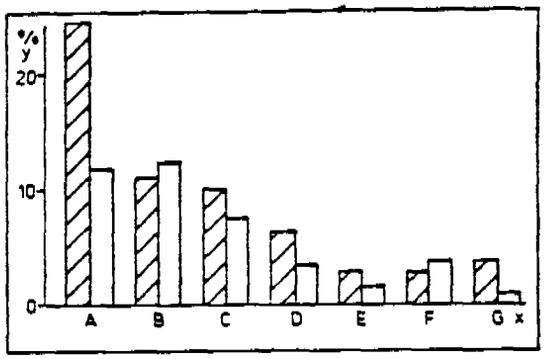
diagnosed in VC-exposed workers were predominantly episodic, in 5 cases combined with the diffuse abnormity. Three EEG recordings revealed only diffuse abnormities. Relatively frequent was also the presence of sleep waves (in 46.5 % of cases). In 16 % of workers the sleep activity manifestations were of



Graph 2: Objectively diagnosed changes in VC-exposed workers in relation to the level of exposure. X-axis objectively diagnosed changes: A-D see Graph 1. Blank column — lower exposure levels, hatched column — higher exposure levels. Y-axis — % of the total number of exposed subjects.

a higher degree of severity (2c to 3, according to Roth (13)). Significant differences were observed also in the photostimulation reaction that was normal only in 40 % of cases. The most frequent was extension of photic driving towards beta and theta waves (in 43.4 % of cases).

The additionally conducted N5 and EOD (6, 7, 8, 9) questionnaire surveys were used to improve analysis of subjective complaints and to complement

Graph 3: Objectively diagnosed changes in VC-exposed workers in relation to the length of exposure. X-axis — objectively diagnosed changes: A-D see Graph 1. Blank column — exposure shorter than 4 years, hatched column — exposure longer than 4 years. Y-axis — % of the total number of exposed subjects.

anamnestic data. The questionnaire N5 examines superficial personal traits as well as certain clinical symptomatology, particularly neurovegetative syndrome, neurasthenic, depressive and anxiety-phobic symptoms, and the so-called toxic syndrome. Data provided by this type of questionnaire were suggestive of

Table 5. Severity of EEG changes in workers occupationally exposed to vinyl chloride, in a comparison to controls

EEG changes		Exposed		Controls	
		number	%	number	%
Normal		148	63.8	57	70.4
Suspect		48	20.7	19	23.4
Abnormal	slight	30	12.9	5	6.2
	medium	6	2.6	0	0.0
	total	36	15.5	5	6.2
Total		232	100.0	81	100.0

a higher frequency of sleep disorders (36 %) than originally revealed by anamnestic data, highly frequent (5 % level of significance) was also somnolence (76 %), which had not been also indicated in personal histories. More frequent were also feelings of bad performance, fear of loosing life or health. Furthermore, the frequency of hyperhidrosis was also very high (73 %). The Eyseneck personality questionnaire examines neuroticism. It reveals subjective tendencies that are evaluated by the examinee and confronted with the objective reality. In the examined group there were not detected any significant deviations from the norm; increased neuroticism could not be demonstrated.

DISCUSSION

Clinical examination of VC-exposed workers revealed significant changes predominantly in neurologic symptomatology. Some of the subjective complaints, such as headaches, vertigo, sleep disorders or increased sleepiness during the day, as revealed by questionnaire N5, are suggestive of the narcotic action of VC, similarly as the occurrence of the cerebellar and/or vestibulocerebellar symptomatology. These changes have been already described by Spirtas and colleagues (16), Langauer-Lewowicka (11), but also by Schwartzová (15) and others. This characteristic symptomatology was also described in our previous studies concerned with the occupational exposure to trichloroethylene, benzene and other organic solvents (17, 18, 20). Here we also observed a high incidence of dysesthesia after exposures to some solvents, particularly to benzene. We ascribed it either to peripheral vasomotor changes, or — at least in some cases — to initial phases of polyneuropathy. In case of VC the presence of peripheral vasomotor changes is evidently very significant: according to literature data

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and to our own experience these changes are frequently associated with Raynaud's syndrome and may presumably lead to even more severe consequencies in terms of stenosis or occlusion, as described by Lange [12]. Peripheral nerve lesions diagnosed in our group of VC-exposed examinees could be then explained by a direct neurotoxic action of VC, or as a consequence of hypoxia accompanying more severe vasomotor changes in the periphery.

The narcotic action of VC can be either transitory, inducing only reversible changes in the brain function, or persistent, causing more permanent, sometime irreversible changes in the CNS. Slight functional changes manifest themselves in EEG recordings by waves typical for various stages of sleep, as confirmed in a relatively high per cent [46.5 %] of cases in our group of examinees as well as in some of the examined subjects exposed to other organic solvents [19, 21, 22]. Detection of episodic or diffuse EEG abnormalities is rather more serious and may be indicative of chronic changes in mediobasal and/or cortical brain structures. In our group of examinees, the joint episodic and diffuse abnormality occurred in 15.6 % of workers. This frequency is in agreement with the cited literature data as well as with our previous experience. This leads us to a conclusion that even VC, particularly at higher exposure concentrations, can produce neurotic changes in the above described brain structures.

VC-induced pathophysiological changes are believed by some authors to manifest themselves by the central neurovegetative dysregulation, as a result of changed hypothalamus functions [2]. This localization, presumed by these authors on the basis of their experimental studies, seems to be in agreement with our findings of EEG episodic abnormalities.

We also believe that even FS reaction changes, recorded in our group of exposed workers, may be of importance in the early diagnosis of VC-induced damage. Comparable FS reaction changes were also described by Rousková [14] in persons exposed to other toxic agents.

CONCLUSIONS

1) Exposure to VC may lead, besides to other changes described in the literature, also to lesions of the nervous system. The onset and development of these neurologic changes depend on the VC exposure level and on the length of exposure.

2) Some of the neurologic manifestations are caused by the narcotic action of VC, such as certain subjective complaints and cerebellar and/or vestibulocerebellar syndrome. These symptoms can be transitory or persistent.

3) Among the important manifestations that are characteristic for VC action is, no doubt, the peripheral vasomotor symptomatology, sometimes in combination with the Raynaud's syndrome described in the literature. These vasomotor changes in the periphery may further develop, leading consequently to

more severe lesions of peripheral blood vessels. Equally important are the general neurovegetative manifestations (gastrointestinal and cardiovascular disorders, hyperhidrosis, etc.) that might result from the central neurovegetative dysregulation. Important are also symptoms of peripheral neuron lesions caused by a direct neurotoxic action of VC or by hypoxia-related mechanisms.

4) Episodic abnormality in EEG recordings seems to agree with the assumed involvement of hypothalamic structures (Basalajev and colleagues). It occurs even at exposure to the other types of organic solvents (15, 19, 21, 22) and may be indicative of a more diffuse affliction of mediobasal and cortical structures of the brain. Less severe manifestations of EEG sleep activity can be ascribed to the nacrotic action of VC, more pronounced sleep manifestations accompanied with abnormal EEG changes may be suggestive of more persistent changes in the CNS.

5) Neurological changes have not been so far sufficiently accentuated in the professional literature and, therefore, the monitoring of workers at risk is not conducted systematically and by suitable methods. It is necessary to ensure a neurological prevention in these occupationally exposed workers. Of the supplementary methods of examination there are recommendable, both for prevention and research purposes, to use EEG examination with photostimulation, questionnaires N5 and EOD, and electromyographic examination.

SUMMARY

Neurological examinations were conducted in 293 workers occupationally exposed to vinyl chloride. Subjective complaints were evaluated on the background of N5 and EOD questionnare survey analysis. EEG examinations, including photostimulation, were performed in 232 persons. The control group comprised 46 nonexposed subjects. Average time of exposure was 2.8 years, the longest time of exposure was 6 years.

Among the most frequent subjective complaints were headache, neurovegetative disorders and dysesthesiae, among objective findings dominated cerebellar and/or vestibulocerebellar syndrome, lesions of peripheral neurons and peripheral neurovegetative symptomatology. Subjective and objective symptoms were found to depend on the exposure level and the time of exposure.

EEG examinations confirmed in 15.5 % of cases abnormities, predominantly episodic, sometimes combined with the diffuse abnormality. 46.5 % of the exposed showed presence of sleep activity as a consequence of VC narcotic action. The episodic EEG activity could be ascribed to lesions of mediobasal structures, or even to changes in brain cortex.

Our data have confirmed that vinyl cloride has a considerable impact on the human nervous system. Most frequent are lesions of vestibulocerebellar system and vigility disorders due to VC narcotic action. Frequent occurrence of peripheral symptomatology can be explained by a direct neurotoxic action of VC, or as a consequence of hypoxia caused by peripheral vasomotor changes.

As a rule, regular check-ups of VC-exposed workers do not include systematic neurological examinations. The systematic neurologic prevention, based on the assessment of clinical, EEG and/or EMG examinations, should become obligatory. Supplementary use of N5 and EOD questionnaire surveys is highly advisable.

RÉSUMÉ

Stýblová, V., Lambl, V., Chumchal, O., Kellerová, V., Pašková, V., Vítovcová, J., Žlab, L.: **L'image neurologique chez les sujets exposés au chlorure de vinyle**

Il a été étudié d'une manière complexe l'image neurologique chez 293 sujets exposés au chlorure de vinyle. Des troubles subjectifs ont été analysés au plan détaillé à l'aide des anquêtes EOD et N5. Il a été mis en évidence un effet neurotoxique significatif produit par chlorure de vinyle qui dépend de la qualité et de la quantité de l'exposition subie.

Les troubles subjectifs rencontrés le plus souvent: maux de tête, symptômes végétatifs et dysesthésie. Les données objectives témoignent pour une affection du système vestibulocérébelleux et pour celle du neurone périphérique et de l'innervation périphérique végétative. La symptômatologie périphérique peut résulter de l'effet toxique direct produit par chlorure de vinyle aussi bien que du mécanisme d'hypoxie ayant lieu lors des changements vasomoteurs périphériques.

Des donnés issues de l'EEG témoignant une activité de sommeil chez 46,5 % de sujets démontrent un effet narcotique du chlorure de vinyle. L'activité épisodique (chez 15,5 %) associée parfois à l'anomalie de diffusion pourrait s'expliquer par une atteinte des structures médiobasales, même liée aux changements du cortex.

Les sujets exposés à l'influence du chlorure de vinyle ne se soumettent, jusqu'à ce jour, aux examens systématiques au plan neurologique. Il est nécessaire de poursuivre, dans ce cas, une prophylaxie neurologique étudiant l'image clinique, les données issues de l'EEG ou même de l'EMG. Il est utile d'employer les anquêtes EOD et N5.

ZUSAMMENFASSUNG

Stýblová, V., Lambl, V., Chumchal, O., Kellerová, V., Pašková, V., Vítovcová, V., Žlab, L.: **Neurologisches Bild bei den dem Vinylchlorid exponierten Arbeitenden**

Man beobachtete komplexerweise das neurologische Bild bei 293 Arbeitenden, die Vinylchlorid exponiert waren. Subjektive Schwierigkeiten analysierte man eingehender mit Hilfe der EOD- und N 5-Fragebogen. Dabei hat man eine signifikante neurotoxische Einwirkung von Vinylchlorid nachgewiesen, die von der Intensität und Dauer der Exposition abhängig ist.

Die häufigsten subjektiven Schwierigkeiten waren Kopfschmerzen vegetative Symptome und Dysesthäsie. Der objektive Befund zeugt von der Affektion des Vestibularzerebellarsystems, ferner von der Affektion des peripheren Neurons und der peripheren vegetativen Innervation. Die periphere Symptomatologie kann man erklären sowohl als direkte Einwirkung von Vinylchlorid, als auch den hypoxischen Mechanismus bei peripheren vasomotorischen Veränderungen.

In dem EEG-Befund stellte man bei 46,5 % Tiele der Gesamtheit die Schlafaktivität fest, die die narkotische Einwirkung von Vinylchlorid dokumentiert. Die episodische Aktivität (bei 15,5 %) manchmal in Verbindung mit Diffusionsabnormität könnte man durch Affektion von mediobasalen Strukturen, gegebenenfals durch Kortexveränderungen erklären.

Die Vinylchlorid exponierten Arbeitenden werden bisher systematisch vom neurologischen Standpunkt nicht beobachtet. Die Verfasser halten die gezielte neurologische

Vorbeugung in Verbindung mit Beobachtung des klinischen Bildes, des EEG- eventuell auch des EMG-Befundes für notwendig. Sehr geeignet ist die Anwendung der EOD- und N 5-Fragebogen.

RESUMEN

Stýblová, V., Lambl, V., Chumchal, O., Kellerová, V., Pašková, V., Vítovcová, V., Žlab, L.: **El cuadro neurológico en trabajadores expuestos al vinilcloruro**

Se ha examinado globalmente el cuadro neurológico en 293 trabajadores expuestos al vinilcloruro. Las dificultedes subjetivos se las analizó detalladamente mediante los cuestionarios EOD y N 5. Se mostró el resultado neurotóxico marcado del vinilcloruro, el que dependía de la altura y duración de la exposición. Las dificultades subjetivas más frecuentes eran los dolores de la cabeza, los síntomas vegetativos así que la disestesia. El hallazgo objetivo muestra la afectación del sistema vestibulocerebelar, así que la de la neurona vegetativa periférica y de a inervación vegetativa periférica. La sintomatología periférica la puede explicar tanto por el efecto tóxico directo del vinilcloruro, como por el mecanismo hipóxico con los cambios vasomotóricos periféricos.

Se halló en hallazgos electroencefalográficos una actividad del sueño en el 46,5 p. c. del conjunto, lo que prueba el resultado narcótico del vinilcloruro. La actividad epizódica (en el 15,5 p. c.), a veces en la combinación con la anormidad difusa podría se explicar por afectación de las estructures mediobasales, eventualmente por cambios de la epidermis.

Los trabajadores expuestos al vinilcloruro no son aún examinados neurológicamente de manera sistemática. Hace falta que se haya realizado neurológica prevención encaminada incluso el cuadro clínico, el hallazgo electroencefalográfico, eventualmente el electromiográfico. Se recomienda usar los cuestionarios EID y N 5.

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R., Mc Michael, A. L., Gamble, J., Van Ert, M.: Am. Ind. Hyg. Ass. J. 36, 1975, 10, pp. 779—789. — 17. Stýblová, V.: Prac. lék. VII, 1955, 5, pp. 260—263. — 18. Stýblová, V.: Acta Univ. Carol. Med. Suppl. 12, 1960, pp. 269—274. — 19. Stýblová, V.: Čs. neurol. 26, 1963, p. 399. — 20. Stýblová, V.: Diagnoza a prevence v průmyslové neurologii. Praha, SZdN, 1968. — 21. Stýblová, V.: Int. Arch. Occup. Environ. Hlth. 38, 1977, pp. 263—282. — 22. Stýblová, V., Holanová, V.: Prac. lék. 25, 1973, pp. 90—96.

Received November 10, 1980

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December 4, 1981

TO: Vinyl Chloride Program Panel

SUBJECT: Up-date of Epidemiology Study

The Vinyl Chloride Program Panel meeting scheduled for December 16, 1981 has been cancelled due to the unavailability of several key supporters of the epidemiology study. A new meeting date is tentatively set for January 20, 1982.

In the interim I would appreciate a reaction (by phone or memorandum) to the present situation. There is also a new proposal to be considered that would split the present study into two parts corresponding to Phase I and Phase II of the present EHA study proposal. A separate contract agreement would be drawn up for each phase. The work product at the end of the first study would include: 1) updated study tapes, and 2) hard-copy summary of data on the tapes and an indication of the completeness of records. EHA would then develop a protocol for the second study and submit a bid for completion. At this point we would have the option of taking the study protocol to another contractor or continuing with EHA.

I look forward to hearing from you on this matter.

Sincerely,

Carol Stack

Carol R. Stack, Ph.D.
Administrator
Vinyl Chloride Program

CRS/seh

CMA

— CHEMICAL MANUFACTURERS ASSOCIATION

May 13, 1981

Mr. Roger Coffman
Stauffer Chemical Company
Westport, Connecticut 06881

Dear Mr. Coffman:

Following our phone conversation, I checked our files to see what Stauffer had committed to in terms of funding the vinyl chloride epidemiology study update. Our records indicate that your company's pro-rata share is 3.45% based on 150 MM VCM and 385 MM PVC 1979 name plate capacity.

Stauffer was invoiced for $11,700 which represents 3.9% of the total study cost. This adjustment was necessary because the twenty-one companies committed to the program represent 89% of the estimated total capacity for 1979.

I understand that Stauffer's capacity has been reduced due to the recent sale of one of your operations. Since the present funding was based on 1979 capacity, this reduction will not affect your present level of funding. Any future funds required for this study however, would reflect your lower capacity. If you will send me the current figures, I will add the information to our files.

Sincerely,

Carol R. Stack

Carol R. Stack, Ph.D.
Administrator
Vinyl Chloride Program

CRS:md

CMA 007977

CMA

— CHEMICAL MANUFACTURERS ASSOCIATION

May 13, 1981

To: Vinyl Chloride Program Panel

Re: EHA Epidemiology Study

Dear Sirs:

Negotiation of a contract agreement with Environmental Health Associates, Inc.,(EHA) has been a rather prolonged process due to difference of opinion on disbursement of funds during the course of the study. We are looking toward a resolution of this issue and hope the study will get off the ground shortly without further delay.

Both Dr. Torkelson and myself feel there is a need for involvement of company representatives with experience in the conduct of epidemiology studies to aid in monitoring the EHA study. If there is someone in your company who would be willing to serve in this capacity please let me know as soon as possible. Depending on the response, such persons may join the present group of Research Coordinators or a new Epidemiology Task Group could be formed.

I look forward to hearing from you in this matter.

Sincerely,

Carol R. Stack

Carol R. Stack, Ph.D.
Administrator
Vinyl Chloride Program

CRS:md

CMA 007978

CHEMICAL MANUFACTURERS ASSOCIATION

April 10, 1981

Chemical Manufacturers Association

Vinyl Chloride Program Panel Progress Report

As there appears to be no immediate need for a meeting of the Program Panel, I thought a mini-newsletter would be appropriate to keep you apprised of vinyl chloride program activities.

Epidemiology Study Update

CMA is in the process of negotiating a contract with Environmental Health Associates to update the 1978 EEH study of vinyl chloride workers. An updated (March 1981) version of the study protocol is enclosed for your information. There are two items of note: 1) the anticipated cost adjustment for FY '81 was made, and 2) EHA has reverted to the exposure classification scheme described in an earlier proposal in which the focus is on duration of exposure only, rather than estimated level of exposure and duration. As you may recall, the multiplication factor scheme (1 = low, 2 = medium, 3 = high) used in the quantification of exposure in the original study was less than satisfactory and EHA was very reluctant to continue its use.

CMA received financial commitment from twenty companies in support of the epidemiology program. Your company will be invoiced for its share of the cost within the next two weeks. The twenty companies represent approximately 90% of the total U.S. VCM and PVC capacity. A list of the company-designated program panel representatives for this phase of the program is attached.

IBT Settlement

Refund checks are in the mail. If your company supported the IBT vinyl chloride inhalation study, you will be receiving a check for your share of the $110,000 settlement.

University of Louisville Study

May 15 is the target date for receipt of the third and final report from the study group headed by Dr. Carlo Tamburro, University of Louisville, School of Medicine.

Formerly Manufacturing Chemists Association—Serving the Chemical Industry Since 1872.
2501 M Street, NW • Washington, DC 20037 • Telephone 202/887-1100 • Telex 89617 (CMA WSH)

SPAG Presentation

Dr. Torkelson will review the vinyl chloride program with members of the Special Programs Advisory Group on April 21. A word of thanks to those of you who provided comments on the background document that Dr. Torkelson and I prepared for this meeting.

Carol R. Stack, Ph.D.
Administrator
Vinyl Chloride Program

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