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Effects of exposure to vehicle exhaust on health

by Ulf Ulfvarson, TechD,[1] Rolf Alexandersson, MD,[2] Leif Aringer. MD,[3] Eva Svensson, MD,[2] Göran Hedenstierna, MD,[4] Christer Hogstedt, MD,[2, 3] Bo Holmberg, PhD,[3] Gunnar Rosén,[3] Marja Sorsa, PhD[5]

ULFVARSON U, ALEXANDERSSON R, ARINGER L, SVENSSON E, HEDENSTIERNA G, HOGSTEDT C, HOLMBERG B, ROSEN G, SORSA M. Effects of exposure to vehicle exhaust on health. *Scand J* Work Environ ***Health*** 13 **(1987)** *505— 512.* Exposure to combustion engine exhaust and its effect on crews of roll-on roll-off ships and car ferries and on bus garage staff were studied. The peak concentrations recorded for some of the substances studied were as follows: total particulates (diesel only) 1.0 mg/m³, benzene (diesel) **0.3** mg/m³, formaldehyde (gasoline and diesel) **0.8** mg/m³, and nitrogen dioxide (diesel) 1.2 mg/m³. The highest observed concentration of benzo(a)pyrene was 30 ng/m³ from gasoline and diesel exhaust. In an experimental study volunteers were exposed to diesel exhaust diluted with air to achieve a nitrogen dioxide concentration of 3.8 mg/m³. Pulmonary function was affected during a workday of occupational exposure to engine emissions, but it normalized after a few days with **no** exposure. The impairment of pulmonary function was judged to have no appreciable, adverse, short-term impact on individual work capacity. In the experimental exposure study, **no** effect on pulmonary function was observed. Analyses of urinary mutagenicity and thioether excretion showed **no** sign of exposure to genotoxic compounds among the occupationally exposed workers or among the subjects in the experimental study.

Key ***terms:*** engine exhaust. genotoxicity, mutagenicity, pulmonary function, thioethers.

e main emission products arising from the combustion of fuels in engines are water and carbon dioxide. Other components of vehicle exhaust are nitrogen and oxygen (in diesel exhaust), soot (mostly in diesel exhaust), a large number of hydrocarbons, and derivatives of hydrocarbons with oxygen and nitrogen, along with carbon monoxide, oxides of nitrogen, and sulfur dioxide (in diesel exhaust). Their Concentrations vary depending on many factors, eg, fuel composition, lubricant composition, engine design, operating temperature, load, degree of engine wear, fuel supply, condition of the system.

Occupations with the highest exposure to engine exhaust include mining; stevedoring; work around loading decks and quays: warehouse work with forklift trucks; loading motor vehicles onto car ferries; and work in bus garages, buildings at airports, parking garages, car-testing stations, and automobile repair shops.

The purpose of the present study was to investigate the acute effects of exposure to engine emissions on the respiratory tract. Furthermore, the mutagenicity method was applied to urine to test for exposures to the complex chemical mixtures contained in engine exhaust, since several earlier studies have shown that components in engine exhaust, especially the particulate fraction, are highly mutagenic in experimental systems **(28, 29).** A review of the literature relevant to this investigation has already been published **(32).**

Subjects and methods

Several workplaces producing comparatively heavy exposure. to diesel exhaust in particular, were chosen for the investigation. (See tables 1 and *2.)* Occupational hygiene measurements were carried out at these workplaces, along with measurements of pulmonary function and genotoxic exposure. In addition, a small investigation with volunteers exposed to dilute engine emission was carried out in which the same occupational hygiene, medical, and toxicologic measurements were used as at the workplaces.

Workplaces, job descriptions and measurement srraregies

Bus garage. In March—April a bus garage was investigated in which there were large and small diesel-powered vehicles and gasoline-driven buses used for transporting disabled persons. The work performed there, in addition to storage and engine warm-up, included refueling, washing and repairs. In the morning, afternoon, and evening elevated concentrations, in particular of diesel exhaust, accumulated in the garage bays when most buses left for or returned from assignments. The occupations represented were marshaler (2 workers), cleaner (1 worker), foreman (2 workers),

[1] The Royal Institute of Technology. Stockholm, Sweden.
[2] Department of Occupational Medicine, Karolinska Hospital, Stockholm. Sweden.
National Institute of Occupational Health. Solna, Sweden.
[4] Department of Clinical Physiology. Huddinge Hospital, ddinge, Sueden.
[5] ıtitute of Occupational Health, Helsinki, Finland.

Reprint requests to: Dr R Alexandersson. Department of Occupational Medicine, Karolinska Hospital, S-104 01 Stockholm, Sweden.

Table 1. Characterization of the workers (men only) exposed to mixed exhaust (gasoline and diesel fumes) or to primarily diesel exhaust in the workplaces chosen for the tnvestigation.

Workplace	Number of subjects			Age (years)		Height (cm)		Weight (kg)	
	Smokers	Nonsmokers	Total	Mean	SD	Mean	SD	Mean	SD
Mixed exhaust									
Bus garage	5	12	17	32	10.3	180	7.6	80	9.2
Car ferries	15	10	25	36	11.4	177	5.7	76	10.5
Diesel exhaust									
Roll-on roll-off ships									
I	12	11	23[a]	34	7 0	180	7 0	a2	9.4
II	13	11	24[a]	36	6.3	181	7 0	a1	11 0

[a] Ten persons took part on both occasions at the ro-ro ships

Table 2. Chemical characterization of the air samples. obtained with a personal sampling technique. from the workplaces and from the experimental study and the occupational exposure limits of the substances determined. The readings from the ro-ro ships are averages for a whole workshift. Other results represent the exposure measured for part of a day. In the latter instances the measurements were carried out during the course of work entailing exposure

	Range of the substances determined											
	Acetaldehyde (mg/m³)	Benzo-(a)pyrene (ng/m³)	Benzene (mg/m³)	Dust (mg/m³)	Formaldehyde (mg/m³)	Carbon monoxide (mg/m³)	Nitrogen dioxide (mg/m³)	Nitrous oxide (mg/m³)	Nitrous acid (mg/m³)	Sulfur dioxide (mg/m³)	Total carbohydrates (mg/m³)	Toluene (mg/m³)
Bus garage	028-15	<10	≤0.2	0.46[b]	004-08	17-24	02-11	03-10		<1.8		<0.2
Car ferry (2 h run)	049-15	<10	≤0.2		0.03-0.31	13-100	<0.6	006		<1.8		<0.2
Car ferry (20-min run)	102-21	≤30		01-03	01-03	5-190	0.2-0.8	02-10			<190	
Roll-on roll-off ships												
I	<1.6		a03	0.13-0.59	a003	14-27	015-10	0.1-0.8	0002-002		12-14	<0.8
II[c]				03-10	01-05	11-51	006-23	002-07				
Experimental study	03	OM	02	06	005	5.3	39	56				13
Occupational exposure limits[d]												
Ceiling				1	5		10					
Short-time value	90	30 000	30			120		60		13		400
Time-weighted average limit	45	5 000	16	5[a]		40	4	30		5		300

[a] Respirable dust
[b] Single measurement.
[c] Second study occasion.
[d] Taken from reference 27

and mechanic (12 workers). Those responsible for the workplace had rated the ventilation as not fully satisfactory.

Car ferry. In June—July two types of car ferries were studied, one serving on a 2-h route and the other on a 20-min route. The job of the upper deck crew on the former was to direct vehicles to and from their parking places on the car deck. Loading and unloading averaged 20 min. In the intervals between the loading and unloading, the deck crew performed other tasks. The first and second mates had duties on the bridge during crossings.

On the second type of ferry, work consisted of directing vehicles to the right place as they came aboard (so the maximum number of cars and lorries could be accommodated on the car deck) and assisting in the unloading of vehicles from the deck after the ferry had docked. Their work also included mooring the ferry. The mate's job was to lower the gangway after docking, check the tickets of passengers traveling in vehicles, and supervise operations while vehicles were driven on and off the car deck. Samples were only taken during the loading and unloading of vehicles.

Roll-on roll-off ships. The investigations aboard the roll-on roll-off (ro-ro) ships were carried out in January—February and in June and covered lower deck crew whose exposure to exhaust gas was judged to be the heaviest. During loading, cargo was moved from the quay onto the ship with large diesel-powered trucks. Once the cargo was on deck, smaller trucks took over and carried out the final stowage. The work of each truck driver was directed by one or two men on the deck. A supervisor was in charge of one or more decks. The truck drivers drove their trucks aboard ship and also spent a short time on deck. Drivers of the big trucks transferred cargo between the quay and the ships. They remained in their cabs the whole workday. One group, made up in part of supervisors, placed padding, etc, under cargo to keep it steady. The supervisors directed the loading and unloading of cargo.

Experiments in the exposure chamber. Six workers were placed in an exposure chamber (interior dimensions 4.9 x 2.9 x 2.5 m) into which exhaust gas, diluted with air, from a diesel-powered vehicle was piped. The dilution was adjusted so that the nitrogen dioxide in the chamber amounted to about 2 ppm.

The test vehicle was a 1980 Volvo 244D automobile with a manual, four-speed transmission. The vehicle was powered by a six-cylinder, precombustion chamber diesel engine (2 383 cm^3). The compression was 23:1, and the engine output 60 kW. During the experiment the vehicle was run at a constant speed, equivalent to 60 k/h in third gear. This rate produced an engine speed of about 2 580 revolutions/min. The engine load was calculated as 18 kW (maximum engine output about 35 kW at the indicated engine speed). This engine load is about four to five times higher than the load daring driving on a dry, level road. The engine was kept running for 3 h and 40 min without interruption.

Hygienic measurements and chemical analysis

Total dust and respirable dust were collected on cellulose acetate filters in personal and stationary sampling equipment. The sampling of formaldehyde and acetaldehyde was performed with personal sampling equipment with chemosorption, and the samples were analyzed with high-performance liquid chromatography (2, 3). Hydrocarbons were collected in an aluminum laminate bag and then analyzed with a nonspecific, direct-reading photoionization detector (HNU PI 101). Some samples were taken with a carbon tube or Tenax® tube and then analyzed with gas chromatography. Hydrocarbons were sampled with personal equipment only.

Both the personal and the stationary sampling was carried out for mass spectrometry determinations of benzo(a)pyrene and total polycyclic aromatic hydrocarbons (PAH). The particles were collected on glass fiber filters, whereas gas samples were collected by two-stage chilling of the samples with water and dry ice and ethanol. The samples were analyzed with a mass spectrometer employing multiple ion detection (15).

Air was collected in an aluminum laminate bag and analyzed for carbon monoxide with a direct-reading instrument containing an electrochemical cell (Interscan 1144) and for nitric oxide and nitrogen dioxide with a direct-reading instrument (Monitor Labs 8440) according to the chemiluminescence principle. Sulfur dioxide was determined with a direct-reading instrument (Interscan) according to an electrochemical measuring principle. Nitrous acid and nitric acid were collected in glass tubes coated with sodium hydroxide. Subsequent analysis was carried out with ion-exchange chromatography (17).

Acetone extracts of the particulate component of three air samples from the exposure chamber experiment were anaiyzed for mutagenicity in the Ames test with two bacterial strains (*Salmonella typhimurium,* TA 98 and TA 100), both with and without metabolic activation (1).

Biological methods

Determination of urinary muiagenicity and urinary thioether excretion. Workers occupationally exposed to engine exhausts were asked to provide urine specimens (on a random basis) immediately before going to work (unexposed sample) and again at the end of or immediately after work (exposed sample). The urine specimens were immediately frozen and stored at −20°C for several months.

The subjects in the experimental exposure supplied urine specimens before and at several times after the exposure (table 3). Since it has been found (5) that diet may have a powerful effect on the urinary excretion of thioechers and it can be assumed that certain drugs are capable of influencing thioether formation, dietary intake was standardized during the experimental day. In addition the subjects refrained from taking any medication. They carefully avoided certain vegetables (the cruciferae family such as cabbage and horseradish) which contain comparatively large amounts of thiocyanate (5, 37). The urine specimens were immediately frozen and stored at −20°C for several months.

Table 3. Thioether concentration and mutagenic activity in the urine of six workers before and after the experimental exposure to diesel exhaust gases (SE = standard error of the mean)

	Thioether concentration (mol/mol creatinine)		*Salmonella typhimurium* TA 98				*Escherichia coli* WP2 uvrA	
			+ S-9 mix (revertants mol creatinine)		− S 9 mix (revertants: mol creatinine)		+ S-9 mix (revertants/mol creatinine)	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Before exposure	2 7	0 4	181[a]	106	300	112	78[b]	56
After exposure	2 6	0 3	88	46	380	143	33	19
Four hours after exposure	2 5	0 3	54	24	0		8	5
Eight hours after exposure	2 7	0 3	153	64			18	8
Next morning	2 3	0 2	170	51			9	6

[a] One sample exceeded 600
[b] One sample exceeded 300

Two bacterial strains were used for the determination of urinary mutagenicity, S *typhimurium* TA 98 and *Escherichia coli* WP2 uvrA. The analyses were carried out at the Mutagen Laboratory of the Institute of Occupational Health, Helsinki, using the copolymer XAD-2 (for the determination of the concentrations in the urine specimens) and the fluctuation method (16, 38).

The urinary concentrations of the thioethers (13) were determined by spectrophotometry. using Ellman's reagent after hydrolysis to thiols according to the method described by van Doorn et al (34, 35).

All the exposed persons (see table 1) were examined with the use of spirometry and the single-breath nitrogen-washout technique. The subjects from the car ferries and bus garage were examined on a Monday after a 2-d break from work. Stevedores on the ro-ro ships were examined after a IO-d break from work. All the exposed subjects were examined before they entered the work premises and after the workday. The exhaust concentrations in the air were determined with a personal sampling technique during the workday. On the basis of these results the study was expanded to include a second examination of the stevedores on the ro-ro ships on a later occasion. Prior to the examination, the stevedores were not exposed to exhaust gases for 5 or 6 d. After exposure to emissions for 1 or 2 d, the group was monitored during unexposed work so as to determine the time needed for pulmonary function to recover after deterioration.

Forced expired vital capacirv was recorded with a low-resistance bellows spirometer (Ohio 740). At least two measurements were taken per person. The best result for each variable was chosen, even if the value had to be taken from different determinations. and the volumes were adjusted to conditions of body temperature and pressure saturated with water vapor (BTPS) (19).

The following variables were determined: foried vital capacity (FVC), forced expiratory volume in 1 s ($FEV_{1,0}$), $FEV_{1,0}$% [(100 × $FEV_{1,0}$)/FVC], and maximal midexpiratory flow (MMF).

Reference values for the spirometric variables were taken from Berglund et al (9) and Birath et al (10).

Single-breath nitrogen washout (4) was studied with the use of rhe aforementioned bellows spirometer and a "bag-in-box" unit. The nitrogen concentration was measured with an analyzer operating on the ionization principle (Ohio 720). The gas concentration and volume were documented on an x-y rzcorder (Bryans 26000). At least two measurements were taken at an interval of 7—10 min. The closing volume (CV) was expressed as the percentage of expiratory vital capacity (CV%). The slope of the alceolar plateau (phase III) was expressed as the percentage of nitrogen per liter of exhaled gas. The nitrogen washout data obtained in this manner were compared to reference values from Buist & Ross (11, 12).

Linear regression analyses were performed in intra- and interindividual comparisons between degree of exposure and lung-function effect. The two-tailed Student's t-test was used (30).

Results

Exposure conditions

An overview of the workplaces visited, the subjects, and the measured concentrations of substances can be found in tables 1 and 2.

The carbon monoxide peaks were lower in the bus garage (where diesel-powered vehicles were predominant) than on the ferries. The carbon monoxide concentrations were also low on the ro-ro ships on which only diesel trucks were used. The blood of exposed nonsmokers before and after a workshift displayed no increase in carboxyhemoglobin. The concentrations of nitrogen oxides were not higher than at the other workplaces where both gasoline- and diesel-powered vehicles were used.

At the concentrations tested, none of the three extracts from the filter samples was toxic to either strain of S *typhimurium* (TA98 or TA 100), but extracts were mutagenic and produced a linear dose-response relationship. The maximal number of observed revertants per cubic meter of air sample was 643 for strain TA 100-S9. ,Mutagenicity was observed both with and without a rat-liver metabolic system (S-9 mix), but the response was slightly lower in both strains when metabolic activation was used.

Urinary mutagenicity and urinary excretion of thioethers

Occupationally exposed workers. Comparisons between the urinary mutagenicity of samples from an exposed and an unexposed period failed to disclose any significant differences between the number of revertants per mole of creatinine, ie, either in the occupationally exposed group as a whole or after the group had been divided into smokers and nonsmokers. A few samples displayed values that were barely above the limits regarded as mutagenic (>600 for *S typhimurium* and >300 for *E coli)* (16). All but one of these urine specimens had been submitted by smokers. For the mutagenicity of the *S typhimurium* strain TA 98, the mean value for the smokers was higher than that of the nonsmokers [mean 231 (SE 58) and 197 (SE 54) revertants/mol of creatinine. respectively].

No significant differences in thioether excretion were found between the samples from the exposed and unexposed periods, ie, either in the occupationally exposed group as a whole or after the group had been divided into smokers and nonsmokers [5.8 (SE 0.5) and 5.5 (SE 0.5) mmol/mol, respectively]. If, on the other hand, all the samples from the smokers are compared to all the samples from the nonsmokers, the value of the smokers is significantly higher than that of the

nonsmokers (7.2(SE 0.6) and 4.7 (SE 0.4) mmol/mol, respectively, P = 0.001.]

Experimental exposure. Neither the thioether findings nor any of the values obtained in the tests for urinary mutagenicity were increased after the experimental exposure to the diesel exhaust-air mixture. (See table 3.)

Pulmonary function studies

For each person, a comparison was made with the reference material on a Monday before work and after a break from work lasting at least 2 d (table 4). The exposed group displayed an average reduction of 0.33 l in FVC ($P < 0.001$) and of 0.23 l in $FEV_{1.0}$ ($P < 0.005$). There were no differences between the smokers and nonsmokers. There were no corresponding significant changes in the MMF, CV%, or phase III variables. As a further check for a possible correlation between exhaust exposure and pulmonary function, various linear regression analyses were used, but they failed to disclose any significant correlations.

The pulmonary function of all the exposed subwas studied before and after a workday. The mean exposure on this day was as follows: nitric oxide 0.6 mg/m³, nitrogen dioxide 0.54 mg/m³, carbon monoxide 1.1 mg/m³, and formaldehyde 0.15 mg/m³. Significant impairment in pulmonary function was found (table 4). The FVC declined by an average of 0.15 l and the $FEV_{1.0}$ by a corresponding value of 0.11 l. No changes were found in the MMF, the CV%, or the alveolar plateau gradient (phase III). There was no significant difference between the smokers and nonsmokers in pulmonary function on Monday before work.

The presence of any correlation between the exposure to various investigated Components in exhaust gas and the investigated pulmonary function variables was studied. However, no correlation was found between the changes in pulmonary function and exposure to nitric oxide, nitrogen dioxide, or formaldehyde in comparison with either peak values or the mean values for the various components in the exhaust gases during one workshift. Nor was any correlation found between the changes in pulmonary function and the carbon monoxide concentration.

The group of stevedores who had only been exposed to diesel emissions on ro-ro ships had a 10-d break from exposure before the medical investigation. There was no difference between the values of this group and the reference values before the start of the workday (table 4). However, pulmonary function did display deterioration during a workshift. The deterioration averaged 0.44 l for FVC and 0.30 l for $FEV_{1.0}$. There was no difference between the smokers and nonsmokers.

A new study was carried our on another group of stevedores (N = 24) to ascertain whether the

Table 4. Spirometric and nitrogen wash-out data for the exposed subjects (according to type of exposure) on a Monday before work and after periods of 2. 5. 10 and 13 days of no exposure and after 3 days of exposure. Reference values were matched with regard to sex. age and height (8. 10, 11) (FVC = forced vital capacity, $FEV_{1.0}$ = forced expiratory volume in 1 s. FEV% = (100 x $FEV_{1.0}$)/FVC, MMF = maximal midexpiratory flow CV% = closing volume expressed as the percentage of expiratory vital capacity, Phase III = slope of the alveolar plateau, N_2 = nitrogen)

	Number of workers	FVC (l)		$FEV_{1.0}$ (l)		FEV%		MMF (l/s)		CV%		Phase III (%N_2/l)	
		Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE
All exhaust exposure													
Reference value	.	5.66	0.06	4.47	0.06	78.8	0.4	4.32	0.06	12.2	0.5	1.04	0.01
			↑		↑		↑						
		P<0.0001		P = 0.005		P = 0.005							
			I		I		I						
Monday before work	65	5.32	011	4.24	010	79.7	0.9	4.42	0.16	12.9	0.8	1.13	0.07
Mixed exhaust exposure	42												
Reference value		5.62	0.07	4.44	0.08	78.7	0.06	4.29	0.08	11.8	0.8	1.02	0.02
After 2 d of no exposure		5.17**	014	4.10*	0.11	807	0.18	4.30	0.18	12.5	1.1	1.00	0.08
Change during a shift		+0.01		0.00		-0.1		−0.10	.	+0.7	.	−0.12	.
Diesel exhaust exposure													
Reference value		5.72	0.18	4.53	0.10	79.13	0.6	4.38	0.00	12.2	0.7	1.04	0.02
After 10 d of no exposure[a]	23	5.62	0 16	4.50	0.17	79.8	1.4	4.65	0.30	13.2	1.3	1.27	1.22
Change during a Shift after 10 d of no exposure		− 044*		− 030**		+ 1.0		− 033		0 10		+ 0 12	
Change during a shift after 5 d of no exposure[b]	24	− 016*		+0 02		+ 2 5*		+ 0.23		0.00		000	
Change from the values measured after the shift following 5 d of no exposure after 3 d of recovery (no exposure)	.	+0.24**	.	+0.13	.	−0.8*	.	+0.04	.	0.00	.	0.00	.

[a] Study occasion 1.
[b] Study occasion 2 (10 of these subjects took part in both investigations)
* $P \leq 0.01$, ** $P \leq 0.001$ (Student's two-sided t-test).

"acute" deterioration in pulmonary function found in the stevedores during one workshift was reproducible and, if so, how long any normalization would take. On this occasion exposure conditions were about the same as in the first investigation series (table 2). In this case, the break in exposure prior to the investigation was 5 to 6 d. As in the first investigation, no significantly impaired pulmonary function was found before the workshift. But acute deterioration was recorded for FVC (which averaged 0.16 l) during one workday. This decline was accompanied by an increase in FEV%. As table 4 shows, this decline in pulmonary function normalized after a 3-d break from exposure.

Ferry and garage personnel exposed to both gasoline and diesel exhaust had a 2-d break from exposure before the measurement of pulmonary function began before work on Monday. A decline in pulmonary function was found in this group (0.15l for FVC and 0.34 l for $FEV_{1.0}$) in comparison to the reference values (table 4). No additional deterioration was found in the pulmonary function during a workshift.

Discussion

Exposure conditions

In the experimental study the nitrogen oxide concentrations were generally higher than any peak concentration found at the workplaces at which only diesel engines were used (table 2). The concentrations of carbon monoxide were comparable with the peak concentrations found at the workplaces using diesel engines.

The total concentration of particulate-bound and gaseous PAH was 638 ng/^{3} in the exposure chamber.

The low molecular-weight compounds (methyl phenanthrenes, anthracenes, and phenanthrene) accounted for 76 % of the total PAH content.

Genotoxicity

The particulate extract of the air samples from the exposure chamber displayed clear genotoxicity with a linear dose-response in the Ames test. Both test strains used, ie, *S typhimurium* TA 98 and TA 100, yielded a higher response when no exogenous metabolic system was used. This finding points to the presence of direct-acting mutagenic substances [eg, nitroarenes such as I-nitropyrene (28, 29)] characteristically found in diesel exhaust.

The ambient air samples taken from the exposure chamber during the voluntary exposure experiment and several previous studies performed on engine exhaust have all shown these emissions to be mutagenic, irrespective of the fuel type (14, 15, 22, 23, *26,* 28, **29).** However no mutagens were found in the urine specimens of our subjects occupationally or experimentally exposed to vehicle emissions.

The negative results of the mutagenicity analysis of the urine do not preclude the absorption of mutagenic substances from engine exhaust. Several earlier studies (31, 38) have shown the test strain *S typhimurium* TA 98, with metabolic activation (S-9 mix) to be sensitive to tobacco smoke. The smokers in the present study also displayed greater mutagenic activity than the nonsmokers.

The excretion of thioethers in urine was similar before and after exposure to engine exhaust. On the other hand, the values of the smokers were significantly higher ($P = 0.001$) than those of the nonsmokers. This finding agrees with results reported earlier (5, 33). The individual results for the occupationally exposed subjects (some values exceeding 10 mmol/mol of creatinine in samples taken before exposure but declining in those taken after exposure) indicate that factors unrelated to the work environment, ie, probably dietary factors (5, 37) or possibly medication, had affected the results obtained for certain individuals in this group. The lower thioether levels and the lower variation in the values obtained in the experimental study, compared to the values of the occupationally exposed persons, might be due to the diet standardization smployed in the experimental study.

The negative results of the urinary assays do not preclude the possibility that exhaust exposures may cause local mutagenic effects in, eg, lungs and airways, the regional lymph system, or the gastrointestinal tract, after exhaust particles are swallowed. Compounds excreted in bile were not detectable with the urinary assay methods used.

Respiratory effects

Exposure to exhaust fumes appeared to impair pulmonary function. These effects were found on a Monday morning, before work began, after cessation of exposure for at least 2 d and were accentuated during a workday with exposure to exhaust fumes.

The subjects comprised stevedores exposed only to exhaust from diesel-powered trucks and ferry and garage personnel exposed to both diesel and gasoline exhaust fumes. The stevedores had had a 10-d break from exposure before the investigation started and displayed normal pulmonary function on the Monday before going to work as compared with the reference material. However, both their FVC and $FEV_{1.0}$ values deteriorated during a workday with exposure to exhaust. Similar but less pronounced effects were found in a second, subsequent study. Pulmonary function returned to normal after 3 d without occupational exposure to exhaust fumes.

The recovery to normal function after three exposure-free days may explain why the stevedore group did not display poorer pulmonary function than the reference group before exposure. This finding is consistent with the fact that no chronic lung effects solely attributable to exhaust gases and particles have been discernible in various cross-sectional studies of persons exposed to diesel exhaust (*6,* 7, 8, 18, **24).**

After a 2-d break in exposure, the ferry and garage personnel exposed to mixed exhausts displayed a deterioration in pulmonary function of the same nature and magnitude as the stevedores after work. The functional deterioration showed no progression after one workday. Thus the same degree of dysfunction was observed in both the stevedores exposed solely to diesel exhaust and in the ferry and garage workers exposed to mixed exhaust emissions. These findings suggest that subjects who display functional deterioration after previous exposure to exhaust gases may not display any additional deterioration after renewed acute exposure and that subjects who have time to recover during a break from exposure may display acute deterioration. However, the interpretation of these findings is complicated by the differences in the exposure of the stevedores and that of the exposure of ferry and garage personnel and by the fact that no dose-related correlation was found between any irritating substances in the exhaust gases (nitric oxide, nitrogen dioxide, and formaldehyde) and an effect on pulmonary function. Nor was any correlation found with the carbon-monoxide exposure, investigated as a possible indicator of exposure to all exhaust compounds.

decline of up to 0.4 l in the FVC during a work- orresponded to a deviation of less than 10 % from prework values. Smaller differences were found for the other variables. Presumably, these changes do not produce any discernible impairment in physical work capacity during moderate physical exertion, but they are a disturbing finding in a cross-sectional study since their prognostic implications are unknown.

The occupational exhaust exposure levels measured are among the highest in Sweden, and they appear to affect pulmonary function during a workday but cause relatively few subjective symptoms. This decline, which is reproducible in repeated measurements, normalizes after a few days without exposure to exhaust emissions. The changes are relatively slight and need not have any significant effect on physical work capacity. Because the changes are small, the nature of the dysfunction is difficult to assess. The decrease in FVC and $FEV_{1.0}$, but not in FEV% or MMF, like the virtually normal. single-breath nitrogen washout findings. may suggest a restrictive rather than an obstructive dysfunction, or a combination of borh.

Possible indicators of exhaust exposure

In group studies, formaldehyde at concentrations of 0.40 mg/m³ in the air has been shown to be capable of affecting pulmonary function, ie, causing mainly obstruction. Formaldehyde alone, at concentrations down to 0.05 ppm (0.06 mg/m³), irritates the nose, e and throat of sensitive people and produces di nfort at somewhat lower concentrations (25. 39). It is possible that aldehydes could explain some of the airway symptoms found in the present study. The levels were relatively low, and a higher incidence of eye. nose, and throat symptoms might have been expected.

High concentrations of nitrogen dioxide are known to cause acute effects on the **lungs (20).** Nitrogen dioxide produced increased respiratory resistance after a 15-min exposure in the 1.6—2.0 ppm (3.6—2.9 mg/m³) concentration range. Lower concentrations produce nasal irritation and laryngitic symptoms but no changes in lung physiology **(21).**

It should be pointed out that the alveolar concentration of several of the gases may be even higher than concentrations in the breathing zone, since additional input of injurious agents could conceivably *oc*cur by adsorption onto the soot particles present in exhaust emissions. The particulate phase in diesel exhaust resembles carbon black, since the particulate matter consists of more than 85 % elementary carbon in the form of nearly spherical particles formed in the partial combustion of hydrocarbons. Diesel particles and carbon black particles are almost always respirable **(36).** A calculation assuming adsorption of a monomolecular layer of nitrogen dioxide on a diesel aerosol indicates that the surface area of aerosol particles is sufficient to permit the particle-bonded nitrogen dioxide to constitute a substantial proportion of the total nitrogen dioxide concentration.

In summary published data on the effects of the substances studied at different concentrations and on measured concentrations of these substances in occupational exhaust exposure do not rule out the possibility that nitrogen dioxide and formaldehyde, or both, may give rise to effects on lung and mucous membranes at the concentrations found in practice.

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Diesel Asthma

Reactive Airways Disease following Overexposure to Locomotive Exhaust

John F. Wade III, MD
Lee S. Newman, MD

While some of the gaseous and paniculate components of diesel exhaust can cause pulmonary irritation and bronchial hyperreactivity, diesel exhaust exposure has not been shown to cause asthma Three railroad workers developed asthma following excessive exposure to locomotive emissions while riding immediately behind the lead engines of caboose-less trains. Asthma diagnosis was based on symptoms. pulmonary function tests. and measurement of airways hyperreactivity to methacholine or exercise. One individual's peak expiratory flow rates fell in a work-related pattern when riding immediately behind the lead diesel engine. None had a previous history of asthma or other respiratory disease and none were current smokers. All three developed persistent asthma. In two cases. physiologic abnormalities suggesting reversible restriction were observed. This is the first report implicating diesel exhaust as a cause of reactive ainways disease.

Diesel-powered equipment has long been used in industrial applications. resulting in diesel exhaust exposure for nilroad workers. miners. bridge and tunnel workers. truck driven and bus maintenance garage workers. among others. The National Institute for Occupational Safety and Health (NIOSH) estimated in 1983 that between 1 and 1.5 million workers were exposed to diesel emissions.[1] Mounting concerns about potential health effects of diesel exhaust have led to numerous studies of the carcinogenicity and respirator), consequences of chronic exposure.[2-11] Much less is known about the acute respiratory effects of high level exposure to diesel exhaust.[14,15]

We have identified three railroad workers who deveioped new asthma from diesel exhaust inhalation. Overexposure to diesel combustion products occurred in these individuals after two railroad companies had discontinued the use of cabooses on freight trains. One of the principle functions of the caboose is to shuttle second railroad crews for future runs, a practice called "deadheading." As a result of caboose-less trains. deadheading crews have to ride in locomotive units trailing immediately behind the lead locomotive. In each of our patients, diesel exhaust from the lead unit entered the second unit, inducing acute or subacute onset of asthma.

Report of Cases

case 1

A 40-year-old white man developed persistent dyspnea beginning acutely during a 5-hour exposure to diesel locomotive exhaust in April 1987.

From the Pulmonary Division and Occupational/Environmental Medicine Division. National Jewish Center for Immunology and Respiratory Medicine (Dr Newman), and Division of Pulmonary Sciences. Department of Medicine (Drs Wade and Newman) and Department of Preventive Medicine and Biometrics, University of Colorado School of Medicine (Dr Newman), Denver, Colo.

Address correspondence to: Dr Newman. National Jewish Center for Immunology and Respiratory Medicine. 1400 Jackson Street, Room D-104, Denver, CO 50106.

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The patient. employed for 14 years as a railroad conductor and brakeman. had been riding in the second locomotive unit trailing immediately behind the lead locomotive. The lead engine's diesel exhaust blew almost continually into the cab in which the patient was riding, producing acute symptoms of shortness of breath, burning chest pain with inspiration. and burning eyes. The patient reported no cough. fever, or hemoptysis and had no intercurrent respiratory infection at the time of exposure. He had no prior history of asthma, allergies. bronchitis, pneumonia, or other respiratory illness. He was a former smoker (17 pack-yean) having quit in 1982.

The patient reponed that he had never experienced work-related respiratory symptoms or previously been overexposed to diesel exhaust until then, noting that deadhead crews did not ride in the second unit of caboose-less trains until approximately 6 months before the onset of his symptoms. He noted that wind direction had contributed to the intensity of his acute exposure.

Upon arrival at the train's destination. the patient was seen at a local emergency room where he was found to be dyspneic, with poor air movement and conjunctival injection. Spirometry was not performed. but arterial blood gas analysis demonstrated profound hypoxemia (pO_2 35 mm Hg, O_2 saturation 69%. pCO_2 34 mm Hg, pH 7.45). He was treated as an inpatient with corticosteroids and supplemental oxygen, leading to gradual improvement in symptoms and oxygenation. Because of penistent dyspnea. the patient saw a pulmonologist 3 weeks later, Reactive airways disease was diagnosed based on the demonstration of airflow limitation and exercise-induced bronchospasm. Theophylline and inhaled beta-agonists produced subjective improvement, and the patient returned to work. Despite medication, a second, similar exposure to excessive diesel locomotive exhaust 2 months later precipitated another severe asthma attack. Since that time. the patient's respiratory symptoms have been precipitated by nonspecific triggers such as exercise, cold air, and fumes. .

Fourteen months following the initial accident, the patient was referred to the National Jewish Center for Immunology and Respiratory Medicine. He had continued to experience episodic aggravation of his respiratory symptoms, although they were fairly well controlled with oral theophylline. an inhaled beta-agonist, and inhaled triamcinolone. Past medical and occupational history was noncontributory, except as noted above.. The patient's father and brother had reactive airways disease, and his two sons had seasonal rhinitis. He had no allergies or atopy.

Physical examination revealed scattered expiratory wheezes and slight prolongation of expiratory phase on forced expiration. Chest radiograph was normal, as were radiographs from 1987 and 1988. Pulmonary function tests suggested a mixed restrictive and obstructive disorder. with improvement in airflow limitation following bronchodilator. Diffusing capacity was normal (see Table 1). Pulmonary mechanics showed the patient to have normal elastic recoil, suggesting that the mildly decreased lung volumes were related to *the* patient's weight rather than to coexisting interstitial lung disease.

TABLE 1
Pulmonary Function Tests in Diesel Asthma Cases'

	Case 1		Case 2		Case 3			
					Initial		Follow-up§	
	Pre†	Post‡	Pre	Post	Pre	Post	Pre	Post
FEV_1	2.57 (59)	3.81 (91)	1.33 (38)	2.54 (73)	3.16 (79)	3.23 (81)	2.65 (65)	3.19 (81)
FVC	3.31 (61)	4.75 (85)	2.17 (45)	3.86 (80)	3.55 (66)	3.62 (67)	3.69 (69)	3.73 (70)
FEV_1/FVC (%)	78	80	61	66	89	89	71	85
Total lung capacity	4.87 (67)	6.56 (90)	6.86 (107)	6.61 (103)	6.03 (86)	5.47 (78)	5.39 (77)	5.27 (75)
Thoracic gas volume	2.92 (72)	3.49 (86)	3.98 (109)	3.80 (103)	2.10 (53)	2.05 (52)	2.62 (66)	2.31 (58)
Residual volume	1.78 (84)	2.08 (98)	2.81 (135)	2.47 (118)	1.54 (95)	1.24 (76)	1.65 (99)	1.17 (70)
DL_{co}‖	106		104		157		143	
Airways hyperreactivity	Positive##		0.2 mg/dL**		6.2 mg/dL**			

* Expressed in liters, with percent predicted in parentheses. unless otherwise indicated.
† Measured prior to administration of inhaled bronchodilator.
‡ Measured after administration of inhaled bronchodilator.
§ Follow-up 3 years after initial exposure. 1 year after initial tests.
‖ Single breath-diffusing capacity for *carbon* monoxide (% predicted).
Positive exercise-induced bronchospasm study.
** Provocative concentration of methacholine producing 20% or greater drop in FEV_1 (PC_{20} FEV_1) (normal > 8 mg/dL).
Note. — FEV_1. forced expiratory volume in 1 second: FVC, forced vital capacity; DL_{co}, diffusing lung capacity for carbon monoxide.

Case 2

A 50-year-old white man nonsmoker had been in good health, without prior history of lung disease or lower respiratory tract symptoms until one evening in January 1987. The patient. employed as a railroad conductor and brakeman for 25 years, was riding in a diesel exhaust-filled second locomotive unit for several hours when he noted the acute onset of shortness of breath. dry cough. chest tightness and wheezing. Although he closed the windows of the cab, diesel exhaust emanating from the lead locomotive entered through the seams in the doors and through the electrical panels, filling the cab with the most intense exposure he had ever experienced. He recalled previous more moderate diesel exhaust exposures. beginning when his employer had removed the cabooses from the trains several months earlier.

When the train's run was completed. he was admitted to a local hospital. He was found to have bilateral rhonchi and hypoxemia (pO_2 53 mm Hg, pCO_2 31 mm Hg, pH 7.49). The patient improved with theophylline, inhaled beta-agonists and corticosteroids, but subjectively never returned to his pre-January 1987 baseline. Upon returning to work he repeatedly experienced aggravation of his symptoms when exposed to diesel exhaust. even on shorter trips of less intense diesel exhaust exposure, as illustrated by his peak expiratory flow rates (see Fig. 1). He gradually required a more intensive medical regimen. including *two* courses of systemic corticosteroids.

Two years after the original incident the patient was referred to National Jewish Center for evaluation of persistent respiratory symptoms. He continued to have episodic aggravation of respiratory symptoms, despite oral theophylline. inhaled and oral beta-agonists, beclomethasone nasal spray, oral antihistamines. and a recent course of oral corticosteroids. Nonspecific triggers included cooking smoke. cigarette smoke. and exenion. Past medical history was notable for preexisting seasonal rhinitis controlled with antihistamines and prior nasal polypectomy. He had no history of aspirin sensitivity, previous asthma, or other lung disease. Family, occupational, and environmental histories were noncontributory except as noted above. Medical records indicated peripheral eosinophilia ranging from 6% to 15%, present since 1987.

Physical examination revealed a Cushingoid male in moderate respiratory distress. He had diffuse, wheezing snd boggy, erythematous nasal mucosa without polyps. White cell count was 5.3 x 10^9/L with 9% eosinophils. Serum immunoglobulin E was normal. Chest radiograph demonstrated hyperinflation and peribronchial thickening, the latter finding having been present at the time of initial presentation. Pulmonary function tests showed airflow limitation with significant improvement following bronchodilator and nonspecific airways hyperresponsiveness. Diffusing capacity was normal (see Table 1).

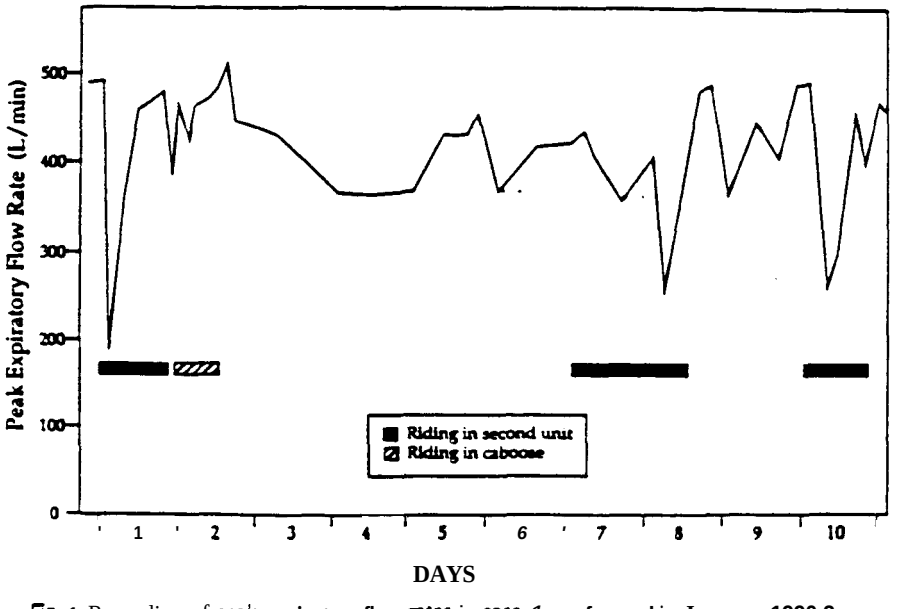

Fig. 1 Recording of peak expiratory flow rates in case 1. performed in January 1990.2 years after initial onset of asthma. Bars indicate all workshifts. Note the fall in peak flow occurring shortly after the start of three shifts in which he rode in the train's second unit *(solid bars)*. The patient's peak flows did not drop during one work period in which he rode in the train's caboose (hatched bar).

Case 3

A 44-year-old Hispanic man never-smoker developed the subacute onset of episodic dyspnea on exenion, cough. wheezing, and nasal congestion beginning in late 1986. He reported a temporal association of these symptoms with high diesel exhaust exposures. usually within the first few hours of exposure. The patient. employed by the nilroad for 23 years, worked for the past 11 years as a brakeman. He had never experienced respiratory problems until he began riding in second locomotive units on deadhead runs where he described being exposed to significantly more diesel exhaust than in previous years.

The patient sought medical attention in early 1987 because of increased frequency of these episodic respiratory symptoms. A graded treadmill test produced bronchospasm and cough. Despite treatment with inhaled beta-agonists. triamcinolone, several courses of oral corticosteroids, and removal from exposure. he remained symptomatic. Two years after symptom onset. he was referred to National Jewish Center with persistent, slowly progressive respiratory symptoms. Past medical history was notable for von Willebrand's disease, rhinoplasty for a nasal bone deformity, and cholecystectomy. He had no allergies or atopy. Except for diesel exhaust. he recalled no significant past occupa-

tional or environmental exposures.

Physical examination revealed a moderately obese male. The mucosa of the anterior nares was mildly hyperemic. Oropharynx was normal. Lungs were clear without wheezes, rales or rhonchi. Chest radiograph was normal. Initial pulmonary tinction tests suggested a possible restrictive process without airflow obstruction. Diffusing capacity was elevated (Table 1). Pulmonary mechanics revealed normal elastic recoil of the lungs suggesting that his reduced lung volumes were probably due to obesity. We observed mild airways hyperreactivity to methacholine (Table 1). A graded exercise treadmill test induced bronchospasm and cough. as had occurred in 1987. Accurate post-exercise spirometry was not obtainable due to severe cough. On a follow-up visit 3 *years* after onset of symptoms. he remained symptomatic, noting nonspecific triggers such as *grasses* and exercise in cold or hot weather. Repeat pulmonary function tests showed airflow limitation with a significant bronchodilator response (Table 1).

Comments

Although millions of Americans are occupationally or environmentally exposed to diesel exhaust,[5] this is the first time that diesel exhaust has been reported as a cause of asthma. Several lines of evidence support the conclusion that railroad locomotive diesel exhaust exposure induced asthma in these three individuals *(see* Tables 1 and 2): 1) ail three demonstrated airways hyperreactivity, air flow limitation. and reversibility with bronchodilators. consistent with asthma: 2) none had preexisting asthma or Significant respiratory tract disease, based on our review of all past medical records and medical history; 3) each developed symptoms within the first hours of the overexposure to diesel exhaust: 4) in two cases. a single unusually high exposure led to immediate fis time hospitalization and treatment for asthma: *5)* all three experienced exacerbation of symptoms upon reexposure to locomotive diesel exhaust: and *6)* in one individual. a work-related pattern of airflow limitation was documented by peak expiratory flow rate records. These three workers were employed by two different railroads and were unaware of the othen or of their shared diagnosis and etiology at the time of presentation.

Asthma resulting from overexposure to diesel exhaust may occur more frequently than is recognized. Kahn and co-workers recently reponed 13 cases of acute overexposure to diesel exhaust among railroad workers, two of whom complained of chest tightness and wheezing.[11] The symptoms were suggestive of asthma however. no other clinical or physiologic data were provided in that report.

While a number of population-based studies have examined the respiratory effects of diesel exhaust. none has tested for the development of asthma. However, data from several of these studies suggest that asthma could be occurring. In a large study of diesel bus garage workers. Gamble and co-workers found a significant increase in eye irritation. labored breathing, chest tightness. and wheezing in a subgroup of "high-exposure" individuals although these symptoms were not associated with pulmonary function decrements at any measured level of nitrogen dioxide or diesel exhaust particulate concentration.[7] These same investigators showed that bus garage workers with longer job tenure had a higher prevalence of dyspnea. wheezing, cough and phlegm. and accelerated decline in spirometry compared *to* nonexposed control subjects.[11] In another stud). diesel-exposed salt miners experienced a small but significant drop in FEV_1 across the workshift. correlating with increasing nitrogen dioxide levels.[11] In a later study of salt miners. this same group found that phlegm production was associated with increasing diesel exhaust exposure. but cough. dyspnea, and pulmonary function were not significantly different between the exposed and unexposed subjects.[11] In contrast, other researchers have found no effect of diesel exposure on respiratory symptoms or spirometry.[6–8,10,15] Many of the cross-sectional studies may be biased by a healthy-worker effect with asthmatics less likely to stay in the work force. Taken in composite. these epidemiologic studies present contradictory results. probably due in part to the heterogeneity of diesel exhaust.[11] variability in exposure conditions[11] and population and methodologic differences. None has anempted to measure outcome variables pertinent to the recognition of asthma. such as airways hyperreactivity or reversibility of airflow limitation.

We do not know the levels of exposure to combustion products that produced disease in our patients. as is

TABLE 2
Demographics and Clinical Features of Disease in Diesel Asthma Cases

	Case 1	Case 2	Case 3
Age (years)	40	50	44
Smoking history	Former	Never	Never
Pnor respiratory tract disease	None	Seasonal rhinitis, nasal polyps	None
Pattern of disease onset	Acute	Acute	Subacute
Chest radiograph	Normal	Hyperinflation, peribronchial thickening	Normal
Subsequent nonspeafic triggers*	+	+	+
Airways hyperreactivity testing†	+	+	+
Airflow limitanon and bronchodilator response‡	+	+	+
Peak expiratory flow records	Not done	Work-related pattern	Not done
Duration of symptoms since onset (months)	14	24	36

* Development of asthma symptoms resulting from nonspecific exposures, since time of diesel exposure.

† By exeruse or methacholine challenge testing (see Table 1).

‡ Based on FEV, pre- and post-albuterol (see Table 1).

commonly the case in occupational asthma Nor can we know, in retrospect. which component parts of diesel emissions may have been causative. Diesel exhaust varies considerably, containing complex, respirable gases and particulates to which a variety of organic compounds adsorb.[18] Due to this complexity and variability, we did not perform specific bonrchoprovocation testing to diesel exhaust in our patients. Many of the component parts of diesel exhaust can cause asthma and/or act as pulmonary irritants. Potentially important constitutents include oxides of nitrogen,[19,20] sulfur oxides,[21-26] aldehyde~.'' and carbonaceous particulates.[29-31]

In addition to the potential for these irritants to cause airways hyperreactivity, intense exposures to the oxides of nitrogen and sulfur can result in bronchiolitis obliterans.[26,32-34] Symptoms of dyspnea and cough generally occur several weeks after recovery from exposure. Pulmonary function tests show a restrictive. obstructive. or mixed obstructive/restrictive pattern. Obstructive physiology is typically fixed and unresponsive to bronchodilator, unlike the reversible airways dysfunction in our patients. We can not exclude the possibility of coexistent bronchiolitis obliterans in our cases. as lung biopsy was not performed.

Interestingly, two of our patients exhibited physiology consistent with 'reversible restricrive'' lung disease.[35,36] Spirometry in cases 1 and 3 revealed a normal FEV_1/FVC ratio with reduced lung volumes characteristic of a classic restrictive defect. Bronchodilator treatment, however, produced a dramatic improvement in flow rates and normalization of lung volumes in case 1 and improved flow rates with reduced air trapping (decreased residual volume) in case 3 on follow-up testing. The pathophysiology of reversible restriction is unknown. but may relate to smooth muscle contraction and constriction of distal respiratory bronchioles and alveolar ducts. Constriction of these small terminal airways may preclude the development of hyperinflation typically seen in asthma. We do not know whether reversible restriction is common in diesel exhaust overexposure. however as cases 1 and 3 demonstrate, this disorder would be easily overlooked if evaluation were limited to simple spirometry without bronchodilator testing.

These cases share many similarities with the patients described by Brooks and others as having reactive airways dysfunction syndrome (RADS).[37-44] This term has been used to describe a persistent clinical picture of asthma resulting from a single massive exposure to an irritant gas, fume. vapor, or smoke. However, our patients worked for the nilroad for many years, and presumably had been chronically exposed to lower levels of diesel exhaust prior to their acute overexposures. One patient had a subacute onset of disease without recognizing a single precipitating exposure: however, recurrent. high exposures resulted in persistent symptoms. Occupational asthma can develop through one of several postulated mechanisms.[45] While the RADS-like presentation in our uses is compatible with an irritant mechanism,[44] it is notable that environmental automotive exhaust exposure has been implicated in the development of allergies,[46] and that diesel exhaust paniculate can function as an adjuvant. enhancing antigen-specific immunoglobulin E formation in mice.[47] Future studies may elucidate the mechanism of diesel-induced asthma

In conclusion, we have described three railroad workers who developed persistent asthma as a result of overexposure *to* diesel exhaust. This is the first time that any form of diesel exhaust has been associated with asthma Future studies should be performed that can relate diesel exhaust dose and constitutents to measures of airways hyperreactivity among diesel-exposed workers. Regulations and work practices that may lead railroad workers to be overexposed to diesel exhaust should be reexamined and rectified.

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