

Monitoring Exposures to Vinyl Chloride Vapor: Breath Analysis and Continuous Air Sampling

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⊗ An environmental survey was conducted to determine the time-weighted average exposure (TWA) of a group of chemical plant workers to vinyl chloride (VCl) vapor. This survey featured continuous multipoint air sampling and analysis using an infrared spectrophotometer. The inhalation exposure data were digitized and recorded on paper tape for subsequent computer analysis and derivation of daily TWA values for each worker. A breath sampling program was conducted concurrently with the environmental survey, and a series of breath decay curves relating post-exposure breath concentration to vapor exposure were derived from the data. To validate the breath curves derived from on-the-job data, postexposure breath curves were also constructed from breath data obtained following experimental human exposures to carefully controlled concentrations of VCl vapor. The close agreement between postexposure breath concentrations at the corresponding TWA's obtained by each of the methods suggests that either continuous air monitoring or breath analysis is valid for estimating the worker's individual daily exposure to VCl, and provides further evidence that breath analysis is a useful industrial hygiene technique for evaluating vapor exposure.

Introduction

THE QUESTION THAT MAY ARISE following an environmental survey is whether the chemical vapor concentrations measured are truly representative of the exposure being experienced by the workmen. Evaluation of the ranges of atmospheric concentrations and estimates of time-weighted average concentration (TWA) are all too often based on a few spot samples obtained under conditions which are not representative of all phases of a given operation. A more exact measurement of vapor exposure would have to be based on continuous monitoring of air in the workman's breathing zone during his entire work shift. Obviously this task is made difficult and often impossible

by the large number and variety of tasks performed by today's modern chemical plant worker.

Recent improvements in automatic monitoring and data processing equipment have provided a means for a more satisfactory solution. Sequential samplers and automatic analyzers and recorders can now be used to continuously monitor several locations or operations to provide more valid data on which to base estimates of chemical exposure. Computers can be utilized to manage the large volume of data generated by continuous monitoring.¹

Meanwhile a technique has been under development which more precisely defines the level of individual exposure. The realization that the total body burden of a volatile chemical is directly related to its concentration in expired air led to the development of techniques for collecting and analyzing breath samples useful in estimating the more indi-

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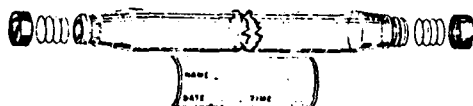


FIGURE 4. Glass pipet (50 ml) used for collecting breath samples. One cap has a predrilled hole for gas sampling. Both caps have Saran liners which seal the pipet chamber.

times. After expelling the fourth breath he quickly caps the tube, trapping a portion of alveolar air. The importance of writing the name, date, exact time of sampling, and the workshift most recently completed, on the label attached to each pipet, was stressed.

Aliquots were drawn from the pipets with a 1-ml Hamilton gas-tight syringe and analyzed in an Aerograph A-600B gas chromatograph using N_2 carrier gas and a hydrogen flame detector. Separations were made with a 6-foot, $\frac{1}{8}$ -inch I.D. stainless-steel column packed with Carbowax 20M alkaline on Chromosorb W 60/80 mesh acid-washed.

Exposure Chamber Operation

Three experimental human exposures to VCI were conducted at nominal vapor concentrations of 50, 250, and 500 ppm. The exposure chamber was a room measuring 41 feet by 6 feet wide by 7.5 feet high. The room had a continuous positive air supply and exhaust system capable of maintaining a slight negative pressure within the chamber. Continuous distribution of the chamber air was achieved by recirculating the air with a squirrel cage fan through a series of inlet and outlet ducts spanning the length of the chamber. The VCI was metered into the duct carrying air exhausted by the squirrel cage fan and entered the room atmosphere via the recirculation system at a rate sufficient to maintain the desired atmospheric concentration. The vapors were introduced from a pressurized storage cylinder through 6 feet of $\frac{1}{8}$ -inch I.D. stainless-steel tubing into a rotometer prior to entering the circulating air duct. A heating tape wrapped around the stainless-steel tubing prevented condensation of the VCI and stabilized the flow of the vapor.

The concentration of VCI in the chamber was constantly monitored with a Perkin-El-

mer infrared spectrophotometer equipped with a 10-meter path-length gas cell. A sampling probe, consisting of 5/16-inch I.D. Saran tubing, was centrally located during the exposure to represent the breathing zone of all subjects within the chamber. The probe was moved about prior to each exposure to detect imbalance of vapor concentrations within the chamber so that necessary corrections in the recirculating system could be made. Air samples collected periodically within the chamber throughout the exposure day were analyzed by gas chromatography for added assurance of analytical accuracy. Both the infrared spectrophotometer and the gas chromatograph were calibrated before each experiment and at intervals throughout the exposure day.

Each 7.5-hour exposure day included a 0.5-hour lunch period in an uncontaminated area outside the exposure chamber. The TWA concentration was calculated on the basis of 7.5 hours of exposure.

Clinical and Laboratory Procedures

Each subject had been under careful medical surveillance by the medical department for a number of years, and each was given a complete medical examination a few days prior to the VCI exposures. Included were a complete urinalysis and 24-hour urine for urobilinogen, complete blood count with sedimentation rate, reticulocyte count, SGOT, SGPT, LDH, alkaline phosphatase, BUN, creatinine, and bilirubin.

Each subject received a repeat physical examination 1 hour before entering the exposure chamber. This examination included measurement of temperature, blood pressure, and pulse rate, a neurological examination, and collection of blood and breath samples. A questionnaire noting the presence of any symptoms of illness (for example, headache, nausea, dry throat) completed the pre-exposure medical evaluation.

After the subject entered the chamber, total expired breath samples were collected every hour by having him breathe out through a Saran tube leading to a Saran plastic collection bag located outside the chamber. Tidal volume and total expiratory capacity

were measured in the morning and again late in the afternoon exposure periods.

Subjective and neurological responses were measured before the subject entered the chamber, 15 minutes after entrance, and at 1-hour intervals thereafter. Flannagan Coordination and Crawford Manual Dexterity Tests were conducted at midmorning and again in the afternoon. Breath sampling began immediately after the subject left the exposure chamber. A 24-hour postexposure urine sample was collected and a blood sample was drawn the following morning for SGPT, LDH, alkaline phosphatase, BUN, creatinine, and bilirubin determinations.

Analysis of Breath Data

The decay curves for the breath vinyl chloride concentrations were constructed by stepwise multiple regression using a digital computer. An empirical relationship of the form $\text{Concentration} = f(\text{TWA}, \text{time})$ was selected from a choice of several terms, each based on TWA and/or time. The resulting regression equation best represents the ordered relationship between breath vinyl chloride concentration, time-weighted average exposures, and postexposure time.

Each breath decay curve has an associated standard error of regression which can be used to compute the confidence band for any chosen level of significance. The 95% confidence band for the mean of a group of observations was chosen in this case to describe the statistical error associated with the breath data and the regression technique.

Results

Experimental Breath Curves

A total of 13 men participated in the three experimental chamber exposures at nominal concentrations of 50, 250, and 500 ppm producing a total of 160 valid breath data points. Five of the six subjects exposed to 50 ppm were re-exposed at 500 ppm 2 days later. There was no measurable residual vinyl chloride detected on the breaths of the subjects prior to the second exposure. Serial breath sampling was initiated immediately after the subjects left the exposure chamber and continued up to 20 hours following the exposures.

TABLE I
Experimental Human Exposure to Vinyl Chloride

Chamber Concentration (ppm)		Range (ppm)	TWA* (ppm)	Number of Subjects
$\bar{X}$	S.D.			
59	2	65-53	48	6
261	8	289-243	248	4
493	7	518-471	459	4
491	5	525-475	491 ^b	7

*Time-weighted average concentration based on 7.5 hours including a 0.5-hour lunch period in an uncontaminated area.

^bContinuous exposure for 3.5 hours.

Table I shows the analyzed concentration to which the subjects were exposed. Calculations of the mean and standard deviation of exposure concentration are based on chart readings from the infrared spectrophotometer taken at 5-minute intervals over the two 3.5-hour exposure periods. The TWA is based on the total 7.5 hours which included a 0.5-hour lunch period in an uncontaminated area.

The final breath decay curves intended for use as an index to VCl exposures were adjusted to TWA concentrations of 50, 250,

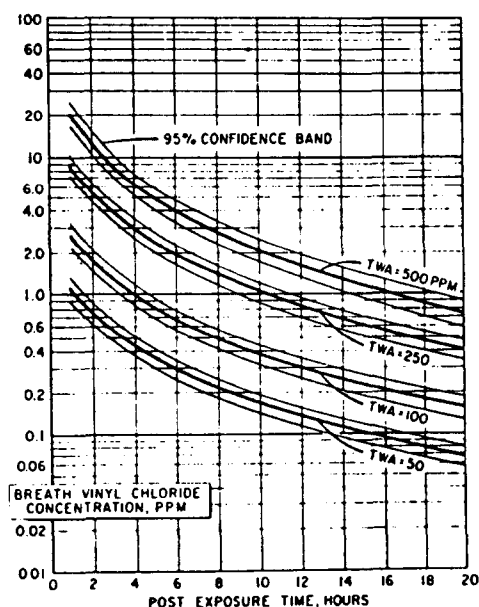


FIGURE 5. Breath decay curves based on experimental human exposures to 50, 250, and 500 ppm of VCl (7.5-hour TWA).

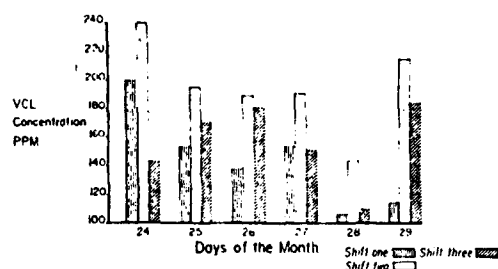
DAILY VARIATION IN EXPOSURE TO VCL VAPOR
(8 hr. TWA)

FIGURE 6. Variation in VCL vapor exposure for three shifts.

and 500 ppm (Figure 5). A 100-ppm decay curve was interpolated from the available data using regression analysis. These curves are presented with the calculated 95% confidence bands for the mean of a group of observations.

On-the-Job Breath Curves

Ten workmen participated in the on-the-job breath sampling program, producing a total of 91 usable sets of data. Ten percent of the breath samples collected were discarded because of pipet leakage or poor sampling techniques.

Absolute breath levels ranged from about 20 ppm in one sample taken less than 1 hour after an 8-hour TWA of 250 ppm, to barely detectable levels (<0.05 ppm) in samples taken after exposures at TWA's below 50 ppm.

The extremely broad variation in the TWA's experienced by workmen during one of the periods in which breath sampling was being conducted is demonstrated for three shifts of men bearing the job classification "coagulator operator" (Figure 6). Minute, hourly, and daily fluctuations in the concentration of a contaminant are most descriptively revealed by continuous monitoring. This method of sampling quickly points out the fallacy of judging TWA and peak exposure concentrations on the basis of spot sampling or periodic surveys of brief duration.

The remarkable correlation between breath concentration and corresponding TWA values made it possible to construct the series of breath decay curves shown in Figure 7.

with confidence bands only slightly wider than those from controlled human experiments. The close similarity between these curves and those constructed from controlled exposure data are further illustrated in Figure 8.

Human Responses

From a subjective standpoint no significant untoward affects were noted at any of the exposure concentrations. The only complaints were those of two subjects who reported mild headache and some dryness of their eyes and nose during the 500-ppm exposure experiments.

No odor was detected by anyone entering the exposure chamber at 50 ppm. At 250 ppm all four subjects entering the chamber initially reported that they could detect a very slight odor of the chemical. Five of the seven subjects entering the exposure chamber at 500 ppm were able to detect the odor of VCL, but after 5 minutes of exposure those five were unable to detect it even with forced inspiration. Three of the four subjects re-entering the chamber after lunch were able

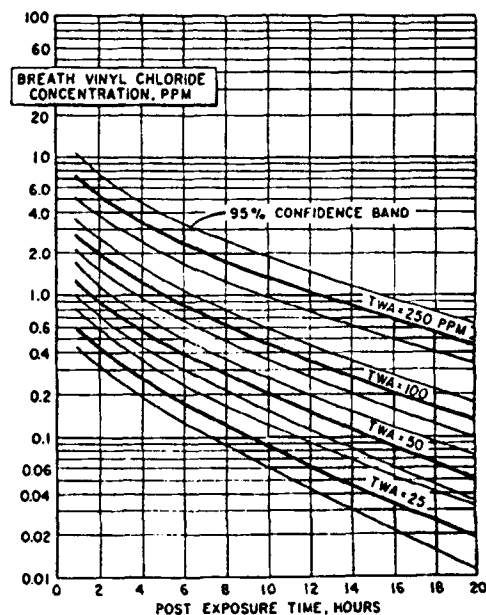


FIGURE 7. Breath decay curves derived from breath data collected from workers following on-the-job exposures to VCL vapor (8-hour TWA).

to detect a faint odor of VCl. One subject could detect a faint odor on deep inspiration for approximately 15 minutes after entering the exposure chamber.

The exposure had no noticeable effect on neurological responses, nor did it produce significant changes in the results of mental, coordination, or manual dexterity tests conducted during the exposure period. All clinical laboratory studies performed in the post-exposure period were normal and not significantly different from pre-exposure values.

Discussion

The object of the environmental health survey is to identify the atmospheric contaminant, determine the exposure level, and relate this to the health hazard it presents. If one is to judge hazard by ambient concentration measurements, then those measurements must accurately describe the exposure on a continuing individual basis. A carefully conducted survey combining continuous analysis of the work room atmosphere with a comprehensive job study will provide data valid for estimating time-weighted average exposure.

On the other hand, breath decay curves constructed from breath data collected during continuous plant monitoring are in close agreement with those obtained from exposure chamber experiments with VCl. These curves should therefore be useful as a second method for assessing exposure to VCl vapor.

The choice of whether one or both methods should be used depends on prevailing circumstances and on the thoroughness desired. For example, data useful in describing peak exposures are obtained from continuous monitoring. Concurrently, exposure trends and concentration gradients may help identify plant operational inefficiencies and equipment malfunctions by revealing specific sources of emission. Correcting these problems not only restores a healthful work environment but often results in bonus savings by reducing losses of raw material and product.

Continuous monitoring, however, is extremely costly both in time and in the equipment required. The scope of data acquired is

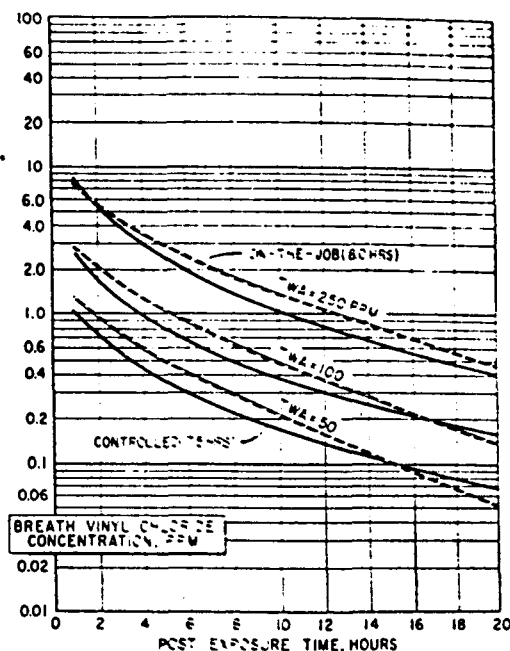


FIGURE 8. Comparison of breath decay curves derived from the on-the-job data and the experimental human exposure data.

limited by the number of sampling probes, and these probes are not always capable of accurately measuring the individual's daily exposure experiences, especially should these involve unusual incidences such as chemical spills or exposures outside the monitored area.

Breath analysis has the advantage of individualizing each worker's integrated daily exposure. Breath decay curves, as an index of exposure, offer a means of estimating the average daily individual exposure on the basis of a few breath samples taken serially in the postexposure period. Consequently breath analysis can be used to diagnose as well as quantitate an exposure which has already occurred. It is a relatively inexpensive and simple method which can be put into operation without extensive and costly preliminary preparations.

However, postexposure breath analysis does not provide information on the daily fluctuations of exposure, and the peak exposure concentrations are not made evident by breath data. Finally, breath analysis is not applica-

ble to all chemicals, and breath decay curves established for one chemical are not useful as an index of exposure to any other chemical.

The decay curves presented here are intended to serve as an index of exposure to vinyl chloride vapor and are based on an exposure duration of 7.5 hours for the experimental exposures, and 8 hours for the on-the-job study. The close agreement between the two sets of curves and the narrow confidence bands obtained in each case demonstrate the usefulness and accuracy of both methods for estimating TWA exposures and indicate the importance of breath analysis and the need for expanding its use in evaluating exposures to other widely used volatile organic chemicals.

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animals. The major difference lies in the larger maintenance requirements of the mouse due to its higher metabolic rate.

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110564k Polymorphism of transferrins of bovine, porcine, and canine sera, as determined by means of acrylamide-gel disc electrophoresis. Dörner, Joseph L. (Univ. of Illinois, Urbana, Ill.). 1968, 66 pp. (Eng). Avail. Univ. Microfilms, Ann Arbor, Mich., Order No. 69-10,687. From *Diss. Abstr. B* 1969, 29(12), 4727. SNDC

110565m Hemoglobin-Lepore Baltimore, a third type of a $\delta\beta$ crossover (δ^{30}, β^{96}). Ostertag, Wolfram; Smith, Ernest Wendell (Sch. of Med., Johns Hopkins Univ., Baltimore, Md.). *Eur. J. Biochem.* 1969, 10(2), 371-6 (Eng). A new Lepore-type Hb in a person of Negro descent has been identified. In this person a minor Hb (Hb-Lepore^{Baltimore}) was detected. An abnormal $\delta\beta$ -chain was isolated and fingerprinted. This hybrid-type protein presumably arose as a consequence of unequal crossing over between the δ and β genes, as was concluded for Hb-Lepore^{Boston} and Hb-Lepore^{Hollandia}. In the new Lepore-type Hb described here the crossover could be placed between residues δ^{30} and β^{96} . This type of crossover should occur with the highest frequency if crossing over is equally frequent between any nucleotides and if selection favors none of the crossover types. RCBV

110566n Genetic and developmental regulation of hepatic δ -aminolevulinate dehydratase in mice. Doyle, Darrell J.; Schimke, Robert T. (Sch. of Med., Stanford Univ., Stanford, Calif.). *J. Biol. Chem.* 1969, 244(20), 5449-59 (Eng). The mechanism by which the levulinate locus (*Lr*) regulates the tissue activity of δ -aminolevulinate dehydratase in mice has been examd. The assayable hepatic enzyme activity in homozygous *Lr^{bb}* mouse strains, represented by C57Bl/6, is between one-third and one-half that of homozygous *Lr^a* strains. This difference in enzyme activity is due to a difference in amt. of enzyme protein as demonstrated by immunochem. techniques with an antibody specific for δ -aminolevulinate dehydratase. Combined immunochem. and isotopic techniques show that the levulinate locus regulates the concn. of hepatic δ -aminolevulinate dehydratase by acting at the level of enzyme synthesis. The rate of degradation of hepatic enzyme is the same in both low and high activity strains; when expressed as a half-life, this is equal to 5-6 days. The pattern of δ -aminolevulinate dehydratase development with age is similar in livers of both low and high activity strains. The specific activity of the enzyme is high in fetal liver, decreases during the several days prior to birth, and increases to the adult level during the first 3 weeks of postnatal life. The activity of δ -aminolevulinate dehydratase in fetal liver is also regulated by the levulinate locus. The enzyme in fetal liver is approx. twice as active catalytically as the enzyme in adult liver relative to its function as an antigen. The fetal enzyme also appears to be different in stability to heat and proteolytic inactivation. However, fetal and adult enzymes are similar by other physiochem. criteria, including electrophoretic mobility, sedimentation coeff., and K_m for the substrate. RCJN

110567p Identification and genetic control of two new low-density lipoprotein allotypes: phenogroups at the Lp_q locus. Albers, John J.; Dray, Sheldon (Med. Center, Univ. of Illinois, Chicago, Ill.). *J. Immunol.* 1969, 103(2), 155-62 (Eng). See C.1 69: 104403z. VNJZ

110568q Modification by crude histones of gene activity for lactate dehydrogenase. Latner, A. L.; Longstaff, E. (Roy. Victoria Infirmary, Newcastle upon Tyne, Engl.). *Nature (London)* 1969, 224(5214), 71-3 (Eng). Addn. of crude calf thymus histone to the mouse kidney organ culture increased the proportion of the lactate dehydrogenase (LDH) isozymes which moved more rapidly toward the anode during electrophoresis. If a crude rat liver histone fraction was added to the culture, the increase was in the direction of the slower moving LDH isozymes. In the cultures exposed to the crude calf thymus histone, the percent of LDH-1 and the H subunit contribution to the total LDH activity significantly increased, whereas the opposite was found with the rat liver histone prepn.; LDH-5 and the M subunit significantly increased. Enrichment of the medium with amino acids present in the calf thymus histone prepn. did not alter the isozyme pattern, indicating that the changes in LDH pattern were not caused by hydrolysis of the histone. Gene masking by histones apparently is nonspecific, and the crude ext.

may contain factors, not necessarily histones, which affect gene activity in a manner that is not species specific. BSJN

110569r Changes in the activity of isolated vascular smooth muscle in response to reduced osmolality. Jonsson, Olof (Univ. Göteborg, Göteborg, Swed.). *Acta Physiol. Scand.* 1969, 77(1), 191-200 (Eng). The effects of hyposmolality on the spontaneous activity of the smooth muscle in the isolated portal vein of the rat have been studied in solns. with varied ionic compn. A comparison between the stimulatory effects of lowered osmolality and increased $[K^+]_o$ (external K^+ concn.) indicated that at normal $[K^+]_o$ in the control state the excitation caused by hyponotonicity is not mediated only via changes in the $[K^+]_i/[K^+]_o$ ratio. The response to hyposmolality at a higher $[K^+]_o$ is, however, more readily explained by the change in $[K^+]_i/[K^+]_o$ which occurs in assocn. with the swelling of the cells. This might be attributed to the fact that the membrane potential of smooth muscle is more dependent on the transmembrane concn. gradient for K^+ at higher levels of $[K^+]_o$. The stimulatory effects of hyposmolality are markedly reduced at a low $[Na^+]_o$ but are not considerably affected by comparable redns. in $[K^+]_o$ or $[Cl^-]_o$. This indicates that the transmembrane Na^+ gradient is involved in the mechanisms by which hyposmolality excites the spontaneous activity of vascular smooth muscle. One possible interpretation is that the swelling of the muscle cells in hypotonic solns. causes an increase in the permeability of the cell membrane to the relatively larger Na^+ . RCVV

110570j Secretion of rat pancreas perfused with plasma from rats fed soybean trypsin inhibitor. Khayambashi, H.; Lyman, R. L. (Univ. of California, Berkeley, Calif.). *Amer. J. Physiol.* 1969, 217(3), 646-51 (Eng). When plasma from rats fed soybean trypsin inhibitor was perfused through an isolated, fasted rat pancreas, amylase secretion was 2-3-fold greater than that of a pancreas perfused with plasma from rats fed the same diet without trypsin inhibitor. Addn. of atropine to the perfusate did not inhibit the secretory response. The plasma factor was relatively unstable upon storage at 4° (50% loss of activity in 4 days) and appeared to be assocd. mainly with those plasma proteins of 10,000 mol. wt. or less. Thus, active soybean trypsin inhibitor enhanced the formation and (or) release of a humoral pancreozymin-like substance that markedly stimulated external enzyme secretion of the rat pancreas. RCDH

110571k Effects of diet and catechol amines on bile acid metabolism in dogs. Gans, Joseph H.; Cater, Marilyn R. (Coll. of Med., Univ. of Vermont, Burlington, Vt.). *Amer. J. Physiol.* 1969, 217(4), 1018-24 (Eng). Five adult male dogs were surgically prepd. with polyvinyl tubing placed in the upper duodenum. Each dog was given cholic-carboxyl-¹⁴C acid and samples of gallbladder bile were withdrawn over a 10-day period. The taurocholic acid pool was 1.09 g./10 kg. body wt. and half-life was 3.2 days when dogs were given a dry dog food diet. Epinephrine in oil, 0.8-1 mg./kg./day, increased plasma cholesterol concns., produced a 23.9% redn. in the taurocholic acid pool size, and increased the rate of decline of specific radioactivity of both taurocholic and taurodeoxycholic acids. The half-life of taurocholic-¹⁴C acid during epinephrine administration was 1.6 days. Norepinephrine in oil, 0.8-1.0 mg. free base/kg./day, produced a modest decrease in the half-life of taurocholic-¹⁴C acid without significant elevations in plasma cholesterol concns. A dietary supplement of 1/4 lb. beef plus 2-3 g. of cholesterol per day resulted in increased plasma cholesterol concns., increases in the taurocholic acid pool size, and a decrease in the half-life of taurocholic-¹⁴C acid. Epinephrine administration further increased plasma cholesterol concns. in cholesterol-fed dogs, but did not significantly alter bile acid metabolism. RCDH

110572m Effect of osmolality on canine renal vascular resistance. Gazitua, Sergio; Scott, Jerry Benjamin; Chou, Ching-Chung; Haddy, Francis J. (Michigan State Univ., East Lansing, Mich.). *Amer. J. Physiol.* 1969, 217(4), 1216-23 (Eng). The effects of changes in renal blood osmolality, produced by close intraarterial infusion of solns. of dextrose, NaCl, and urea, on renal resistance were systematically examd. in the dog. Infusion of a hyperosmotic soln. of dextrose for 3 min. produced a fall in renal vascular resistance which was sustained for the entire infusion period. On termination of the infusion, resistance returned to the control level. Infusion of a soln. of hyperosmotic NaCl or urea, on the other hand, produced a fall in resistance which waned with time. Furthermore, on stopping the infusion, resistance transiently rose well above the control level, particularly in the case of urea. Intraarterial infusion of an isosmotic soln. of urea and of hyposmotic solns. of all three substances produced large increases in resistance. Studies concerning lymphatic vessel pressure and cell-free perfusion, as well as the findings of others, are consistent with the hypothesis that the changes in resistance result, to a large extent, from active vasomotion, possibly due to osmotic changes in the water content of the smooth muscle cells. RCDH

110573n Metabolism of allyl compounds in the rat. Clapp, J. J.; Kaye, C. M.; Young, Leslie (St. Thomas's Hosp. Med. Sch., London, Engl.). *Biochem. J.* 1969, 114(1), 6P-7P (Eng). A mercapturic acid was isolated from the urine of rats treated s.c.

with CH_2CHIOAc or CH_2CHIOH and identified as 3-hydroxypropylmercapturic acid (*N*-acetyl-S-(3-hydroxypropyl)-L-cysteine, I). There was no evidence for the presence of allylmercapturic acid (*N*-acetyl-S-allyl-L-cysteine, II) in the urine of these animals. II, however, was detected in the urine of rats injected s.c. with CH_2CHCl , S-allylglutathione, and S-allyl-L-cysteine. Rats treated with CH_2CHCl also excreted I. Mercapturic acids apparently arise by the reaction of allyl compounds or their active derivs. with glutathione. BQJN

110574p Metabolites of octoclotheptine eliminated in human and rat urine. Queisnerova, Milena; Svatek, E.; Metysova, Jirina (Res. Inst. Pharm. Biochem., Prague, Czech.). *Biochem. J.* 1969, 114(2), 339-42 (Eng). Four metabolites and unchanged octoclotheptine were extd. with dichloroethane from the urine of humans given octoclotheptine. These substances were isolated and purified by column and thin-layer chromatog. By chromatographic, spectrophotometric, and polarographic anal., unchanged octoclotheptine and 3 of the metabolites were identified (noroclotheptine, noroclotheptine N-oxide, and octoclotheptine S-oxide). The presence of glucuronides in human urine was shown. The same metabolites and unchanged octoclotheptine were also found in rat urine by chromatog. RCFG

110575q Mechanism by which leucine and arginine stimulate insulin release in vitro. Milner, R. D. G. (Univ. West Indies, Kingston, Jamaica). *Biochim. Biophys. Acta* 1969, 192(1), 154-6 (Eng). Basal insulin release in young rabbit pancreas slices in vitro was higher in the presence of leucine (5mM) than of arginine (5mM) (in the absence of glucose). Glucagon (5 $\mu\text{g./ml.}$), theophylline (1mM), dibutyryl cyclic AMP (1mM), or L-arginine (5mM) stimulated insulin release in the presence of leucine but not in the presence of arginine. Arginine-stimulated basal insulin release perhaps works by releasing glucagon from the α -cells. The mechanism of the leucine-induced stimulation is different, probably via the adenyl cyclase system. BSJN

110576r Cytochemical study of the distribution and content of nucleoproteins and of some functional groups of proteins in isolated formations of the central nervous system following foreign protein injection. Tumanyan, E. L. (Erevan. Med. Inst., Erevan, USSR). *Biol. Zh. Arm.* 1969, 22(5), 97-8 (Russ). Cytoplasm of various parts of rabbit central nervous system (including intervertebral ganglia, nuclei of the XII cranial nerve, and skin motor area of brain cortex) displayed higher ribonucleoprotein content in animals treated with repeated i.v. injection of normal horse serum. The peak effect was observed on the 4th day after the last injection. No changes were seen in content and distribution of protein SH groups. N. Jasinczuk

110577s DNA synthesis in mouse embryonic fibroblast-like cells in vitro, stimulated by various factors. Vasil'ev, Yu. M.; Gel'fand, I. M.; Gel'shtein, V. I.; Fetisova, E. K. (Mosk. Gos. Univ., Moscow, USSR). *Dokl. Akad. Nauk SSSR* 1969, 187(4), 913-15 [Cytol] (Russ). Autoradiography was used to follow the DNA synthesis in single-layer cultures of mouse embryo fibroblast-like cells in lactalbumin hydrolyzate and ox serum media in the presence of thymidine- ^3H added at various periods of culture age. The index of ^3H inclusion was increased by addn. of testicular or bacterial hyaluronidases, RNase, and digitonin. The rise of ^3H intake was the result of stimulation of the entry of the cells into the S-phase of development. G. M. Kosolapoff

110578t Effect of pregnancy and oral contraceptives on glucose and insulin metabolism. Taskinen, Maria R. *Duodecim* 1969, 85(11), 676-83 (Finnish). A review. The effect of both pregnancy and oral contraceptives is diabetogenic, and they may cause deterioration of glucose tolerance in healthy women. The organism tends to compensate this by enhanced insulin secretion, which leads to hyperinsulinism. 43 references.

110579u Effect of pyridoxal 5'-phosphate on the strength of skin in vitro. Harkness, Robert D. (Univ. Coll. London, London, Engl.). *Experientia* 1969, 25(10), 1048-9 (Eng). Treatment with 10mM pyridoxal 5'-phosphate (I) in vitro reduced the strength of rat tail skin progressively with time of incubation. The redn. was reversible, with strength returning when the skin rings were placed in buffered saline. Pyridoxamine or pyridoxine at 10mM had no comparable effect. The effect of I was reduced in the presence of lysine. Pretreatment of the skin with NaBH_4 , followed by washing in saline buffer, largely inhibited the effect of I. Pretreatment with NH_4OH also inhibited the effect of I. Treatment with NH_4OH after I prevented the recovery of strength on subsequent transfer to the saline buffer; H_2NNH_2 had a similar effect. The effect of I on skin strength is apparently brought about by rupture of a methine linkages formed between an aldehyde and an amino group. BSJN

110580n Diabetogenic effect of L-asparaginase. Khan, Amanullah; Adachi, Mitsuo; Hill, Joseph McGlashan (Wadley Inst. of Mol. Med., Dallas, Tex.). *J. Clin. Endocrinol. Metab.* 1969, 29(10), 1373-6 (Eng). The effects of *Escherichia coli* L-asparaginase (500-50,000 I.U./kg. body wt.), which has been used to induce remission of human acute lymphatic and myelogenous leukemias via depletion of an amino acid essential for some neoplastic cells, on rabbit blood and urinary glucose levels were

studied. A dose of 2000 I.U. L-asparaginase/kg. evoked hyperglycemia and glycosuria in most of the animals; this is equal to a dose which induced hyperglycemia when given to patients. AK rabbits receiving 10,000 I.U. L-asparaginase/kg. or more showed diabetogenic responses, but these effects were temporary (2-13 days) and were not assoc. with any histological changes in the pancreatic islets, except in 1 rabbit which showed islet hyalinization. DDJN

110581p Effect of Bidrin on the metabolism of dietary components by the bovine. Lowrey, R. S.; Bowman, Malcolm C.; Knox, F. E. (Coastal Plain Exp. Sta., Agr. Res. Serv., Tifton, Ga.). *J. Dairy Sci.* 1969, 52(9), 1460-3 (Eng). Six steers averaging 400 kg. in wt. were used in a switchback trial to study the effect of spiking corn silage with 15.7 ppm. (0.24 mg./kg. body wt.) of the pesticide Bidrin [3-(dimethoxyphosphoryloxy)-N,N-dimethyl-cis-crotonamide] on blood cholinesterase, digestibility of dietary components, utilization of N, and rumen fermentation. Bidrin residues were not found either in the urine or in the feces of animals ingesting Bidrin. Azodrin, a metabolite of Bidrin, was not present in the feces of treated animals but averaged 0.430 ppm. in the urine. Based on urine vol. this represented 1.5% of the ingested Bidrin. Blood cholinesterase was depressed to 30% of pretreatment values by the end of the 42-day exptl. period, whereas activity of steers fed untreated silage was unaffected. In the metabolism trial conducted during the last 14 days of the 42-day period Bidrin had no effect on the digestibility of dietary components (dry matter, crude protein, ether ext., crude fiber, N-free ext., and gross energy), the utilization of N, or rumen fermentation. RCLD

110582q Effect of a second dose of cadmium salts on vascular permeability in the rat testis. Clegg, E. J.; Carr, Ian; Niemi, M. (Univ. Sheffield, Sheffield, Engl.). *J. Endocrinol.* 1969, 45(2), 265-8 (Eng). Two doses of CdCl_2 were given to rats at intervals varying from 76 to 194 days. After the second dose the blood vessels in the testis and initial segment of the epididymis showed increased permeability, as demonstrated by i.v. markers. In the testis, leaking vessels were usually found in areas where interstitial cells were abundant. RCKV

110583r Acid-base and electrolyte changes induced by acute isotonic saline infusion in the nephrectomized dog. Rosenbaum, Barry J.; Makoff, Dwight L.; Maxwell, Morton H.; Houghoughi, Michael (Cedars-Sinai Med. Res. Inst., Los Angeles, Calif.). *J. Lab. Clin. Med.* 1969, 74(3), 427-35 (Eng). The mechanism and extent of "dilution acidosis" by acute infusions of isotonic saline was studied in nephrectomized dogs. Infusions of 50, 75, and 100 ml./kg. of body wt. (BW) (Groups 1, 2, and 3) over a 30-min. period resulted in extracellular fluid expansions of $24.4 \pm 1.7\%$, $28.8 \pm 2.2\%$, and $33.9 \pm 5.5\%$, resp. pCO_2 was kept const. Body spaces were measured isotopically, and intracellular H^+ activity by 5,5-dimethyl-2,4-oxazolidinedione- ^{14}C . The extracellular bicarbonate concn. decreased only -2.4 ± 0.7 meq./l. and -2.5 ± 0.4 meq./l. in Groups 1 and 2 and -3.0 ± 1.0 in Group 3. The total amt. of extracellular bicarbonate increased $+0.6 \pm 0.2$ meq./kg. of BW, $+0.8 \pm 0.2$ meq./kg. of BW, and $+1.5 \pm 0.4$ meq./kg. of BW in each group, resp. Concomitantly, the total amt. of extracellular fluid K increased $+0.3 \pm 0.0$ meq./kg. of BW, $+0.5 \pm 0.1$ meq./kg. of BW, and $+0.4 \pm 0.1$ meq./kg. of BW, resp., while there was no decrease in extracellular K concn. It was suggested that the extracellular bicarbonate and K concns. were defended by shifts of H^+ into cells (or bicarbonate out of cells), in conjunction with a shift of K out of cells. Despite the presumed H^+ (or bicarbonate) flux, there were no net changes of H^+ activity. The conceptual theory of extracellular "dilution acidosis" is valid but of limited magnitude and little clin. significance when expansion is relatively slow. Cellular buffering minimizes the extracellular acidosis, and the shift of K out of cells prevents hypokalemia. RCKY

110584s Effect of erythropoietin on bone marrow α -amino-levalulinic acid synthetase and heme synthetase. Bottomley, Sylvia S.; Smithee, G. Ann (Veterans Admin. Hosp., Oklahoma City, Okla.). *J. Lab. Clin. Med.* 1969, 74(3), 445-52 (Eng). An in vitro culture method has been adapted for rabbit bone marrow and has permitted measurement of the effect of erythropoietin on Δ -aminolevalulinic acid synthetase and heme synthetase activities in marrow cells. In this system, erythropoietin enhanced Δ -aminolevalulinic acid synthetase activity. This effect was detectable as early as 6 hrs. after contact with erythropoietin. The max. enzyme activity observed was 200% greater in stimulated than in control cultures. Studies with inhibitors of protein synthesis suggested that erythropoietin increased the synthesis of the enzyme. No stimulatory effect by erythropoietin on heme synthetase activity was observed. RCKY

110585t Action of adenosine triphosphate on the depressed spontaneous electrical activity of the dog cerebral cortex. Benzi, Gian; Arrigoni, Elena; Ferrara, A.; Masciapa, P. (Univ. Pharmacol., Univ. Pavia, Pavia, Italy). *J. Pharm. Sci.* 1969, 58(9), 1161-3 (Eng). The repeated suppression of the ventilation and the circulation of the brain in the dog induces a high depression or a silence of elec. activity of the cortical and subcortical centers. The recovery of respiratory and circulatory

Pb poisoning and manic-depressive psychosis are discussed and the striking similarities between them noted. It is suggested that Pb may be a toxic determinant in this psychosis. The Davis test (Davis and Andelman, 1967) was used for the detn. of urinary δ -aminolevulinic acid (I) levels in patients and controls. Results showed an increasingly significant rise in I levels between controls and untreated patients and patients treated with Li_2CO_3 . Li may interfere with Hb synthesis in a similar way to Pb. 41 references. S. M. Maxwell

89616s Effects of DTPA [diethylenetriaminepentaacetic acid] aerosol on lung contamination by lanthanum. Pasquier, Christian, Voisin, Dominique; Thieblemont, Pierre; Perrault, Gerard; Bayard, Jean P. (Dir. Prot. Surete Radiol., C.E.N., Fontenay-aux-Roses, Fr.). *Commis. Energ. At. [Fr.], Rapp.* 1969, CEA-R-3735, 19 pp. (Fr). Avail. CEA. By use of DTPA aerosol in the treatment of pulmonary contamination by La, its effectiveness was detd. as a function of time. Provided that it is administered at an early stage, in the 2 hrs. after exposure, >80% can be eliminated using lower therapeutic doses than those prescribed for other methods of administration. Its assocn. with some enzymes did not enhance the therapeutic effect of the chelator. The const. for the passage of the DTPA-La complex from the lung to the blood is $\sim 0.016/\text{min.}$, corresponding to a period of 44 min. A significant nonchelatable fraction, persisting after prolonged action of the DTPA, of the order of 40-45% is observed. DWJF

89617: Ferric cyanoferrate(II): an effective antidote in thallium poisoning. Heydlauf, Horst (Inst. Strahlenbiol., Kernforschungszentrum, Karlsruhe, Ger.). *Europ. J. Pharmacol.* 1969, 6(3), 340-4 (Eng). The influence of orally administered ferric cyanoferrate(II), (Prussian Blue, PB) on the distribution and excretion of ^{201}Tl was studied in the rat. PB lowered the retention of ^{201}Tl by inhibition of its absorption and reabsorption from the intestinal tract. The toxicity of Ti_2SO_4 was decreased by PB. PB is suggested as an antidote in Tl poisoning. V. N. Gupta

89618u Cycloheximide-induced ultrastructural changes in the adrenal cortex of the rat. Dzsinich, Cs.; Szabo, D.; Okros, I. (Inst. Exp. Med., Hung. Acad. Sci., Budapest, Hung.). *Experientia* 1969, 25(8), 835-6 (Eng). Wistar rats of both sexes weighing about 180 g. were used. Conspicuous changes in the ultrastructure of the zona fasciculata cells were observed following decapitation at 50 min. even after the lowest (5 mg.) dose. At low-power magnification, compact masses of irregular shape, medium d. and blurred outlines were seen to have accumulated between organelles. In expts. involving both cycloheximide and ACTH treatment, the changes were similar, although the cells appeared swollen. Similar observations were made in some cells of the zona reticularis, but not in the zona glomerulosa. The findings suggested a correlation between the substance seen to accumulate among organelles and the increased cholesterol content of the adrenal cortex. The ultrastructural changes were the consequence of an impairment of the enzyme system. P. J. Parisek

89619v Effect of acetone on the level of ketone bodies in the blood and urine of experimental animals of different species. Linyucheva, L. A.; Tiunov, L. A.; Kolosova, T. S. (USSR). *Farmakol. Toksikol. (Moscow)* 1969, 32(4), 465-7 (Russ). Rats and mice exposed to 30 mg. $\text{Me}_2\text{CO}/\text{l.}$ and rabbits and guinea pigs exposed to 72 mg./l. for 2 hrs. showed increased levels of Me_2CO , acetoacetic acid, and β -hydroxybutyric acid in their blood and urine immediately after inhalation and 24 hrs. later. In all 4 species the β -hydroxybutyric acid level increased to a greater extent than did the other ketone bodies. The largest increases in the Me_2CO and acetoacetic acid levels in the blood both immediately and 24 hrs. after acute inhalation occurred in rats and the smallest changes appeared in rabbits. BJJR

89620p Nature of the acute action exerted on the organism by monoethanolthylenediamine. Tikhonova, G. P.; Sidorov, K. K. (Inst. Med.-Biol. Probl., Moscow, USSR). *Farmakol. Toksikol. (Moscow)* 1969, 32(4), 473-5 (Russ). Monoethanolthylenediamine (I) injected into the stomach of rats in a max. tolerable dose (2.5 g./kg. in 30% aq. soln.) disrupted the acid-base balance in the blood after 3-5 hrs., increased the pH from 7.18-7.35 (control) to 7.4-7.49, and increased the level of free bases. One day after I injection the Ca level in the serum increased, the time of blood coagulation decreased, the blood pH dropped to 7.11-7.24, and the amt. of free bases was below normal. The level of globulins decreased and the content of albumins increased in the blood; the level of chlorides in the urine decreased. I caused necrosis in the mucous membranes of digestive system organs, probably through its alk. properties. BJJR

89621q Changes in adrenaline-like substances in rabbit blood following chronic exposure to vinyl chloride fumes. Vazin, A. N.; Plokhova, E. I. (Inst. Gig. Tr. Profzabol., Gorki, USSR). *Gig. Tr. Prof. Zabol.* 1969, 13(6), 46-7 (Russ). A group of 8 chinchilla rabbits was exposed for 4 hrs. daily, during 5 months, to the vapors of vinyl chloride (I) in air at 0.02-0.03 mg./l. Samples of blood were taken from the ear veins and analyzed for adrenaline (II) and adrenaline-like (IIa) substances.

Before the exposure to I and also in the control group of rabbits the II and IIa levels varied little and averaged 3.5 $\mu\text{g.}\%$. After 20 days exposure the level of II and IIa rose to 6.15 $\mu\text{g.}\%$, after 40 days it reached 6.6 $\mu\text{g.}\%$ and it remained const. thereafter. The biopotential of the posterior hypothalamus also changed. These effects of I are the direct cause of hypertension. CPJR

89622r ATP and lipid contents in the liver of mice after inhalation of chlorinated hydrocarbons. Ogata, Masana; Tomokuni, Katsumaro; Watanabe, Shinsaku (Med. Sch., Okayama Univ., Okayama, Japan). *Ind. Health (Kawasaki, Japan)* 1968, 6(3), 116-9 (Eng). The hepatic ATP level decrease and the onset of fatty liver as indicated by the increase in the amt. of the total lipids and triglycerides in the mice exposed to 2 kinds of chlorinated hydrocarbons are in the following order: CCl_4 , tetrachloroethylene, and trichloroethylene. The total lipid and triglyceride contents increased proportionately to the fall in the ATP level before and after the exposure to 3 kinds of chlorinated hydrocarbons. It was suggested that there is some close relationship between the decreased hepatic ATP levels and the development of fatty liver in chlorinated hydrocarbon poisonings. B. V. Shetty

89623s Influence of subacute intoxication with manganous chloride and carbon tetrachloride on the lethal dose of digitoxin, lanatoside C, and strophanthoside in guinea pigs. Lence, P.; Valentic-Budihna, Metka (Med. Fac., Ljubljana, Yugoslavia). *Jugoslav. Physiol. Pharmacol. Acta* 1968, 4(2), 157-64 (Eng). In guinea pigs the toxicity of the title cardiotonic glucosides is modified in subacute intoxications with MnCl_2 and CCl_4 (when evident morphological changes are restricted to the liver). The following doses were used: 0.01 ml./kg. CCl_4 in 2% oil soln. and 0.003 g./kg. MnCl_2 in 3% aq. soln., i.m., twice a week, or 10 times successively; glucosides were administered 30-39 days after the last dose of CCl_4 or MnCl_2 . In intoxicated guinea pigs the lethal dose of digitoxin did not differ significantly from that of controls. The lethal dose of lanatoside C was significantly smaller only in CCl_4 treated animals and the lethal dose of strophanthoside was significantly smaller in both intoxicated groups. G. Muacevic

89624t Antidotes for phosgene-induced pulmonary edema. Boyd, Eldon M. (Queen's Univ., Kingston, Ont.). *J. Pharm. Pharmacol.* 1969, 21(8), 557 (Eng). Death rates from phosgene were reduced in rabbits, cats, and rats if the animals were allowed to inhale the phosgene through the nose rather than directly into the trachea. David B. Sabine

89625u Demethylphalloin. Puchinger, Herwig; Wieland, Theodor (Univ. Frankfurt, Frankfurt, Ger.). *Justus Liebig's Ann. Chem.* 1969, 725, 238-40 (Ger). Demethylphalloin- ^3H (I) was obtained by redn. of the CO group of ketophalloidin with ^3H -labeled NaBH_4 . I had almost the same toxicity as phalloidin. During storage I gave a degradation product whose uv spectrum indicated a sulfoxide structure. BTJG

89626v Histochemical study of cytochrome oxidase and succinic dehydrogenase activity in encephalon of rabbits poisoned by alcohol. Lo Menzo, G.; Chiara, A. (Univ. Catania, Catania, Italy). *Med. Leg. Assicurazioni* 1968, 16(3-4), 163-72 (Eng). An increase in both cytochrome oxidase and succinic dehydrogenase was observed in the cells of the cerebellar cortex of rabbits which had undergone either chronic or acute alc. poisoning, as compared to the nonpoisoned control animals. No change was evident in other encephalic regions. The increase of these enzymes at cerebellar level agrees with the symptomatological data indicative of functional damage of the area during alc. poisoning. Murrie W. Burgan

89627w Nicotine degradation in hamsters and rats and its modification by foreign substances. II. Effect of carbon monoxide treatment of the animals on their nicotine metabolism. Harke, Hans P.; Frahm, B.; Schultz, Ch.; Döntenwill, W. (Inst. Wiss. Forschungstelle Verband, Cigarettenind., Hamburg, Ger.). *Naturwissenschaften* 1969, 56(8), 418 (Ger). Degradation of nicotine to cotinine in rat and hamster liver homogenates was not affected by prior exposure to CO. GKJG

89628x Toxic effects of calcium, titanium, and niobium borides in rats. Kasparov, A. A.; Zhilova, N. A. (USSR). *Nov. Dannye Toksikol. Redk. Metal. Ikh Soedin.* 1967, 152-60 (Russ). From Ref. Zh., *Farmakol., Khimioter. Sredstva, Toksikol.* 1968, Abstr. No. 7.54.779. LD $_{50}$ of CaB_2 (I), during i.p. administration to rats, was 1.045 mg./kg. Intoxication with I is expressed by depression and disorder in movement coordination. Chronic oral administration of I to rabbits (100 mg./kg./day for 4 months) caused leukocytosis, lymphocytosis, increase in concn. of α -globulins and activity of aldolase, and decrease in albumin in blood. Prothrombin in blood at beginning decreased and then increased to the end of expt. In lungs there was polyemia of tissues and thickening of interalveolar septums. In intestines there was sclerosis of all vessels in submucosal layer, decreased glycogen in liver, and accumulation of acid mucopolysaccharides in the region of hepatic triad. Moderate intensification of lung pattern was observed by x-ray studies in animals 0-9 months after single intratracheal administration to rats of Ti boride (II), Nb boride (III), and esp. of I (50 mg.).

ences in the fatty acid compn. of the brain between HCN-treated and untreated rats. N. Constantas.

113452n Curative antagonization of liver damage caused by phalloidin with silymarin as a model of antihepatotoxin therapy. Vogel, Guenther; Temme, Inge (Biol. Inst. Madaus, Cologne, Ger.). *Arzneim.-Forsch.* 1969, 19(4), 613-15 (Ger.). Silymarin, the antihepatotoxic agent in the seeds of *Silybum marianum*, prevented the toxic effects of phalloidin in mice. Silymarin was also effective in reversing the toxic effects of phalloidin in mice intoxicated first with this compd. and then treated with silymarin. The antiphalloidin effect of silymarin depended on the time interval between intoxication and treatment, and on the degree of liver damage. BQJC

113453p Evidence for the bioactivation of slaframine. Aust, Steven D. (Michigan State Univ., East Lansing, Mich.). *Biochem. Pharmacol.* 1969, 18(4), 929-32 (Eng). Max. salivary activity in pentobarbital-anesthetized cats occurred ~1 hr. after i.v. administration of slaframine (0.3 mg./kg.); the duration of salivation was extremely long, usually lasting for 6 hrs. after a single dose. In addn. to salivation, most of the exocrine glands were specifically stimulated by slaframine. Upon administration of slaframine to cows, sheep, and goats with pancreatic cannulas there was also a substantial delay before an increase in pancreatic flow was observed. In mice, a longer delay occurred after i.v. injection of 2 mg./kg. than with i.p. administration at the same dose; this delay was decreased by injection directly into the portal vein. Delay of the effect of the drug at 4 mg./kg. was significantly extended by briefly isolating (with clamps) the liver of rats; the effect was completely eliminated by the permanent isolation of the liver. Common inducers of liver drug-metabolizing enzymes consistently reduced the delay in the induction of salivation in mice, while inhibitors of the enzymes consistently lengthened the delay. Thus, slaframine seems to require activation by the liver before stimulating exocrine glands. The enzymes involved in this activation are probably those responsible for the metabolism of most xenobiotics. BYJN

113454q Metabolism of phospholipids in the brain and liver of rats during intoxication with organophosphorus compounds. Dvorkin, V. Ya.; Tofilo, A. P. (Pavlov Inst. Physiol., Leningrad, USSR). *Byull. Eksp. Biol. Med.* 1969, 67(3), 50-2 (Russ). Organophosphorus compds. LG-63 (5 mg./kg.) and GA-81 (0.4 mg./kg.) administered i.m. to rats did not affect the level of phospholipids in the brain and liver or the rate of restoration of phospholipids in the brain. The metabolism of phospholipids in the liver was increased 24.8% by organophosphorus compd. LG-63 and 32.4% by GA-81. The increased intensity of phospholipid metabolism may be connected in some way to increased activity of the hepatic cells during detoxication of the cholinesterase inhibitors. BJJR

113455r Toxicity studies in mice treated with 1- β -D-arabinofuranosylcytosine (ara-C). Leach, William B.; Laster, W. Russell, Jr.; Mayo, Joseph G.; Griswold, Daniel P., Jr.; Schabel, Frank M., Jr. (Med. Center, Univ. of Alabama, Birmingham, Ala.). *Cancer Res.* 1969, 29(3), 529-35 (Eng). Optimum therapeutic dosage schedules of 1- β -D-arabinofuranosylcytosine (ara-C) administered i.p. in mice (15 mg./kg., every 3 hrs. for 24 hrs.) result in karyorrhectic damage to the crypt epithelial cells of the intestinal mucosa. This damage is most severe at 4 hrs. (earliest observations made) after the end of the 24-hr. course, after which there is a rapid recovery to completion in 72 hrs. The damage is thus transitory and resembles that of hydroxyurea. This cycle of transitory intestinal damage followed by recovery occurs after each therapeutic dosage schedule of ara-C as long as the schedule is not repeated more often than every 4th day. Progressive damage to the intestinal mucosa accompanied by changes in the hematopoietic tissues occurs only if this optimum therapeutic dose (15 mg./kg., every 3 hrs.) is continued uninterrupted to the LD₁₀₀ dose (360 mg./kg. in 72 hrs.) and beyond. Irreversible changes are seen in the intestinal mucosa, and a progressive depopulation of the bone marrow with ultimate aplasia ensues as the LD₁₀₀ dose is reached and surpassed. RCTT

113456s Effect of butylated hydroxytoluene (BHT) on rat liver cytochrome oxidase activity. Pascal, Gerard; Terroine, Therese (Centre Rech. Nutr., C.N.R.S., Bellevue, Fr.). *C. R. Acad. Sci., Paris, Ser. D* 1969, 268(11), 1529-31 (Fr). The oral administration of BHT (0.05% in the food, a concn. 50-fold greater than that authorized for human food) for 8 weeks caused a 13.4-22.4% decrease in hepatic cytochrome oxidase activity in rats of both sexes. The addn. of BHT to rat liver homogenates at the level of 10 mg./g. liver caused a 12% decrease in cytochrome oxidase activity. Thus, BHT appears to exert an antioxidant effect on *in vivo* metabolism. DFJF

113457t Activity of guanine deaminase in rat kidney, liver, and blood during experimental uranyl nitrate intoxication. Bastide, Janine; Bastide, Pierre (Fac. Mixte Med. Pharm., Clermont-Ferrand, Fr.). *C. R. Soc. Biol.* 1968, 162(5-6), 1169-71 (Fr). Guanine deaminase activity (I) was studied in the liver, kidney, and blood of rats during exptl. intoxication

with uranyl nitrate (1 ml. i.p. of a soln. contg. 2 g./l. per 100 g. body wt.). As early as 24 hrs. later a progressive elevation of I was noted in all organs, but there was a definite lowering of I in the kidney for the first 12 hrs. after the start of intoxication.

Dorothy J. Buchanan-Davidson

113458u Excretion of tetraethylgermanium in the rat. Oustrin, J.; Clavel, M. J.; Pitet, G. (Centre Rech. Toxicites, C.N.R.S., Toulouse, Fr.). *C. R. Soc. Biol.* 1968, 162(5-6), 1226-9 (Fr); cf. G. Pitet (1967). EtGe (I), a very resistant compd. *in vitro*, is degraded very easily in the rat. Although I has a very high b.p., it is eliminated in large amts. during respiration. The metabolites of I found in rat urine are GeO₃ or the germanates. The metabolism of I is different from that of tetraethyllead (II) or tetraethyltin (III). No evidence was found for the formation of triethylgermanium, which explains the weak toxicity of I compared to II and III.

Dorothy J. Buchanan-Davidson

113459v α -Hydroxybutyrate dehydrogenase activity of rat kidney homogenate fractions after experimental uranyl nitrate intoxication. Bastide, Janine; Bastide, Pierre (Fac. Mixte Med. Pharm., Clermont-Ferrand, Fr.). *C. R. Soc. Biol.* 1968, 162(8-9), 1492-3 (Fr). Most of the α -hydroxybutyrate dehydrogenase activity of the rat kidney is found in the supernatant after centrifugation at 24,000 g for 2 hrs. This activity decreased with time during exptl. uranyl nitrate poisoning, whereas the contents of protein, DNA, and RNA were relatively low and underwent but little variation. C. W. Ackerson

113460p Effect of ethyl bromide on the liver. Karimullina, N. K.; Gizatullina, A. A. (Ufim. Nauch.-Issled. Inst. Gig. Profzabol., Ufa, USSR). *Farmakol. Toksikol. (Moscow)* 1969, 32(2), 165-7 (Russ). EtBr fumes (2.4 mg./l.) inhaled by rats and rabbits for 4 hrs. daily for 6 months disrupted the functional ability of the liver, decreased the hepatic glycogen and fat levels, and prolonged hexenal sleep. Granular dystrophy in the hepatic cells and a decreased RNA level in the cytoplasm were detected. BJJR

113461q Hemopoiesis in chronic heliotrine poisoning of Wistar rats. Levin, G. S.; Novachenko, Z. I. (Uzb. Nauch.-Issled. Inst. Gematol. Pereliv. Krovi, USSR). *Farmakol. Toksikol. (Moscow)* 1969, 32(2), 170-1 (Russ). Heliotrine administered s.c. at 3-10 mg./100 g. once a week for 1-8 months to Wistar rats caused hepatic lesions, hypochromic anemia, severe reticulocytosis, normoblastosis, and leukopenia. Erythroblastic sprout hyperplasia, an increased no. of mitoses, and an increased no. of reticular and esp. plasmatic cells were observed. The observed changes in the blood and bone marrow suggest development of an autoimmune form of hemolytic anemia in response to chronic heliotrine poisoning. BJJR

113462r Benzene metabolism in the liver of experimental animals and man. Tiunov, L. A.; Sokolova, T. I.; Bandman, A. L. (USSR). *Farmakol. Toksikol. (Moscow)* 1969, 32(2), 185-8 (Russ). The rate of C₆H₆ metabolism during 24 hrs. of incubation was similar in liver homogenates from humans and rats, more rapid in homogenates from guinea pigs, and slower in rabbit liver homogenates. Species-specific differences seemed to be involved in C₆H₆ conversion, since the activities of aryl-4-hydroxylase and glucuronyltransferase increased while the sulfonating system activity did not change in C₆H₆-treated rats. In C₆H₆-treated rabbits the sulfate adenylyltransferase and aryl sulfotransferase activities decreased during disruption of the sulfonating system. The high rate of C₆H₆ conversion in guinea pigs may be connected with the relatively high liver catalase activity. BJJR

113463s Effect of the sodium salt of adenosine triphosphate on experimental cyanide poisoning of rats (mechanism of the antidotal action). Mosketi, K. V.; Ganzhara, P. S. (Odess. Med. Inst., Odessa, USSR). *Farmakol. Toksikol. (Moscow)* 1969, 32(2), 214-15 (Russ). Na ATP (0.5 ml. of a 1% soln.) given s.c. or i.m. to rats 1 hr. prior to administration of the min. lethal dose of NaCN prolonged survival. When given s.c. immediately after lethal cyanide poisoning it substantially extended the life span of 50% and prevented death in the other 50% of the rats. The antidotal effect of ATP may result from its ability to restore respiration by bypassing cyanide-sensitive enzymes. BKJR

113464t Changes in the cardiac activity of rats chronically exposed to vinyl chloride vapors. Vazin, A. N.; Plokhova, E. I. (Gor'k. Nauch.-Issled. Inst. Gig. Tr. Prof. Zabol., Gorki, USSR). *Farmakol. Toksikol. (Moscow)* 1969, 32(2), 220-2 (Russ). Chronic (5 months) exposure of rats to vinyl chloride vapors at 0.03-0.04 mg./l. disrupted cardiac work rhythm, induced bradycardia and arrhythmia, and reduced the relative duration of I-II and T-II sound intervals. The relative duration of the Q-T complex did not change significantly. Within 15 days after termination of poisoning, the rat cardiac activity rhythm returned to normal, but the duration of the I-II and T-II sound intervals remained below the initial level for another 15 days. The maximal permissible concn. of vinyl chloride apparently is significantly less than the 0.03 mg./l. level previously estd. BJJR

14—TOXICOLOGY

T. R. TORRELSON

41109x Toxicology of vinyl chloride. Schottek, Wolfgang (Abt. Arbeitstoxikol., Holzweissig, Ger.). *Chem. Tech. (Leipzig)* 1969, 21(11), 708-11 (Ger.). A review with 24 refs. The toxicity of vinyl chloride in animals and humans, and the relation of the chem. structure of the compd. to its toxicity were discussed. CCJG

41110r Microscopically contrasted heavy metal intoxication. Silver sulfide process, a method for localized histochemical detection of heavy metals in tissues. Haider, Gerhard (Ger.). *Mikrokosmos* 1969, 58(9), 272-5 (Ger.). A review of work is presented which illustrates the value of the combination of light microscopy with histochem. techniques for the detection, localization, and identification of Hg, Pb, Bi, Fe, Zn, and Cu in cells and tissues. Highlights of the silver sulfide histochem. procedure are presented along with representative photomicrographs. 6 refs. Nellie G. Dehnhostel

41111s Development of the hemodynamic, biochemical, and morphologic changes in experimental endotoxin shock. Stengert, Krzysztof (Z Zakl. Anestezjologii, AM, Lodz, Poland). *Postępy Hig. Med. Dosw.* 1969, 23(5), 601-59 (Pol.). A review is given of methods for detg. hemodynamic, biochem., and morphol. changes, the course of changes in dogs, clin. evaluation and patterns, and damage to tissues and organisms during exptl. endotoxin shock. 146 refs. Y. Pomeranz

41112t Saponins. Birk, Yehudith (Hebrew Univ., Rehovoth, Israel). *Toxic Const. Plant Foodst.* 1969, 169-210 (Eng.). Edited by Liener, Irvin E. Acad. Press: New York, N.Y. Dietary source, metabolism, and effects of various saponins are given with methods for qual. and quant. analyses. 167 refs. E. A. Hodgdon

41113u Chromatographic identification of psychotropic drugs. Phillips, Geoffrey F.; Gardiner, Jane (Lab. Govt. Chem., London, Engl.). *J. Pharm. Pharmacol.* 1969, 21(12), 793-807 (Eng.). The thin-layer chromatog. of 3 classes of psychotropic drugs, phenethylamines, tryptamines, and erganes, has been investigated. Published methods are reviewed and R_f data, normalized by a graphical technique, are reported for extensions and modifications of some of these systems. Optimum forensic sorting procedures are recommended. RCHQ

41114v Estimation of lead in urine by atomic absorption analysis. Taira, Yoshiko. *Nippon Eiseikensha Gishikai Zasshi* 1969, 18(5), 389-91 (Japan). The Pb^{++} was extd. into iso-Bu-COMe soln. from 30% NH_4OH . The recovery rate was 99.9%. The reproducibility of at. absorption measurement was 1.4%. No interference from other ions was noticed. T. L. Chang

41115w Determination of toxic substances and their metabolites in biological fluids by gas chromatography. I. Trichloroethanol in urine. Sedivec, Vaclav; Flek, Jan (Ustav Hyg. Prace, Prague, Czech.). *Prac. Lek.* 1969, 21(7), 301-5 (Czech). See CA 70: 113446p. VNJZ

41116x Aflatoxin B₁ in the excretion of aflatoxin-poisoned rats. Chou, Ming-Wu; Tung, Ta-Cheng (Coll. Med., Nat. Taiwan Univ., Taipei, Taiwan). *T'ai-Wan I Hsueh Hui Tsa Chih* 1969, 68(8), 389-91 (Eng.). Aflatoxin B₁ was detected in the rat urine and feces after i.p. injection of the toxin. Most of the aflatoxin B₁ was excreted in the first 24 hr. The percentage recovery was about 1.5%. A thin-layer chromatographic method was a simple way for detg. the aflatoxin concn. of the excretions, and could provide useful information for detecting it in humans. N. M. Wright

41117y Paper chromatography of *Taxus baccata* toxin. Buben, Zenon (Wyzsza Szk. Roln., Wroclaw, Poland). *Zesz. Nauk. Wyzsz. Szk. Roln. Wroclawiu, IVet.* 1968, No. 23, 215-21 (Pol.). The presence of toxin in *T. baccata* (English yew) needles, in fodder, and in the alimentary tract content was detected by paper chromatog. The alkaloid was extd. from the biol. material by Et_2O , purified with active C, and chromatographed in the form of aq. HCl soln. The chromatograms were developed at 18° by the ascending technique, using as solvent either $BuOH-80\% AcOH-anhyd. EtOH-H_2O$ (50:7:2:15), or 75% aq. $(NH_4)_2SO_4$. The R_f values were 0.95 and 0.75, resp. The toxin spots were stained by the Dragendorff reagent. Irena Kloczko

41118z Errors of converting a urine alcohol value into a blood alcohol level. Kaye, Sidney; Cardona, Eduardo (Sch. Med., Univ. Puerto Rico, Rio Piedras, P.R.). *Amer. J. Clin. Pathol.* 1969, 52(5), 577-84 (Eng.). Evidence is presented for the inadvisability of calcg. blood $EtOH$ levels on the basis of urine $EtOH$ content. $EtOH$ content was detd. in the blood and urine of 148 patients and the ratio of urine/blood was calcd. The range of ratios was 0.21-2.66 with a mean ratio of 1.28. Blood levels were calcd. from urine levels using a conversion factor of 1.28 and compared with measured values. Calcd. values exceeded actual values by at least 0.02 g/ml in 21.5% of the cases and were lower by the same amt. in 34.5% of the cases. J. R. Macnab

41119a Ethylene glycol toxicity in the monkey. Roberts,

James H. Seibold, H. R. (Tulane Univ., Covington, La.). *Ann. Appl. Pharmacol.* 1969, 15(3), 824-31 (Eng.). The toxic effects of ethylene glycol in several macaque species are reported. The compd. was administered in the drinking water at concns. of 0.25-10%, and histol. studies were made after acute and chronic administration. With the exception of a few animals (which had Ca oxalate crystals in the brain), significant pathol. alterations were limited to the kidneys. Animals receiving 15 ml/kg or more of ethylene glycol had Ca oxalate crystals within proximal renal tubules and assocd. tubular degeneration. Despite the absence of crystals in animals receiving <15 ml/kg, mild glomerular damage was found, and azotemia occurred in some animals, suggesting a toxic effect of ethylene glycol apart from its conversion to oxalic acid. RCZB

41120u A clinicopathologic study of the effects of riot control agents on monkeys. IV. o-Chlorobenzylidene malononitrile (CS) grenade. Striker, G. E.; Streett, C. S.; Ford, D. F.; Herman, L. H.; Helland, D. R. (Edgewood Arsenal, Md.). *U.S. Clearinghouse Fed. Sci. Tech. Inform., AD 1967, AD-808-732*, 39 pp. (Eng.). Avail. CFSTI. From *U.S. Govt. Res. Develop. Rep.* 1969, 69(19), 123. A study was made of the order, severity, and resolution of pathol. changes in monkeys exposed to CS. Monkeys were exposed to CS (2700, 8500, 28,500, or 80,000 mg min/m³). The most prominent lesions seen after the 2 lower doses were mild pulmonary congestion, bronchorrhea, emphysema, and atelectasis. These lesions cleared by 72 hr but recurred at 1 week and 30 days. Oral and nasal discharges and dyspnea appeared early after a level of 28,500. They were most severe between 12 and 24 hr and were resolved by 72 hr. Pneumonia, emphysema, and atelectasis were present 1 week and 30 days after exposure. Significant lesions were seen radiographically only in those monkeys exposed to a level of 80,000. These lesions paralleled those seen on necropsy. At this level edema appeared by 12 hr, peaked between 24 and 48 hr, and cleared by 1 week. Emphysema and bronchiolitis were present 1 week and 30 days after exposure. TCVL

41121v Experimental study on gas embolism with particular reference to the differentiation between embolic gas and gas from putrefaction. Pierucci, Giovanni; Gherson, Gemma (Inst. Med. Legale, Univ. Pavia, Pavia, Italy). *Zaccchia* 1968, [3] 4(3), 347-73 (Ital.). Embolism was induced by injecting air or He i.v. into living (followed by instant death), and i.v. or intracardially into sacrificed, rabbits, and gas was aspirated from the heart at intervals. Putrefaction gas was aspirated from the heart and abdominal cavity of rabbits and human cadavers 1-13 days, and 15-236 days, after death, resp. In samples of air embolic gas, O_2 decreased and 1 hr after death was insignificant; CO_2 was present immediately; N_2 levels were relatively stable, similar to air, for 2 days, then decreased sharply. In He embolic gas, O_2 , N_2 , and CO_2 were present immediately. Results were essentially the same in rabbits injected before and after death. Av. values for putrefaction gas contents in rabbit and cadaver heart were, resp.: O_2 1.32 and 2.05%, N_2 (usually <50%) 12.13 and 22.06%, CO_2 31.08 and 50.62%; CH_4 appeared early and almost constantly in the rabbit. F. Farnam

41122w Early effects of carbon tetrachloride on the synthesis of phospholipids in the rat liver and their possible pathogenetic role in fatty liver induction. Halbreich, A.; Mager, J. (Haddassah Med. Sch., Hebrew Univ., Jerusalem, Israel). *Biochim. Biophys. Acta* 1969, 187(4), 584-7 (Eng.). In rats, i.p. injections of CCl_4 in doses as low as 0.5 μ l/100 g reduced the ability of liver microsomes to incorporate choline-¹⁴C into total phospholipids and labeled L-leucine-¹⁴C into protein, discernible as early as 10-15 min postinjection and lasting for ≥ 20 hr. Incorporation patterns of choline were identical whether the radioactive choline was labeled in the Me groups or in the 1,2-carbon atoms. The magnitude of choline inhibition was not altered by varying the dose of labeled choline over a 1000-fold range, attesting to the independence of this phenomenon of the attendant variations in the internal pool size of free choline. Ethionine (1 mg/g) and dimethylnitrosamine (10 mg/100 g) did not affect the incorporation of choline into liver phospholipids, although they inhibited protein synthesis. CCl_4 enhanced the incorporation of ethanolamine-²⁻¹⁴C into liver microsomal phospholipids. The early onset and the long persistence, as well as the specific nature, of the derangement of phospholipid synthesis by CCl_4 suggest a possible role of this phenomenon in the pathogenesis in fatty liver. BKJN

41123x In vitro inhibition of succinate and pyruvate oxidation by ethanolic extracts of grasses, legumes, and dystrophogenic forages. Cheeke, Peter R.; Oldfield, James E. (Oregon State Univ., Corvallis, Oreg.). *Can. J. Anim. Sci.* 1969, 49(3), 402-4 (Eng.). $EtOH$ exts. of title plants inhibited in vitro oxidn. of both succinate and pyruvate by rat liver homogenates. Exts. of 2 dystrophogenic forages did not inhibit succinate oxidn. more than those of two nondystrophogenic samples. The succinic