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A PETROLEUM SOLVENT MORTALITY STUDY OF OKLAHOMA DRY CLEANERS

Final Report on
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Departments of Biostatistics and Epidemiology
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College of Public Health
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The records of the Board of the Oklahoma State Dry Cleaners were used in a study on the effects of chronic, occupational exposures to petroleum dry cleaning solvents. The historical licensure records maintained by the Board made it possible to study a a well defined cohort of dry cleaners for which there is information on solvent exposure and duration of exposure. Volume 1 consisted of a review of the literature with information provided concerning the history of dry cleaning, description of the industry, legislation affecting the industry, a description of the process, equipment used, emission sources, levels of solvent exposure, exposure limits, the chemistry of petroleum hydrocarbons, animal toxicology, mutagenicity, teratogenicity, tumor production, human effects, and cancer mortality among oil refinery workers.

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BACKGROUND AND RATIONALE

Cancer is the second leading cause of death and lost years of potential life in the United States (1), and will account for approximately 494,000 deaths in 1988 (2). A high proportion of all cancers are thought to be caused by environmental and behavioral factors including diet, cigarette smoking, ionizing radiation, alcohol, and exogenous hormones, as well as toxic exposures in the workplace and the community (3). Evidence for these relationships has been principally developed through epidemiological and toxicological studies. The main epidemiologic observations have included differences in the incidence of cancer between groups with different exposures, case-control studies, and changes in the incidence of cancer over time, or following migration. Toxicologic studies have led to the identification of specific agents that cause cancer in experimental animals (3) or have induced an inheritable change in genetic material via bioassay testing (4).

Although general agreement exists concerning the overall incidence of cancer, considerable controversy surrounds the proportion of cancer cases attributable to occupational exposures. Estimates have been made of the proportion of cancers related to occupation, and span a broad range from less than four per cent (3, 5) to more than 20 per cent (6). While these estimates are unquestionably imprecise (7), little doubt remains that occupational factors are significantly related to an increased risk of developing cancer. Moreover, in specific groups of workers exposed to known or suspect carcinogens, the proportion who ultimately develop a site specific cancer may be large (8, 9). Several characteristics of cancer contribute to the difficulty in making such estimates.

Latency in the development of cancer

Occupational cancer usually becomes evident long after initial exposure to the carcinogen; this interval may vary from five years to more than 40 years (9), making it difficult to characterize important exposures long past.

Influence of exposures to multiple carcinogens

Cancer victims may have been occupationally exposed to many carcinogens; interaction of these agents or interactions between them and other factors may greatly increase the risk of cancer (10).

Influence of behavioral factors

Cigarette smoking, alcohol drinking, and dietary habits also influence the development of cancer (11). Moreover, these factors, especially cigarette smoking, interact with chemical and physical agents in the working environment to increase the risk of cancer (12-14); e.g., exposure to asbestos interacts with cigarette smoking to greatly increase the risk of lung cancer.

In addition, problems with the documentation of cancer and the nature and extent of etiologic exposures obscure important epidemiologic associations.

Errors in diagnosis and classification of cancer

Unusual neoplasms are often misdiagnosed; even correct diagnoses may be improperly categorized according to the International Classification of Diseases (ICD); an example is mesothelioma (10).

Lack of meaningful occupational histories

In only a few states is information collected on the work histories of cancer victims; hence, for many cases, crucial associations with occupational carcinogens are not apparent.

Difficulty in assessing exposures quantitatively

Precise measurements of levels and duration of exposures have not generally been available (13). Consequently, the ability to delineate dose-response relationships has been very limited.

The frequency of specific types of cancers

The occupational etiology of a very rare cancer due to a specific agent (e.g., hemangiosarcoma of the liver due to vinyl chloride) is much more readily documented than the occupational etiology of a cancer type potentially caused by several factors (e.g., lung cancer associated with exposure to chromates).

The "dilution factor"

Highly significant differences in the rates of cancer among small subgroups of a population may be overlooked because these rates affect the overall rate for cancer in the larger study population only slightly, if at all (15).

Epidemiologic studies provide a unique opportunity to observe the mortality experience of workers with relatively high levels of chronic occupational exposures to physical and chemical agents. These circumstances suggest that if a particular substance has the potential for inducing a carcinogenic effect in humans, the best opportunity of observing such an effect may be in the occupational setting. Occupational exposures are often associated with well defined and circumscribed populations that make natural study groups. DeCoufle (11) described at least four reasons for conducting epidemiologic studies of industrial populations:

> 1) the monitoring or surveillance of various groups, such as steel or rubber workers (16-19), can detect previously unsuspected hazards by noting unusual disease patterns,

2) epidemiologic studies assist in the reevaluation of current thinking on what are "safe" levels for known hazards, such as vinyl chloride (20),

3) epidemiologic studies of workers can provide leads for experimental research. Thus, identification of high-risk occupational groups suggests a set of potentially carcinogenic substances that can be tested individually and jointly in laboratory animals, and

4) there will always be work environments in the real world of industrial processes that will be difficult to recreate under experimental conditions.

The epidemiologic study of occupational carcinogenesis presents a unique opportunity to identify work groups in which methods of risk reduction, as well as early diagnostic and therapeutic interventions, can be particularly effective in decreasing cancer morbidity and mortality.

Dry cleaners represent a group of workers with past and present exposures to a variety of chlorinated and/or non-chlorinated petroleum hydrocarbon solvents. Previous mortality studies of dry cleaners have reported significant elevations in overall proportionate mortality due to cancer (21), or elevations in lung (21, 22), kidney (22-24), urinary bladder (25), colon (26), small intestine (27), cervix uteri (21), buccal cavity and pharynx (26), genitals, unspecified (23), biliary passages and liver (26), or skin cancer deaths (21). These studies (21-24, 26, 27) made no attempt to be solvent or duration of exposure specific, or were in the case of Brown and Kaplan (25), seriously confounded by antecedent solvent exposures.

Due to the limitations inherent in the design of these previous studies, it is likely that only a relatively small number of solvent exposed dry cleaners were actually studied, and that any solvent specific effects on mortality were diluted or confounded by the inclusion of a large proportion of dry cleaning and/or laundry workers with little or no exposure to the solvents of interest.

The existence of a set of historical licensure records, archived and maintained by the former Oklahoma State Dry Cleaners Board, has created the opportunity to study the effects of chronic, occupational exposures to petroleum dry cleaning solvents on a well defined cohort of Oklahoma dry cleaners whose specific solvent exposures and durations of exposure are known, and among whom the expression of an effect, if any, on site specific cancer mortality can be measured.

LITERATURE REVIEW

Dry cleaning has been defined as "the cleansing of fabrics with substantially nonaqueous organic solvents . . . to which special detergents and soaps are often added (28). The Federal Trade Commission has defined dry cleaning as "a process by which soil may be removed from products or specimens in a machine which uses any common organic solvent . . . . The process may include moisture addition to solvent up to 75 per cent relative humidity, hot tumble drying up to 71°C (160°F), and restoration by steam press or steam air finishing (29)." This process has evolved into a two billion dollar industry with employment in the United States estimated at nearly 140,000 (30).

History of Dry Cleaning

Bowra (31) reported that the use of nonaqueous substances for cleaning textiles may have been practiced in Greece as early as 1600–1100 B.C.E., and that the term "dry cleaner" was included in a list of over one hundred occupations inscribed in Mycenaean clay tablets. According to Van Sigworth (30), these "dry cleaners" probably used grease absorbent earths and sands to remove spots from clothing. Johnson (32) mentions that these natural cleaning agents, such as "fuller's earth," have been used since Roman times and suggests that the term "dry cleaning" was coined in reference to cleaning with these powders. Contemporary dry cleaning is accomplished by using nonaqueous organic "dry" solvents. Wet solvents, principally water, glycols, and other hydroxylic compounds swell hydrophylic textile fibers and can cause local distortions (wrinkles) or shrinkage. Dry cleaning solvents remove oily soils at low temperatures and do not swell the textile fibers. These advantages have established dry cleaning as a highly effective, low cost, and safe method for cleaning delicate textiles.

There are no clear records indicating the origin of the solvent using dry cleaning process. Despite the early knowledge of organic solvents such as turpentine, their use as spot removers did not become widespread until the nineteenth century. With the birth of the chemical industry in the 1800's, solvents such as camphene, benzene, benzol, naphtha, and gasoline became available (30). Jean-Baptiste Jolly noted that camphene from an overturned lamp removed grease spots from a table cloth (33-35), and is credited with the accidental discovery of the efficacy of nonaqueous solvents, and with opening the first dry cleaning plant in Paris about 1845 (30). Edelstein (36) argues that " . . . the dry cleaning industry is not the result of some crude accident which took place in the middle of the 19th century . . . ," but rather, " . . . the result of developing skills over a long period . . . ." By the mid-nineteenth century, dry cleaning plants were established in all of the large cities of Europe. Pullar's, a cleaning firm in Firth, Scotland, introduced solvent cleaning in the British Isles in 1866, and introduced the first power machinery for dry cleaning in 1869. References to dry cleaning establishments in the United States can be found as early as 1870 (33) and by 1910 dry cleaning technology was widespread in America. Garfield (37) identified two trends in the United States dry cleaning industry which emerged early in this century and had a considerable impact on the economic and sociologic role of the dry cleaning trade. One trend was to combine the new dry cleaning service with the already existing wet cleaning laundry trade. In 1924, Brannt and Gray (38) noted " . . . the growing tendency to combine the two methods under the same roof . . . ." The second major trend was the decentralization of cleaning services noted by Johnson (32). He attributes this decentralization to the " . . . virtual abandonment of the practice of redyeing garments and household furnishings . . . ." The art of dyeing required considerable skill and was accomplished most efficiently at a centralized facility, where technical knowledge could be shared and dye vats of different colors could be maintained simultaneously. The higher quality of modern, nonfading dyes made redyeing unnecessary and, in the 20th century, it has become more common to discard and replace old goods than to refurbish them. The trend toward decentralized neighborhood dry cleaning plants would probably not have been possible without the development of less volatile or nonflammable solvents. Brannt and Gray (38) reviewed the elaborate safety precautions needed in order to set up a dry cleaning plant using flammable solvents such as benzene, benzol, or gasoline. Gasoline, produced on a large scale for the expanding automobile market, was the major dry cleaning solvent until 1928 when a less flammable, odor-free solvent was developed, largely through the efforts of W. J. Stoddard, president of the National Institute of Drycleaning (now the International Fabricare Institute, IFI). This petroleum fraction was designated Stoddard solvent and standardized specifications were adopted by the United States Department of Commerce in 1928 (39).

Johnson (32) traced the history of the synthetic solvents used today in the dry cleaning industry. The first nonflammable synthetic solvent, trichloroethylene, was introduced in Germany in 1920. Its tendency to damage certain fibers and cause bleeding of many acetate dyes limited its use in the United States. In the 1930's, carbon tetrachloride (CCl_4) and perchloroethylene (PCE) were introduced. CCl_4 was widely used as late as the 1950's. Its toxicity prompted a recommendation by the Consumer Bulletin, in 1968, that CCl_4 be banned in the United States (40) and caused the Environmental Protection Agency (EPA) to recommend that it be considered a suspect human carcinogen (41). PCE or "perc" has become the most widely used solvent in the United States dry cleaning industry (42). More recently, synthetic fluorinated chlorohydrocarbons, such as 1,1,2-trichloro-1,2,2-trifluoroethane (fluorocarbon 113), have been introduced and are being used in less than five per cent of dry cleaning plants (43).

Industry Description

The dry cleaning industry is a service industry involved in the cleaning and/or renting of apparel. The total industry is subdivided according to the type of solvent used and the type of services offered. The solvents currently used are generally categorized as (a) petroleum solvents, (b) PCE, or (c) chlorofluorocarbon solvents.

Petroleum dry cleaning

Petroleum dry cleaning represents about 30 per cent of the total quantity of fabrics cleaned by the dry cleaning industry. Petroleum dry cleaning services are offered only by the commercial and industrial sectors of the industry, and represent about 25 and 30 per cent, respectively, of the total throughput for each of these industry sectors (44, 45). Coin operated or self-service petroleum dry cleaning plants are prohibited by National Fire Protection Association (NFPA) codes due to the volatility and flammability of petroleum solvents (46). Consequently, most commercial and industrial petroleum dry cleaning plants are located away from densely populated residential areas and shopping centers.

Commercial petroleum dry cleaning plants offer dry cleaning services to the general public, and include both independently owned dry cleaners and franchised companies. Typically, these plants clean personal items such as suits, coats, and dresses. In both franchised and independent facilities, a central cleaning plant may support one or more pickup and distribution outlets. Of the 25,000 domestic commercial cleaners, approximately 6,000 (representing 25 per cent of the dry cleaning industry throughput as of 1979) use petroleum solvents (44).

Industrial dry cleaning plants are much larger than their commercial counterparts and cater to industrial, professional, and institutional customers. Articles such as work uniforms, mats, mops, and rugs are cleaned by industrial dry cleaners, often in conjunction with rental operations. There are approximately 1,000 industrial cleaning plants nationwide. In 1979, approximately 230 of these industrial plants used petroleum solvent in some portion of their cleaning operation (45).

Table I lists and describes the Census Bureau's standard industry classifications (SIC) of nine types of firms in the cleaning industry, based on primary lines of business

TABLE I

STANDARD INDUSTRY CLASSIFICATIONS (SIC) OF TYPES OF FIRMS IN THE CLEANING INDUSTRY, BASED ON PRIMARY LINES OF BUSINESS

SIC	Type of Firm	Line of Business
7211	Power laundries, family and commercial	Mechanical laundries using steam or other power.
7212	Garment pressing, and agents for laundries and dry cleaners	Laundry and dry cleaning services but do not do their own cleaning. May do pressing and finishing.
7213	Linen supply	Supply to institutions or households, on a rental basis, linens, towels, and certain garments.
7214	Diaper service	Supply diapers and baby linens to homes, often on a contract basis.
7215	Coin-operated laundries and dry cleaners	Coin-operated or other self-service laundries or dry cleaners.
7216	Dry cleaning plants, except rug cleaning	Dry cleaning or dyeing, other than rugs. For households. Press shops and agents are not included.
7217	Carpet and upholstery cleaning	Carpet or upholstery cleaning, in-plant or on customers' premises.
7218	Industrial launderers	Supply laundered or dry cleaned work uniforms and garments, often on a rental basis.
7219	Laundry and garment services, not elsewhere classified.	Other laundry services, including repairing, altering, and storing clothes for individuals, as well as hand laundries.

(47). In practice, many cleaners are diversified into several markets, cleaning processes, and related fields. It is not uncommon to find firms that have both dry cleaning and laundry operations or, in some cases, both petroleum and PCE dry cleaning equipment. Among commercial dry cleaners, a portion of plant revenues may come from related lines of business like drapery, leather, or carpet cleaning, tailoring, or laundry. Among industrial dry cleaners, at least 50 per cent of cleaning volume is commonly done by laundering, while many industrial cleaners launder 80 to 100 per cent of their throughput (47, 48).

At one time, virtually all commercial dry cleaning plants used petroleum solvent, but today the majority of existing commercial dry cleaning plants use PCE, especially those plants established in recent years (44). Despite their gradual decrease in numbers, petroleum dry cleaners continue to account for a substantial share of total dry cleaning volume.

Industrial cleaners are better able to install the necessary fireproofing for a new petroleum solvent dry cleaning facility than are commercial plants (49). Petroleum solvent is preferred for certain cleaning applications, such as leather cleaning, because it causes less damage to garments than does PCE (44). In both sectors, petroleum and PCE dry cleaning use different washing and drying equipment, and the solvents cannot be used interchangeably in the same equipment.

Two Census Bureau classifications are most representative of petroleum dry cleaners; the commercial dry cleaning sector is represented by SIC 7216, and the industrial cleaning sector by SIC 7218. It is necessary to note that some operations within each classification include nonpetroleum dry cleaning operations, and some petroleum dry cleaning also takes place in other sectors. In particular, the linen supply industry (SIC 7213) has diversified to the point where it shares many of the characteristics of industrial cleaning and may include many petroleum dry cleaning facilities.

Commercial sector

In 1981, there were approximately 25,000 commercial dry cleaners in the United States. Of these, approximately 6,000 used petroleum solvent (44). The commercial dry cleaning industry has had periods of growth and consolidation, as shown in Table 2 (51-55). Using SIC 7216 as a proxy for the commercial sector, the number of plants in SIC 7216 increased from 26,000 in 1954 to 32,000 in 1963 and dropped in 1977 to approximately 22,000. Demand for dry cleaning dropped in real terms during the mid-1970's, in large part due to the introduction of easy to care for polyester garments. Since the late 1970's however, dry cleaning demand has recovered slightly and reached a plateau. Little or no real growth is projected for the near future. Profit-

TABLE 2

NUMBER OF PLANTS AND TOTAL REVENUE IN THE COMMERCIAL SECTOR OF THE DRY CLEANING INDUSTRY, BY YEAR

Year	Number of plants	Total Revenue[a]
1954	26,287	3,531
1963	31,722	4,086
1967	30,625	4,882
1972	28,422	3,765
1977	21,868	2,796
1981	25,000	4,000

[a] Revenue in millions of first quarter 1981 dollars

ability has recovered to a point of general stability. Unexpected changes in consumer fashions, income, leisure time, work patterns for women, and population growth could influence future revenues (44).

Most commercial dry cleaners are small businesses. Family ownership or sole proprietorships are common. More than half the commercial dry cleaners employ fewer than five employees as shown in Table 3 (55).

Imports are not a significant factor in the supplier industries for petroleum dry cleaning. While there are some imports of equipment for dry cleaning, essentially none is for cleaning with petroleum solvent.

Regional trends

Dry cleaning is a local business. Local fashions, fire codes, economic trends, and other factors shape the dry cleaning industry in different regions. Regional trends in revenues among commercial and industrial cleaners are shown in Table 4 (57-60). The most salient regional differences concern the percentages of petroleum dry cleaning among commercial dry cleaners in different states, by IFI district, and can be found at Appendix A (52, 61-62). Region VI, which includes Arkansas, Kansas, Louisiana, Missouri, Oklahoma and Texas, has had a consistently higher proportion of petroleum dry cleaners than the nation as a whole. The Northeast has the lowest concentration of petroleum dry cleaners. State and local fire codes have been less

TABLE 3

NUMBER AND PER CENT OF COMMERCIAL DRY CLEANING PLANTS IN 1977, BY NUMBER OF EMPLOYEES

Number of Employees	Number of Plants	% of Plants
0 to 4	11,272	55.75
5 to 9	5,627	27.83
10 to 19	2,458	12.16
20 to 49	741	3.67
50 to 99	97	0.48
100 or more	23	0.11
Total	20,218	100.00

TABLE 4

TOTAL REVENUES FOR COMMERCIAL DRY CLEANERS DURING 1972 AND 1977, BY REGION

	Total Revenue[a]	
Region	1972	1977
Northeast	1,000	640
North Central	940	680
South	1,230	930
West	590	510
All Regions	3,760	2,760

[a] Millions of first quarter 1981 dollars

restrictive in the South, allowing more dry cleaners to use petroleum solvent (64).

Appendix A also shows that the nationwide share of dry cleaners using petroleum solvent has decreased markedly from the 48 per cent estimate in 1963. A 1974 survey on the extent of petroleum dry cleaning use indicated that approximately 32 per cent of commercial dry cleaners were using petroleum solvent (62); this share is currently estimated by Fisher (45) to be 24 per cent.

Dry Cleaning in Oklahoma

Oklahoma is a state well suited for the conduct of a mortality study of petroleum solvent exposed dry cleaners. The ready availablility of petroleum products has maintained Stoddard solvent as the primary solvent in use. Most importantly, only Oklahoma and California have required licensure of the dry cleaning industry in recent years.

The Oklahoma legislation

The first bill to provide for regulation of the Oklahoma dry cleaning industry was introduced in 1939. The proposed aim of the bill was to protect the public from frauds, to reduce fire hazards, to prevent unfair competition, and to make the occupation of dry cleaning a respectable profession. To accomplish these ends, the bill authorized a State Dry Cleaning Board to:

> . . . promulgate rules and regulations to enforce sanitary and health regulations and to reduce fire hazards of clothes cleaning and pressing establishments; empowering and authorizing said

> Board to promulgate rules and regulations to promote occupational security of operators engaging in said business; and to promulgate rules to prevent unfair trade practices; and to require the issuance of licenses by said Board to persons, firms, corporations or associations, as a prerequisite in engaging in said cleaning and dyeing and/or pressing business; to determine fitness and reliability of applicants to engage in said business; authorizing said Board to approve agreements and make orders fixing minimum prices for all dry cleaning, dyeing and/or pressing services; and providing penalties for the violation of any of the provisions of this Act; and providing for judicial review of the acts of said board (65).

The Act which was in force until July 1, 1985, was substantially the bill that was introduced in 1939. It was reintroduced in the Oklahoma House of Representatives in February, 1941, and did not contain a minimum price clause. It received considerably more legislative support and became law without the Governor's signature (66).

The Act created a State Board of Dry Cleaners. The members were appointed and served at the discretion of the Governor. At least three of the members of the Board must have been actively engaged in the dry cleaning business for at least five years. The Board was an instrument of the state vested with the power to supervise and regulate the cleaning industry within the framework of existing health, sanitation, and labor laws, to investigate and regulate matters pertaining to "the proper supervision and control" of the cleaning industry with the power to subpoena to carry out the purposes of the Act, and to act as mediator in controversies between employee and employer (66).

The Act set forth five main functions of the Board:

> 1. The Board is to adopt and promulgate rules and regulations necessary to identify to the public all licensed practitioners and prohibit false and misleading statements.
>
> 2. Separate licenses for each place of business are to be granted by the Board.
>
> 3. As a prerequisite for obtaining a license, the Board is to require all persons to comply with the standards deemed necessary by the Board for the protection of the public.
>
> 4. The Board is to enforce and assist in the enforcing of fire, sanitation, labor and other laws applicable to the industry.
>
> 5. The Board is to "act with the purposes of this Act, as a competent authority in connection with matters pertinent thereto: provided, however, that nothing herein shall be construed as granting said Board the right or power in any manner to fix prices" (66).

In 1945, the Act was amended to read substantially as the first bill of 1939 had read. The primary change to the 1941 law was the empowering of the Board to set minimum prices.

> The Board shall have the authority and power to approve price agreements establishing minimum prices for cleaning, pressing and dyeing services signed and submitted by at least seventy-five percentum (75%) of the duly registered and licensed cleaning and pressing operators in any county of this state, after ascertaining by such investigation, and proofs as the condition and under varying conditions will best protect the public health and safety by affording a sufficient minimum price for cleaning and pressing services to enable the persons engaged in such business to furnish modern and healthful service and safe appliances so as to minimize the danger to the public health and safety incident to such work (67).

This legislation created a unique setting in which to study the potential health effects of chronic petroleum solvent exposures. First, it established a repository for the official records involved in the implementation of the law. Second, it spawned a vital and active professional association of Oklahoma dry cleaners. Third, it set an economic milieu which enhanced the quality of this cohort mortality study. These economic influences were studies by Plott (68) in 1966, in which he concluded:

1. Neither the Board nor its regulations tended to restrict entry into the industry.
2. A fall in market demand reduced profits rather than the number of firms.
3. When compared to Kansas and the entire United States, Oklahoma maintained:
    - a) higher prices and greater per capita spending for dry cleaning services,
    - b) more, and smaller solvent using dry cleaning plants per capita, and
    - c) a greater number of dry cleaning employees and proprietors per capita.

These factors created a stable population of solvent exposed Oklahoma dry cleaners whose numbers are greater than expected, whose turnover is markedly reduced, and whose average duration of exposure to dry cleaning solvents are relatively long.

Dry Cleaning Process Description

The following sequence of operations is used in the normal drycleaning process (69):

1. Soiled garments are marked and sorted;
2. Prespotting is performed when required;
3. Garments are rotated in a tumble-type washer or washer/extractor containing the dry cleaning solvent;
4. Solvent is drained from the tumbler and most of the residual solvent removed by centrifugal extraction in the washer/extractor, or separate extractor;
5. The small amount of solvent remaining in the garments is removed in heated dryers;
6. Dirty solvent from the wash cycles is continuously passed through diatomaceous earth and activated carbon, or disposable cartridge filters, to remove as much of the fugitive dyes and insoluble soils as possible;
7. Soils not removed by filters, diatomaceous earth, or activated carbon can be removed from the solvent by vacuum distillation;
8. Dry, solvent-free garments are inspected and spot cleaned a second time, if necessary;
9. A garment may be "wet cleaned" at this point, but this is usually omitted when operating a "charged" solvent system;
10. Clean garments are finished on suitable presses, puff irons, steam tunnels, or on adjustaforms;
11. After a final inspection, the garments are assembled according to customer's order, and are bagged and placed on racks, ready to be picked up. Mechanical conveyors aid in fast recovery of a

customer's garments.

Petroleum dry cleaning operations are similar to detergent and water wash operations. Unlike PCE dry cleaning which can have both washing and drying operations in the same machine, petroleum dry cleaning is a batch operation in which articles are washed and dried in separate machines. Figure 1 depicts a typical two-bath petroleum dry cleaning operation. Articles to be dry cleaned are sorted into lots according to color, fabric and degree of soiling. Articles are then agitated in the solvent with a total wash cycle time ranging from 20 to 40 minutes, depending on the load size, fabric, and soil loading (70). The more heavily soiled articles go through two or more wash cycles: the first with recycled, soiled solvent and the second with clean solvent.

Industrial dry cleaning plants often use a cleaning process where water soluble materials are removed from articles in a water and detergent wash followed by a solvent wash operation to remove solvent soluble materials. This process, sometimes called a "dual" or "double phase" process, takes place in modern washers and is used by more than 90 per cent of industrial plants (71).

Commercial dry cleaning plants also use a dual phase process for cleaning articles; however, up to 90 per cent of the commercial plants use a "charged" system, a process where both soap (up to four per cent by volume) and control-

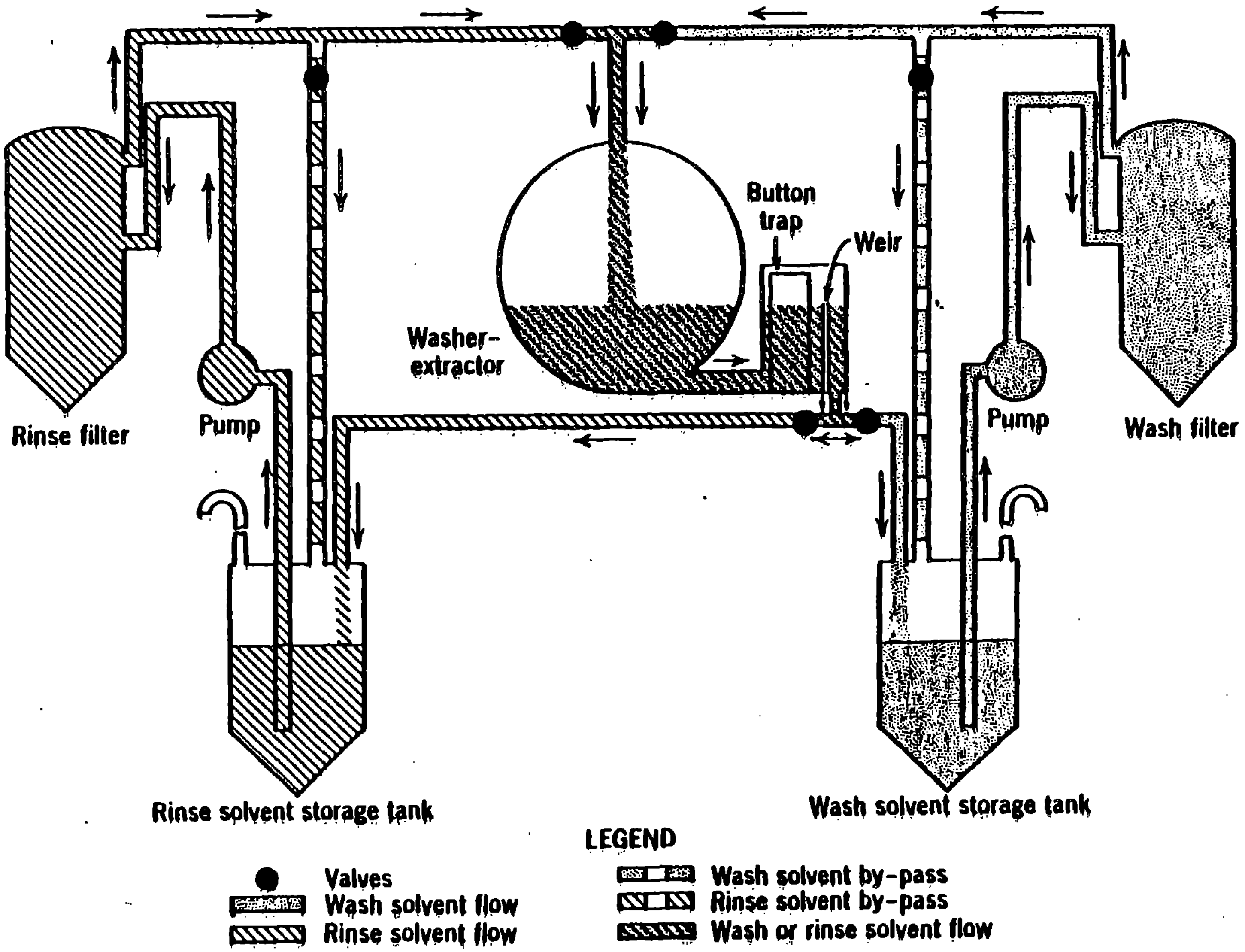

Figure 1. Modern petroleum solvent washer/extractor using a two-bath system with two filters. The arrows indicate the direction of solvent flow.

led amounts of water (0.1 per cent to 0.3 per cent by volume) are manually or automatically added to the solvent (44, 72). The volume of soap and water added to the solvent is controlled by the load type, load weight, moisture present in the solvent, relative humidity of the air, or a combination thereof.

After completion of the wash cycle, articles are spun at high speed to remove excess solvent. This spin cycle usually occurs in the same equipment used for washing; however, approximately 23 per cent of the plants existing in 1975 had separate, high speed centrifugal extractors (73). In 1980, it was estimated that a minimum of three per cent of these plants have been converted to washer/extractors. When the spin cycle has terminated, articles are transferred from the washer/extractor or extractor to a tumble dryer. Inside the dryer, any remaining solvent is removed from the articles by evaporation in a heated air stream and is vented to the atmosphere.

Soiled solvent extracted during the washer spin cycle is passed through a filter to remove insoluble soils and other suspended particles. When the soil load in the solvent is excessive, soil laden solvent may be transferred directly from the washer to a vacuum still or to a settling tank prior to distillation. After settling (usually overnight), the heavy oils, dirt, and grease are decanted, and the solvent is sent to a vacuum still where it is purified.

When oil and grease loading is low, distillation is often bypassed and filtration serves as the only means of solvent purification. Finally, the distilled solvent is pumped into a holding tank or is returned to the washer or washer/extractor.

Spotting

"Spotting" involves the selective application of chemicals, steam, detergent, and/or water to loosen or remove specific stains from soiled garments. Spotting is sometimes done prior to dry cleaning (pre-spotting), but may also be necessary following the dry cleaning step to remove stubborn stains. Depending upon the size of the dry cleaning plant and the nature of the dry cleaning process, spotting can require a full-time employee; however, this step is usually handled by the dry cleaning machine operator. Industrial dry cleaning plants generally do not conduct spotting operations.

The chemicals typically utilized by spotters include chlorinated solvents, amyl acetate, bleaching agents, acetic acid, aqueous ammonia, oxalic acid, hydrogen peroxide, and dilute hydrogen fluoride solutions. A more extensive list of spotting solutions can be found at Appendix B (74). These chemicals generally are applied from plastic squeeze-bottles and are then either rubbed into the fabric with a brush, a spatula, or by hand, allowed to soak into the fabric (which is subsequently handled), or flushed with steam applied from a steam gun. Thus, employees engaged in spotting may be exposed to toxic materials through both skin contact with liquids and inhalation of airborne vapors and mists. However, the problem of inhalation exposures is minimized by the small amount of time that an employee is typically engaged in spotting, the small quantity of chemicals used, and the intermittent nature of this operation.

Washers

The dry cleaning power washer removes an estimated 80 to 90 per cent of the soil and stains found on garments received by the dry cleaner. The washer itself is a horizontal or vertical rotating or oscillating perforated basket which is within a solvent holding drum. Separated petroleum units are those in which only washing takes place, and are connected to appropriate filters and stills. Garments are removed after washing, dripping with solvent, and placed in extractors. Semiautomatic petroleum units are used in small to moderate volume operations where available floor space is limited. The semiautomatic units wash and extract garments in the same basket. Cleaning efficiency is determined by the specific solvent used and the mechanical action of the washer. Mechanical action is the motion required to produce friction on the fabric surface for the purpose of loosening insoluble soil and putting soluble soil into solution. Machine mechanical action takes place within the washer and includes (75):

a) dropping of the garment from the top side of the basket back into the solvent,
b) rubbing of the garments against one another, against the solvent and against the basket side,
c) squeezing of the garments by the weight of other garments and the force of the rotating wheel,
d) bending and flexing of the fibers as the garments are tossed about in the solvent, and
e) spilling of the solvent as it is agitated and is dropped on the garments during the washing cycle.

The factors which determine the extent or degree of mechanical action include the (75):

a) type of washer, usually a single or two pocket rotating drum,
b) size of the washer, determined by the washer or "wheel" diameter,
c) size of the wash load,
d) wash time,
e) speed of the washer, in revolutions per minute (rpm),
f) solvent weight (pounds/gallon), and
g) solvent level.

Extractors

Separate extractors or washer/extractors remove most of the solvent from dry cleaned garments by the centrifugal force generated by the rapid rotation of the perforated extractor basket. Extraction efficiency is determined by the speed of the extractor, usually 400 to 900 rpm, by the diameter of the basket, and by the extraction time (usually three minutes). Wrinkling increases in proportion to the extraction time. Garments which are dry cleaned in moisture-laden "charged" systems and then "hard" extracted at high speeds tend to get difficult wrinkles.

All washer/extractors and some separate extractors are piped to deliver extracted solvent to filters, stills, or storage tanks. Many separate extractors, however, were originally designed to collect any extracted solvent in open, portable containers.

Dryers

Standard, nonrecovery, petroleum solvent dryers remove liquid solvent by forcing ambient air over steam heated coils and directing the heated air stream over and through the articles in the dryer tumbler and out through the lint filter to the atmospheric exhaust. Typically, these units are manufactured with at least two operating cycles, door-open and drying, and frequently have a third cool-down cycle. The standard dryer is loaded and unloaded in the door-open cycle. During this operation, solvent laden articles are loaded into the perforated tumbler basket with the exhaust blower operating in order to remove solvent vapors from the loading area. Thus, in the door-open cycle, ambient air from the dryer door area is drawn into the dryer through the dryer door and exhausted to the atmosphere. Loading and unloading durations vary between one and five minutes, depending on the levels of automation and operator efficiency.

The drying cycle begins when the dryer door is closed and the drying cycle timer is activated. The tumbler basket rotates, a solenoid valve in the steam chest supply permits steam to enter the heating coils, and the blower pulls ambient air into the tumbler over the steam coils where the air is heated to about 100 °C (212 °F). In the tumbler, the heated air forces solvent and water to evaporate from the tumbling articles at an optimum drying temperature range of 60 °C to 66 °C (140 °F to 150 °F), measured at the dryer lint filter (76). Because the evaporation process absorbs heat at a relatively constant temperature, the actual temperature of the drying articles is a function of their solvent and water content and gradually increases during the drying cycle. Upon leaving the tumbler basket, the solvent laden vapor stream passes through a bag-type lint filter, through the exhaust blower, and finally is exhausted to the atmosphere. The duration of the drying cycle typically ranges from 15 to 50 minutes, with short durations reflecting smaller loads of heat sensitive fabrics, such as silks containing little solvent, and longer drying cycle times indicating larger loads of heavy fabric, such as wools containing large quantities of solvent (77).

Volatile organic carbon (VOC) emissions associated with the drying of articles washed in petroleum solvent can occur during all three standard dryer operating cycles. During the door-open cycle, solvent evaporated from the articles being loaded or unloaded contributes to the overall level of fugitive VOC emissions in the plant. Those emissions in the vicinity of the dryer door are drawn into the dryer by the exhaust blower and are vented to the atmosphere through the dryer exhaust. Although articles removed from the dryer are assumed to be solvent-free, Environmental Protection Agency (EPA) tests have indicated that the solvent content of dried articles may be significant (78).

Drying cycle VOC emissions occur when liquid solvent and water are evaporated from the tumbling articles and exhausted to the atmosphere. The principal determinant of the extent of these emissions is the solvent content of the drying articles, determined by the type of fabric, the extraction efficiency of the washer/extractor or extractor, and the weight of articles being dried. The rate and total quantity of solvent evaporated from drying clothes is a function of the quantity of solvent available, the drying temperature, air flow rate, and the duration of the drying cycle. In dryers with a cool-down cycle, VOC emissions from the dryer atmospheric exhaust are produced, but it is assumed that very little additional solvent is evaporated during this cycle.

Recovery dryers

A solvent recovery dryer is essentially a standard dryer that has been fitted with a condenser to remove solvent vapor from the dryer exhaust by condensation. After partial removal of both solvent and water vapors in the condenser, the air stream is ducted from the condenser to a steam chest where it is reheated. The reheated air stream then passes to the tumbler where the cycle of solvent evaporation repeats. In contrast, a standard dryer forces heated air through the tumbling articles and then exhausts it to the atmosphere.

As the vapor stream is forced through the condenser, chilled water circulates downward through the condenser coil and cools the vapor stream until a liquid solvent and water mixture condensate is produced. This condensate flows to the bottom of the condenser where it is piped to a solvent/water separator.

The level of atmospheric emission reduction attained by the recovery dryer is based on the assumption that all solvent entering the dryer in garments is either recovered or emitted to the atmosphere during the cool-down/exhaust phase in contrast to standard dryers which emit their entire solvent content to the atmosphere. Thus, the total VOC atmospheric emission reduction is equal to solvent recovered.

Solvent filters

Filtration in dry cleaning operations is a process used to remove most insoluble contaminants, such as dirt and lint and, to a lesser extent, certain water-soluble contaminants, such as perspiration and food stains, from dry cleaning solvents. This is accomplished by rapidly passing large volumes of solvent through a porous medium that traps and simultaneously removes contaminants suspended in the solvent. Although diatomaceous earth filtration has traditionally been used in the industry, cartridge filtration is becoming the predominant form of solvent filtration. In 1980, about 50 per cent of the petroleum dry cleaning plants that utilized filtration used multicharge diatomite filters, while the remaining 50 per cent employed cartridge filters for solvent filtration; in 1986, between 80 and 90 per cent of petroleum plants used cartridge filters (44).

Diatomite filters.

Diatomaceous earth filtration systems are composed of the filter medium and the structure that holds the filter medium, known as the septum. The filter medium, diatomaceous earth mixed with activated carbon, is used to remove insoluble contaminants by entrapping them on its porous surface. The septum is a rigid, porous surface (screen, cloth, or wire mesh) to which the filter medium adheres, thereby allowing pressurized solvent to flow through while simultaneously blocking the passage of particles. During a wash cycle, articles are agitated in a bath of solvent. After the wash cycle, the soiled solvent is pumped to a filter for filtration. Filter media is replaced when the pressure across the filter, due to the buildup of contaminants on the medium, reaches a predetermined level (usually 40 psi or 270 kPa). Spent filter media or "filter muck" is usually allowed to drain in the filter housing overnight or for 24 hours before it is discarded. An industry trade association determined that discarded filter media that has been allowed to drain for 24 hours may contain from 5 to 10 kg of solvent per 100 kg dry weight of articles cleaned (79). Devices such as centrifugal separators, and pressure or vacuum muck strippers have been used by a few large petroleum dry cleaning plants to recover solvent from diatomite filter muck (44). These devices are not widely distributed throughout the industry and there is currently little data on their performance as an emission source or control technique.

Cartridge filters.

Cartridge filtration is a continuous, two-stage process of filtration in which soil laden solvent is forced under pressure through a paper filter to remove entrained solids and then through a layer or layers of activated carbon which selectively entrap molecules of impurities such as fabric dyes. The term "cartridge" is used to denote replaceable units or canisters containing filtration paper and activated carbon or activated carbon only. Soil laden solvent is pumped from a washer or washer/extractor to a vessel having a removable, pressure-sealed lid or top containing from two to 36 filter cartridges. After passing through the dual component cartridges, the solvent is diverted to one or more filter cartridges containing only activated carbon and is finally transferred to a storage tank to await distillation and reuse (80).

The operation of a cartridge filtration system can be based on either continuous (during washer operation) or batch processing (at predetermined intervals) of spent solvent. In continuous operations, the spent solvent in the washer is pumped through the filter and back to a filtered solvent tank. The outer surfaces of the filter paper in each carbon-core cartridge eventually become clogged with dirt and lint, while the carbon granules contained in both types of cartridges become coated with dyes and particles until they no longer purify the solvent stream. Under typical commercial conditions of soil loading and throughput, the filter cartridge may need to be replaced after every 450 to 500 kg (1,000 to 1,100 lbs) of articles washed (81).

Atmospheric emissions from cartridge filters are limited to fugitive emissions that evolve from leaks, filter cartridge replacement, and evaporation of solvent contained in disposed cartridges. An EPA test of the amount of solvent contained in discarded filter cartridges was conducted at a medium-size commercial petroleum solvent dry cleaning plant (82). Results of this test indicated that draining the filter cartridges in their closed housing for at least eight hours would result in an average solvent emission per cartridge of 1.6 kg or 0.35 kg of solvent emitted per 100 kg of clothing throughput (82), and is in general agreement with a dry cleaning trade association estimate of 0.75 kg per 100 kg of articles cleaned (79). The majority of the drainage takes place during the initial few minutes when liquid solvent is running freely from the canisters. After eight hours of drainage and evaporation, the cartridges have lost 37 per cent of their undrained solvent content. After an additional four hours, they lose only three per cent more, indicating that extended drainage periods are unnecessary.

Settling tanks

Settling tanks are used to separate oils, grease and suspended particles from petroleum solvent. Settling tanks are utilized when other methods such as cartridge filtration are not economical due to heavy soil loadings in processed articles. The difference in densities of the solvent, oil, grease, and suspended particles forms the basis for the separation process. Petroleum solvent is less dense than oils, grease, solids, or water, and rises to the top of the tank while the other materials settle to the bottom. Settling tanks are conical-bottomed, cylindrical containers with two or more orifices for solvent flow and for the venting of solvent vapors. These tanks vary in size, the maximum size being 5,680 liters (1,500 gal). Only two 5,680 liter tanks are allowed per plant by the NFPA codes (46). Settling tanks operate in either batch or continuous modes. The batch operated settling tank is used where contaminated solvent is pumped from the washer and stored in the settling tank. The time allotted for settling depends upon the tank capacity, the extent of solvent contamination, and the variation in densities of the contaminants in comparison to that of petroleum solvent. After allowing sufficient time for settling, a valve is manually opened at the base of the tank to drain off the residue. The viscous, liquid residue is normally collected in a drum and allowed to set for a few hours to several days. Solvent is skimmed from the top of the residue at the end of this period, and the residue is then discarded, mixed with boiler fuel, or sold to solvent reprocessors (45). The solvent remaining in the settling tank after the removal of the residue is conveyed to the vacuum still for further purification.

The continuously operated settling tank, also known as a separator tank, has solvent flowing in and out on a continuous basis. Contaminated solvent from a washer is pumped to the settling tank. The solvent flows from the top of the tank as the heavy contaminants settle to the bottom. Periodically, residue is drained from these tanks and is discarded or utilized in the same manner as that from the batch operated tank.

Vacuum stills

The purpose of vacuum distillation in the petroleum dry cleaning industry is to separate petroleum solvents with lower boiling points from "high boilers" such as oils, grease and solid residue such as dirt, lint, or detergents. The mixture of petroleum solvent, oils and grease that is conveyed to a still is typically a mixture of liquids with a wide range of boiling points. Consequently, a still is operated at a temperature that will evolve the liquids that fall within the boiling range of petroleum solvents while leaving behind the oils, grease, and solid residue. Petroleum dry cleaning solvents have boiling ranges from 150 to 215 °C (300 to 415 °F) at atmospheric pressure. A steam pressure greater than 100 psi (670 kPa) is required to boil petroleum solvents under atmospheric conditions (83). Consequently, distillation of petroleum solvents takes place under a vacuum of 22 to 27 inches Hg (75 to 92 kPa) which lowers the boiling range for petroleum solvents to 107 to 113 °C (225 to 235 °F) at steam pressures of 35 to 90 psi (235 to 600 kPa).

A vacuum still is composed of a) the boiling chamber, b) the condenser, c) the gravimetric separator, and d) the moisture separator. Spent solvent from a washer, filter or settling tank is pumped to the boiling chamber of the vacuum still. In the boiling chamber, steam heated coils volatilize the solvent, leaving behind still residue, composed of oils, grease, and dirt. Solvent vapor and moisture pass from the boiling chamber into a water cooled condenser where the vapors condense to a mixture of liquid solvent and water. This mixture is then piped to a gravimetric separator where the solvent and water are separated by the differences in their densities. The solvent is then pumped to the moisture separator, a tank containing cotton rags or salt pellets, where any remaining water is absorbed. When the concentration of "high boilers" has reached a prespecified level, the liquid contained in the boiling chamber is allowed to boil for a period of up to 30 minutes in a process commonly called "boildown," in which most of the remaining solvent is evolved. After "boildown," the still residue is collected for disposal.

Fugitive Emission Sources

There are a number of sources of fugitive emissions in a dry cleaning operation. A dry cleaning trade association has estimated that approximately 1.0 kg of VOC is emitted by fugitive sources for every 100 kg of articles cleaned in a typical dry cleaning plant (84). In an EPA test of fugitive emissions at a large industrial dry cleaning plant, it was found that more than 0.5 kg VOC per 100 kg dry weight of articles cleaned was emitted from various sources within the plant (85). Fugitive emissions essentially encompass all sources other than dryers and filters and typically include emissions from the extraction cycle of a washer, emissions given off during the transfer of solvent laden articles from washers and dryers, emissions resulting from solvent remaining in articles removed from the dryer, liquid and vapor leaks in tanks and piping, and the evaporation of solvent from open containers. Fugitive emissions may also occur from filter muck, still, and settling tank residues which may be stored in open containers prior to disposal.

Atmospheric emissions resulting from the operation of vacuum stills are a function of the still design, operation, and the frequency of still utilization. Solvent vapor losses from settling and storage tanks contribute significantly to overall fugitive emissions. These emissions generally occur as a result of "breathing" and "working" losses. Breathing losses occur when the vapor volume in storage tanks expand or contract in response to changes in temperature. This results in air being drawn into the tank (vapor contraction) and solvent vapor being expelled to the atmosphere (vapor expansion). In contrast, working losses result from changes in the vented free volume above the stored liquid solvent. Solvent vapor is expelled when the tank is filled. Draining draws in atmospheric air, thereby producing additional breathing losses as the air becomes saturated with solvent vapor.

An EPA sponsored test program conducted at a large industrial dry cleaning facility included sampling and evaluation of VOC concentrations in the general dry cleaning environment (85). Significant concentrations of solvent vapor, at times approaching 70 per cent of the solvent lower explosive limit (LEL), were found around both the settling tank and the solvent storage tank vents. Another significant source of VOC atmospheric emissions was the washer which produced concentrations nearing 10 per cent of the solvent LEL in its immediate vicinity. Additional measurements of VOC concentrations in dry cleaning room roof exhaust vents yielded an estimated VOC atmospheric emission rate of 0.5 kg solvent per 100 kg of articles cleaned.

The broad category of "leaks" can contribute significantly to overall plant fugitive VOC emissions. Liquid solvent which drips from pipes, fittings, valves, hoses, couplings, and pumps adds to the constant background of solvent vapor inherent to many dry cleaning plants. Vapor leaks from dryers, exhaust ducts, filter housings, stills, and open or improperly sealed containers of solvent and solvent laden waste all contribute to the quantity of solvent emitted to the workplace environment.

Levels of Solvent Exposure

The exposure conditions indicated in this study are limited to the identification of a specific solvent or solvent category and the number of years of exposure to that solvent, without regard to the level of exposure. The actual exposure levels experienced by the members of this historical cohort, as in virtually every historical cohort, will never be known. This study, like most in occupational epidemiology, is restrained by this lack of exposure data, and is concerned with providing evidence regarding qualitative questions of whether particular exposures or work conditions are associated with adverse health effects.

Petroleum dry cleaning in Oklahoma has utilized a few simple technologies which have remained virtually unchanged over the past forty years. Plants have employed general dilution ventilation and have not routinely utilized local exhaust ventilation, solvent recovery devices, or personal protective equipment.

There is a paucity of petroleum solvent inhalation exposure studies of dry cleaning plants in the published literature. The only specific reference found was a 1967 survey by Oberg (87) of 30 petroleum dry cleaning plants in Detroit. The time weighted average (TWA) exposure for the entire dry cleaning cycle was 65 ppm (range of 15-200 ppm), and the eight-hour TWA was estimated to be 25 ppm. Data are available from a passive dosimeter sampling program conducted by the IFI of ten petroleum dry cleaning plants in which the eight-hour TWA's ranged from 29 to 145 ppm (88).

The results of a sampling program of dry cleaning plants conducted by the City of Houston Health Department (89) included several petroleum plants in which the eight-hour TWA exposures to Stoddard solvent were estimated to be between 20-40 ppm (90).

Solvent exposure levels in five commercial or industrial petroleum dry cleaning plants were included in a 1980 publication by NIOSH (91) which assessed engineering control technologies in the dry cleaning industry. Operators of these five petroleum solvent plants were reported to have eight-hour TWA exposures of 15 to 95 ppm, with fifteen minute ceiling exposures of 121 to 160 ppm during garment transfers.

The dry cleaning machine operator is generally exposed to the highest concentration of solvent within each plant. One major source of direct employee exposure to solvent vapor is the transfer of garments. The transfer from the washer to the dryer of garments which are damp or wet with petroleum solvents is usually done manually, and typically involves holding these garments directly in the employee's breathing zone. Most dry cleaners comply with OSHA's current permissible exposure levels of 500 ppm of Stoddard solvent over an eight-hour TWA as specified in 29 CFR 1910.1000. It is unknown how many dry cleaners currently meet the peak exposure level of 306 ppm (550 mg/m^3) recommended by the NIOSH criteria document on refined petroleum solvents (74).

Considerably more data are available regarding exposure levels of dry cleaners to the synthetic solvents, most notably PCE (92-94). Although the solvent and actual exposure levels in ppm are different, the pattern of exposure within petroleum dry cleaning plants should be similar to that measured in synthetic dry cleaning plants.

> Among the various jobs in a dry cleaning facility, the machine operators (dry cleaners) had the greatest PCE exposure. Analysis of variance showed a statistically significant difference ($p < 0.05$) between the geometric mean TWA exposure to PCE of the dry cleaners (22.0 ppm) compared to the exposures of the pressers (3.3 ppm) or seamstresses (3.0 ppm) or the front counter (3.1 ppm) concentrations. The machine operators have higher exposures because most of their time is spent in the vicinity of the processing machinery. Their duties usually include loading and unloading textiles, cleaning and maintaining equipment, spotting or other tasks nearby. Conversely, the pressers, seamstresses and front counter personnel usually are located away from the process machinery, often in separate rooms, and normally have no direct exposure to PCE (93).

The National Institute of Occupational Safety and Health (NIOSH) has published a sampling procedure, S-382, using activated charcoal as an adsorbent, carbon disulfide as a desorbent, and flame ionization gas chromatography for quantitation (86).

Exposure Limits

Cook (95), in his 1945 compilation of maximum allowable concentrations (MACs), reported a limit for Stoddard solvents set by New York State at 750 ppm as a guide for assessing occupational exposure. Cook recommended a MAC for Stoddard solvents of 500 ppm (2,950 mg/m^3) basing his proposal on work done with gasoline in 1927 by Sayers et al.

(96) and in 1943 by Drinker et al. (97), believing the higher boiling constituents of Stoddard solvents to be more toxic than those included in gasoline.

In 1946, the Subcommittee on Threshold Limits of the American Conference of Governmental Industrial Hygenists (ACGIH) (98) adopted a MAC for Stoddard solvents of 500 ppm (2,950 mg/m^3) based on recommendations by Cook (95). In 1948, the ACGIH changed the name of maximum allowable concentration to threshold limit value (TLV). The ACGIH TLV tables for both 1948 (99) and 1949 (100) listed the TLV for Stoddard solvents at 500 ppm as a time weighted average (TWA) concentration. This recommended airborne concentration was set to prevent subjective symptoms. The recommended TLV was based on work done with gasoline by Sayers et al. (96), Drinker et al. (97), and Elkins (101). In 1970, however, the ACGIH (102) lowered its TLV recommendation for Stoddard solvents to 200 ppm (1,180 mg/m^3) as an eight-hour TWA concentration. The 1971 Documentation of the Threshold Limit Values for Substances in Workroom Air (103) proposed a TLV of "150 or 200 ppm (800 or 1,100 mg/m^3)" for Stoddard solvents. To estimate the toxicity of Stoddard solvents, the ACGIH defined this solvent as a mixture of 85 per cent nonane, isodecane, and their isomers, and 15 per cent aromatic hydrocarbons, predominately 1,3,5 trimethyl benzene (mesitylene). For nonane and isodecane, a combined air concentration of 250 ppm was recommended based on a comparison of the increasing toxicity of pentane through octane series, and 50 ppm was recommended for mesitylene. These two recommended limits were incorporated into a composite formula for the determination of the TLV's for mixtures, yielding the estimated TLV of 150 to 200 ppm as a TWA concentration for Stoddard solvents (104). In 1974, the ACGIH (104) published a notice of an intended reduction of the recommended limit for Stoddard solvents from 150 to 200 ppm to 100 ppm (575 mg/m^3). In 1976, this change was adopted (105). An additional statement was made that Stoddard solvents having flash points above 45 °C should have a limit below 100 ppm. The short-term exposure limit for Stoddard solvents was suggested to be 150 ppm (approximately 720 mg/m^3). In 1976, the ACGIH suggested a limit of 25 ppm (150 mg/m^3) for 140 flash aliphatic solvent, a type of Stoddard solvent (105).

The current federal occupational standard (29 CFR 1910.1000, Table 2) for Stoddard solvents is 500 ppm (2,950 mg/m^3) as an eight-hour TWA concentration. NIOSH (74) recommends a threshold limit TWA of 200 ppm (350 mg/m^3) for a 10-hr day, 40-hr work week with the same action level, and a ceiling of 306 ppm (550 mg/m^3). The International Labour Office (106) published a report in 1970 on the permissible levels of toxic substances in the working environment for numerous countries. Finland was reported to have a standard for Stoddard solvents of 500 ppm (2,950 mg/m^3). The 1975 permissible level of Stoddard solvents for Sweden was listed as 600 mg/m^3, and the 1972 level of these solvents for the USSR as 300 mg/m^3 (107).

Chemistry and Composition of Petroleum Hydrocarbons

Petroleum derives its name from the Greek "petra," meaning rock, and Latin "oleum" meaning oil; hence, "rock oil." Petroleum products are derived from crude oils composed of thousands of chemical compounds ranging from gases, like methane, liquids, and substances which are solids at standard temperature and pressure, such as waxes and asphalts. The gases and solids are normally dissolved in the liquids under very high pressure. The principal elements in crude oils are hydrogen and carbon, with hydrocarbons composed only of these two elements. Gerarde (108) has pointed out the ubiquitous nature of hydrocarbons, showing how extensively they occur in nature. The four principal types of hydrocarbons are paraffins, olefins, naphthenes, and aromatics.

Paraffin hydrocarbons

Paraffins are also referred to as alkanes or saturated aliphatic hydrocarbons. The term aliphatic refers to a non ring, open-chain structure. In paraffin hydrocarbons, carbons are bonded tc carbons with single bonds in the carbon skeletal structure, and all remaining bonds are carbon to hydrogen single bonds. When a skeletal carbon structure has all of the single bond hydrogens it can have, it is said to be saturated with respect to hydrogen.

Normal paraffins

In normal paraffins, carbons are joined to carbons in one long chain and are identified by using "n-" as a prefix to the name or formula. The early members of the paraffin series, along with boiling points of the normal paraffins are shown in Table 5. Paraffin hydrocarbons have the general formula C_nH_{2n+2} where n = number of carbon atoms present. Increasing the number of carbons in a molecule increases its molecular weight and increases the boiling point of the compound, thus decreasing its volatility, or tendency to vaporize.

Isoparaffins

Isoparaffins have their carbons and hydrogens joined to form branched chains and are isomers of the corresponding n-paraffins. Isomers are defined as compounds with the same formulas but with different structures and varying physical and chemical properties. The lowest member of the paraffin series to have isomers is butane. As the number of carbons increases, the opportunity for isomerization also increases and accounts for the vast number of possible chemical compounds in crude oil and petroleum products. For decane, $C_{10}H_{22}$, there are 75 isomers, and the number of isomers is approximately doubled for each additional carbon beyond ten. Motor gasoline is predominantly composed of hydrocarbons ranging from C_4 through C_{12} but also may include

TABLE 5

EARLY MEMBERS OF N-PARAFFIN SERIES

Name	Formula	Boiling Point	
		°C	°F
Methane	CH_4	-161.7	-259.0
Ethane	C_2H_6	-88.9	-128.0
Propane	C_3H_8	-42.1	-43.8
Butane	C_4H_{10}	-0.5	30.9
Pentane	C_5H_{12}	36.1	96.9
Hexane	C_6H_{14}	68.7	155.7
Heptane	C_7H_{16}	98.4	209.1
Octane	C_8H_{18}	125.7	258.3
Nonane	C_9H_{20}	150.8	303.4
Decane	$C_{10}H_{22}$	174.1	345.4
Undecane	$C_{11}H_{24}$	195.9	384.6
Dodecane	$C_{12}H_{26}$	216.3	421.3

traces of C_3 and C_{13} hydrocarbons. In the case of paraffins alone, this may represent the presence of more than six hundred compounds. Isomers are not restricted to paraffins and exist for olefins, naphthenes and aromatics as well. Motor gasoline has the potential for containing 1,200 to 1,500 or more individual hydrocarbons, at least in trace amounts.

Olefins

Olefins resemble paraffins in structure but they have one or more double bonds between carbon atoms. As a result, they are unsaturated with respect to hydrogen. Olefins are also called alkenes and have the general formula C_nH_{2n}. There are normal olefins and isoolefins, just as with paraffins. Olefins with two double bonds are called diolefins. As a result of the strained bonding forces associated with carbon to carbon double bonds, olefins are much more reactive chemically than compounds that have only single bonds. Olefins do not occur to any significant degree in crude oils. They are formed in certain refinery processing operations, primarily in catalytic cracking.

Naphthenes

Naphthenes are also known as cycloparaffins or cycloalkanes. At least some of the carbon atoms in naphthenes are linked together to form a ring. Like the normal and isoparaffins, naphthenes are saturated with respect to hydrogen, but they have two fewer hydrogen atoms because of their ring structure. Larger molecules consist of several naphthene rings joined together. They may be joined with one or more carbon atoms or they may be built up from naphthene ring "building blocks," possibly with paraffinic side chains. If these paraffin side chains are large enough, a molecule may have more paraffinic than naphthenic characteristics. The contribution to the complex composition of petroleum products due to naphthenic hydrocarbons becomes apparent as one appreciates the many variations in structure that can exist as the molecular weight of naphthenes increases.

Aromatics

Aromatic hydrocarbons are characterized by the presence of the benzene ring as a part of the molecule. Benzene is the first member of the aromatic hydrocarbon family, and has six carbons in a ring, joined by alternating single and double carbon to carbon bonds. Multiring structures and side chains provide for a broad variety of individual aromatic hydrocarbons. As the name of this type of hydrocarbon suggests, many aromatics have pronounced odors. Benzene exhibits chronic toxicity and is considered to be among the most highly toxic of the petroleum hydrocarbons. Some of the multiring polycyclic aromatic hydrocarbons are known human carcinogens (109-110).

Solvents

Petroleum solvents, like gasoline, are complex mixtures of hydrocarbons. However, because of their specialized uses, most petroleum solvents have appreciably narrower boiling ranges than gasoline and are predominantly mixtures of C_8 to C_{12} hydrocarbons. As a result, petroleum solvents, though complex in composition, are generally less complex than gasoline. Most aliphatic solvents are derived from virgin petroleum stocks or are synthesized from petroleum gases. Petroleum solvents that are widely available, especially those used in consumer products, have low concentrations of benzene, normally below one per cent, with many being below 0.1 per cent.

Elkins and Pagnotto (111) felt that ordinary use of the petroleum solvent would not produce a benzene vapor hazard if the benzene content of a solvent ranged from one to four per cent by volume, but the possibility of substantial exposure to benzene vapors resulting from the "free" use of the solvent must be considered if the concentration of benzene was greater than five per cent.

Table 6 gives the physicochemical properties of several types of petroleum solvents and gasoline. Stoddard solvent is a mixture of hydrocarbons, predominantly C_9 to C_{11}, produced from a straight-run distillate of paraffinic or mixed base crude oil, and has a boiling range between 160 and 210 ^{o}C (320 to 410 ^{o}F) (112, I13). It is a clear, colorless, flammable liquid and has a minimum flash point of 38 ^{o}C (100 ^{o}F). Chemically, Stoddard

TABLE 6

PHYSICOCHEMICAL CHARACTERISTICS OF PETROLEUM NAPHTHAS

Common Name	Alternate Name	B.P. °C(°F)	Flash Pt. °C(°F)	Approx. Mol.Wt.	Carbon Number
Gasoline	Benzin, petrol, motor or aviation gasoline	32-210 (90-410)	40-70 (100-150)	100	C_4-C_{12}
VM&P Naphtha	Range of 80 thinner	95-160 (203-320)	-7 to 13 (20-55)	87-114	C_5-C_{11}
Mineral spirits (petroleum spirits)	Refined petroleum solvent, White spirits	150-200 (302-392)	0-35 (0-95)	130	C_6-C_{12}
Stoddard solvent	White spirits	160-210 (320-410)	38-43 (100-110)	140	C_7-C_{12}
High flash naphtha		150-204 (302-400)		140	C_7-C_{12}
140' flash naphtha	Aliphatic solvent naphtha	185-207 (364-403)	59-60 (138-140)	154	C_5-C_{13}
Aromatic petroleum naphtha	Coal tar naphtha	93-315 (200-600)	2-38 (35-100)	140	C_8-C_{13}
High aromatic naphtha	High aromatic solvent	184-206	62 (144)	140	C_8-C_{13}

solvent is a mixture of 30 to 50 per cent straight and branched chain paraffins, 30 to 40 per cent naphthenes, and 10 to 20 per cent aromatic hydrocarbons (114-116). A detailed analysis of the typical composition of Stoddard solvent was reported by Carpenter (113), and is presented in Table 7. Because Stoddard solvent contains 17 per cent C_9 and 65 per cent C_{10} and higher molecular weight hydrocarbons, proper recognition of the toxicity of nonane, decane, undecane, and their homologs must be taken.

Flash point values have been used by the NFPA to classify all solvents used in the dry cleaning industry into four classes (117). Class I solvents are flammable liquids having a flash point below 38 °C (100 °F). Class II solvents are flammable liquids with flash points at or above 38 °C (100 °F) but below 60 °C (140 °F). Class IIIA solvents are combustible liquids with flash points at or above 60 °C (140 °F) and below 93 °C (200 °F). Class IIIB solvents are combustible liquids with flash points at or above 93 °C (200 °F). Class IV solvents are classified as nonflammable.

Dry cleaning plants or systems are categorized into five classes according to the solvent used (117). For example, a class I dry cleaning plant would use a class I solvent such as 50 flash point naphtha, a class II dry cleaning plant would use a class II solvent such as Stoddard solvent, a class IIIA dry cleaning plant would use a class IIIA sol-

TABLE 7

COMPOSITION OF STODDARD SOLVENT

	Mass Spectral Analysis (Volume %)						
Hydrocarbon Class	Total	C_7	C_8	C_9	C_{10}	C_{11}	C_{12}
Paraffins	47.7		0.9	9.5	20.6	13.3	3.4
Monocycloparaffins	26.0	2.4	4.3	5.0	8.4	4.9	1.0
Dicycloparaffins	11.6			2.7	4.7	3.2	1.0
Benzene	0.1						
Alkylbenzenes	14.1						
Indans & Tetralins	0.5						

TABLE 8

PHYSICAL AND CHEMICAL PROPERTIES OF PETROLEUM HYDROCARBON DRY CLEANING SOLVENTS

	Type I	Type II	Type III	Type IV
Commercial reference	Stoddard	140 F Solvent	odorless	low dry point
Flash point, min. $^{\circ}$F	100	140	100	100
Distillation, ($^{\circ}$F):				
Initial boiling pt., min.	300	350	300	300
50 per cent recovered, max.	350	385	375	345
Dry point, maximum	407	412	412	365
Kauri-butanol value:				
minimum	29	29	...	29
maximum	45	45	29	45
Residue from distillation;				
Percent, maximum	1.5	1.5	1.5	1.5
Acidity	neutral	neutral	neutral	neutral
Doctor test	negative	negative	negative	negative
Copper corrosion, max rating	1	1	1	1
Bromine No., maximum	5.0	5.0	5.0	5.0

vent such as 140 flash aliphatic solvent, and class IV and V dry cleaning plants or systems would use a nonflammable class IV solvent such as PCE. Class I dry cleaning plants or systems are prohibited by law.

There are three other solvent grades similar to Stoddard solvent, all belonging to the petroleum solvent category. These are (a) 140 flash solvent, with a flash point of 139 to 142 °F, (b) odorless Stoddard, flash point 121 to 130 °F, and (c) low end point Stoddard, flash point 100 to 108 °F (966). They contain paraffins, naphthenes, and alkylbenzenes, with a trace of benzene. The American Society for Testing and Materials (ASTM) has published specifications regarding these four types of petroleum hydrocarbon dry cleaning solvents (118) which are presented in Table 8. While Stoddard solvent and white (mineral) spirits are not always considered the same petroleum products and are used differently for different purposes in industry, their boiling ranges (Stoddard solvent, 160 to 210 °C; white spirits, 150 to 200 °C) are almost identical and therefore their chemical compositions are similar. In fact, many investigators use the terms white spirits and Stoddard solvent interchangeably, and some consider Stoddard solvent to be a specific type of white spirits (113, 116, 119-121).

Annual petroleum solvent consumption by professional dry cleaning plants was approximately 87 x 10^6 L (23 million gal) in 1978 (69). Industry wide, dry cleaning employment is estimated at 140,000 (122), of which about 25 per cent work with petroleum solvents (44). In addition to the dry cleaning process, Stoddard solvent and white spirits are widely used as general cleaners and universal solvents. NIOSH (74) has compiled a list of occupations with potential exposures to petroleum solvents which can be found at Appendix C. It was estimated by NIOSH (74) that in 1976, 600,000 workers in the United States were potentially exposed to all "specialized" petroleum naphthas, 61,000 were potentially exposed to white (mineral) spirits, and 75,000 were potentially exposed to Stoddard solvent.

Animal Toxicology

Renal effects

Hydrocarbon-induced nephropathy is a nephrotoxic response to a variety of petroleum derived materials which appears to be unique in the male rat and is characterized by renal tubular degeneration/regeneration, hyaline droplet formation, granular proteinaceous casts and tubular calcification. Petroleum-derived materials that have been shown to be nephrotoxic to the male rat include various naphthas (123), solvents (124-127), certain distillate fuels (128), and gasoline blends (123, 129).

A recent study by Halder et al. (123) has demonstrated that the alkane (paraffin) components of petroleum hydrocarbon exposures are primarily responsible for the observed nephrotoxicity, with a positive structure-activity response relating the degree of alkane branching to the potency of the nephrotoxic response. In 1986, Halder et al. (130) documented that occupational exposures to gasoline vapors consist predominantly of the more volatile components of this petroleum hydrocarbon blend. They found that C_4 and C_5 hydrocarbons constituted approximately 75 per cent of the typical gasoline exposures and that four C_4 and C_5 hydrocarbons in particular, namely n-butane, isobutane, n-pentane, and isopentane comprise greater than 90 per cent of the C_4 and C_5 fraction or 61 to 67 per cent of the total vapor composition. Subsequently, Halder et al. (131) conducted a 21 day inhalation study of a mixture consisting of 25 per cent (by weight) of each of these four compounds and were unable to demonstrate hydrocarbon-induced nephropathy in the male rats exposed.

Aranyl et al. (132) exposed male and female Fisher 344 rats to a 50/50 per cent mixture (by weight) of n-butane/n-pentane or isobutane/isopentane six hours per day, five days per week for a total of 90 days. No differences in renal pathology scores were observed between the treatment and control groups at the study termination. An apparently transient, treatment-related effect was observed at the 28th day interim sacrifice in the kidneys of male rats exposed to 1000 ppm of the isobutane/isopentane mixture.

In 1984 McFarland et al. (129) reported on a chronic inhalation study which showed that whole unleaded gasoline vapor caused kidney carcinomas and sarcomas in male rats, with some evidence of a dose-response relationship. An increase in liver masses and nodules was observed in female mice. However, parallel experiments involving female rats and male mice were essentially negative. Exposure to whole unleaded gasoline vapor was for six hours per day, five days a week for 107 weeks. All of the primary renal tumors were observed in rats which died after 18 months or when the experiment was terminated at 24 to 26 months. In serial sacrifices during the first year, an early and progressive renal tubular disease was observed. During the second year, preneoplastic changes were observed and were believed to have preceded the development of the primary renal tumors. The Cancer Assessment Group at the EPA concluded that the study furnished sufficient evidence of the carcinogenicity of unleaded gasoline vapor in rats under the conditions of the bioassay and that the evidence for the carcinogenicity of unleaded gasoline vapor in rats and mice indicates that this material could be considered a potential human carcinogen (134).

Effects on the nervous system

Acute intoxication by paraffinic hydrocarbons results in central nervous system depression (135). Chronic intoxication may lead to a more persistent effect, such as polyneuropathy, because saturated paraffinic hydrocarbons have a particular affinity to nervous tissue due to its high lipid content (136). Since the discovery of the special neurotoxicity of n-hexane and the hexacarbon ketones (137), efforts have been made to investigate the neurotoxicity of other petroleum products (138).

Savolainen and Pfaffli (139) reported on the neurochemical effects in male Wistar rats of extended exposure to white spirit vapor at three concentration levels. The rats were exposed to 575, 2,875, or 5,750 mg/m^3 (100, 500 or 1,000 ppm) of white spirit vapor for 4 to 17 weeks, five days a week, for six hours each day. The neurochemical effects included a dose dependent decrease in the cerebellar succinate dehydrogenase activity with an increase in creatine kinase activity. Creatine kinase in the brain is almost solely associated with astroglial cells (140), and therefore may indicate an early astroglial proliferation. The serum creatine kinase activity, originating mainly from striated muscle, was decreased at the two higher concentration levels of exposure. Analysis of isolated muscle membrane, sialic acid and uronic acid residues, showed decreased concentrations. Sialic acid has been suggested to have a crucial role in the regulation of transmembrane calcium flux (141). Myopathic changes were found on electromyographic examination while peripheral nerve motor conductive velocities appeared normal. The authors concluded that white spirit mixtures had neurochemical effects, possibly caused by paraffinic fraction of white spirits, and that this fraction may have caused the effects seen in muscle cell membranes. The authors concluded that the lowest exposure concentration (575 mg/m^3, 100 ppm) represents a virtual "no effect" level for rats in the 17 week exposure.

Verkkala et al. (142) reported on the comparison of local neurotoxicity of three white spirit formulations by percutaneous exposure of rat tail nerve. The three white spirit formulations differed in their aliphatic and aromatic hydrocarbon concentrations. Formulations I and III contained over 10 per cent n-nonane, whereas its concentration was negligible in formulation III. Formulations II and III contained 12 and 17 per cent aromatics respectively, while formulation I contained no aromatics. Formulation I and II caused local axonopathy by neurophysiological and morphological criteria after six weeks of percutaneous exposure for five days a week, three hours per day. The appearance of the polyphasic motor response was gradual, most probably related to the local cumulative effect of the absorbed solvent molecules on the axons. No nerve motor conduction velocity changes were found to be caused by exposure to formulation III, while morphological analyses revealed infrequent demyelinative foci after six weeks of exposure. Rats exposed to formulation II containing one per cent trimethyl benzene isomers showed that urinary excretion of dimethylbenzoic acid isomers were a reliable method for biological monitoring of exposures.

Effects on the respiratory system

Rector et al. (143) exposed rats, guinea pigs, rabbits, dogs, and monkeys eight hours per day, five days per week for 30 exposure days and also for 90 days continuously to vapor of mineral spirits having a boiling range of 284 to 374 °F, and containing 13 to 19 per cent aromatics, 1 per cent olefins and 80 to 86 per cent paraffinic hydrocarbons. In the eight hour exposures at 114 mg/m^3 the only effect noted was minor congestion and emphysema in guinea pig lungs. Gross pathologic examination revealed lung congestion in all test animals exposed to the highest level of 1,271 mg/m^3, accompanied by evidence of bronchitis and mixed inflammatory cell infiltration.

Carpenter et al. (124), in 1975, reported no differences in the lung histopathology of rats or beagle dogs exposed to 480 mg/m^3 (84 ppm), 1,100 mg/m^3 (190 ppm), or 1,900 mg/m^3 (330 ppm) six hours daily for five days per week for 13 weeks when compared to unexposed controls. In 1984, Riley et al. (144) reported on the response of the upper respiratory tract of the rat to white spirit vapors at a concentration of 214 mg/m^3, for four hours per day for four consecutive days. Histological examinations of tissues from the respiratory tract revealed the presence of inflammatory cell infiltrates in the nasal cavity, trachea, and larnyx of the exposed rats. In addition, the epithelial lining of the nasal cavity and trachea showed a loss of cilia, hyperplasia of the mucus and basal cells, and squamous metaplasia. No evidence of lung parenchyma injury was noted other than the presence of numerous alveolar macrophages. The relative absence of tissue damage in the lung is consistent with the findings of others who have tested chemically similar materials (124, 143). The authors inferred that the lung escapes injury because only a small portion of the inhaled vapor remains in the lung, whereas the upper respiratory tract is continuously exposed to the full atmospheric concentration of inhaled white spirit, a theory which has been demonstrated in man with benzene vapor exposures (145).

Hepatotoxicity

It has been observed that the lower- and medium-chain alkanes are hydroxylated in the liver microsomes of mammals by monoxygenase system involving NADPH, O_2, and cytochrome P-450 (146, 147). Carpenter, et al. (148) studied the toxic manifestations produced by n-nonane vapor up to the level of 1,600 ppm in rats. There was a consistent suppression of body weight gain and signs of toxic stress after repeated exposure to n-nonane vapor at this dose level. However, there was no indication that the 13 week inhalation exposure, even at the 1,600 ppm level, produced any liver abnormalities: BUN, SGOT, SGPT, alkaline phosphatase, and liver histopathology were all normal at week 13.

Reports by Kahn and coworkers (149, 150) reveal that there is a decrease in hepatic protein content and microsomal damage after intraperitoneal administration of n-octane and n-nonane to albino rats as well as an increase in the activity of hepatic alkaline phosphatase (151). In 1985, Kahn and Pandya (152) reported on the effects of n-octane and n-nonane on hepatic and serum enzymes, lipids, and nucleic acids. They reported a significant decrease in serum acetylcholinesterase activity and albumin content, possibly due to disturbance in secretory mechanisms because of liver cell necrosis, as well as an overproduction of some proteins such as alkaline phosphatase. A fall in carboxylesterase was apparently associated with parenchymal cell degeneration and necrosis (153, 154). An increase in serum FDP aldolase activity was present. A decrease in total and esterified cholesterol in the serum and an increase in hepatic free cholesterol contents were observed, indirectly indicating destruction of the hepatic smooth endoplasmic reticulum membrane which may lead to alteration in the esterification process in the liver (155). Serum albumin and total protein were also significantly decreased.

Other effects

Nau et al. (156) reported the earliest study of the potential toxicity of aromatic-rich naphthas in which rats, mice, rabbits, and monkeys were used and exposures included inhalation, skin application, and subcutaneous injection.

Test animals were exposed to a $C_9 - C_{10}$ aromatic rich fraction distilled at 311 ^oF to 392 ^oF, a $C_{11} - C_{12}$ aromatic-rich fraction distilled at 392 ^oF to 480 ^oF, n-decane, and benzene. Exposure levels ranged from 50 ppm to 1,000 ppm for 23.5 hours per day, seven days a week for between 51 to 150 days for the rats studied, and between 50 and 200 ppm for 90 days for the monkeys studied. It was reported that the inhalation of $C_9 - C_{10}$ and $C_{11} - C_{12}$ fractions at greater than 500 ppm decreased the total leukocyte and lymphocyte counts but did not produce the myelotoxic effects characteristic of benzene. The inhalation by monkeys of 50 or 200 parts of $C_9 - C_{10}$ or $C_{11} - C_{12}$ for 90 exposures of seven hours each led to skin irritation, a reversal of the polymorphonuclear/lymphocyte ratio, depression of the myelocytic activity and stimulation of the erythrocytic activity of the bone. There was also a pronounced early tremor and a decrease in the white blood cell count in those monkeys exposed to $C_9 - C_{10}$. Exposure by inhalation of n-decane at 560 ppm produced significant increases in total leukocytes and expected animal body weight gain. Skin application of $C_9 - C_{10}$ or $C_{11} - C_{12}$ led to pathological changes in the skin and internal organs (unspecified) of greater intensity and severity than that produced by benzene or n-decane. They noted the results of subcutaneous injection of test materials were not consistent with the inhalation toxicity or percutaneous toxicity of the same compounds. It was recommended that eye contact and percutaneous exposures to these liquid hydrocarbon fractions be carefully avoided by use of protective shields and clothing. In 1974, Grant (157) reported that Stoddard solvent was essentially innocuous to the rabbit cornea.

Mutagenicity, Teratogenicity and Tumor Promotion

In 1984, Conway et al. (158) utilized a test battery consisting of the Ames salmonella assay, the L5178Y mouse lymphoma assay, and rat bone cytogenetics to evaluate mutagenic activity of petroleum base stocks, fuels, and lubricants. Unleaded gasoline, kerosene, and Stoddard solvent were judged not mutagenic by each of the three bioassays utilized for testing. Also in 1984, Gochet et al. (159) assessed the mutagenic and clastogenic potential of white spirit solvent using the Ames test, the induction of sister chromatid exchanges in vitro in mammalian cells, and the micronucleus test of mouse bone marrow cells. The authors concluded that white spirit does not display mutagenic properties based on the negative results obtained in all three test systems.

As early as 1957, Horton et al. (160) reported that repeated applications of pure n-dodecane promotes skin tumors in mice that have received an initiating dose of 7,12-dimethylbenz(a)anthracene and that n-dodecane, without preliminary initiating treatment, is inactive. In 1966, Sice (161) reported on the tumor promoting activity of n-alkanes and 1-alkanols applied to the skin of mice following treatment with an initiating dose of 7,12-dimethylbenz(a)anthracene. Decanol, dodecane, and tetradecane were the most potent promoters of papilloma growth of the pure n-alkanes and 1-alkanols tested. Tumor promoting potency was related to carbon chain length with a distinct peak in activity appearing for dodecane (C_{12}) among the alkanes and for decanol (C_{10}) for the 1-alkanols.

In 1981, Philips <u>et al.</u> (162) reported on the potential for embryotoxic, teratogenic and mutagenic effects of commercial white spirit and $C_8 - C_9$ isoparaffinic hydrocarbon solvents. Mated CD female rats were exposed six hours a day, by inhalation, to either white spirit (100 or 300 ppm) or $C_8 - C_9$ isoparaffin (400 or 1200 ppm) from day six to day fifteen of gestation. There were no treatment related effects on implantation, implantation efficiency, number of live fetuses, or fetal resorption. External, soft tissue, and skeletal examination of fetuses recovered from white spirit and $C_8 - C_9$ isoparaffin exposed females revealed no treatment related effects. A statistically significant increase in the total incidence of fetuses with ossification variation was observed in the high exposure $C_8 - C_9$ isoparaffin group; however, the types and relative incidence of ossification variation were generally comparable to historical controls. The mutagenic potential of white spirit and $C_8 - C_9$ isoparaffin was assessed by the dominant lethal test. White spirit (100 or 300 ppm) and $C_8 - C_9$ isoparaffin (400 or 1200 ppm) were administered by inhalation to male CD rats previously proven fertile. Animals were exposed six hours a day, five days a week for eight consecutive weeks prior to mating. Pregnancy and implantation rates, implantation efficiency and fetal deaths for females mated to white spirit or $C_8 - C_9$ isoparaffin exposed males were considered comparable to controls. Therefore, at the exposure concentrations employed, neither white spirit nor $C_8 - C_9$ isoparaffin was considered as embryotoxic, teratogenic, or mutagenic to rats.

Human Effects

Case reports

In 1940, Braunstein (163) reported that a 26 year old man who worked in a dry cleaning plant and had his forearms and hands wetted with or immersed in Stoddard solvent during most of the workday developed follicular dermatitis of the exposed skin after two weeks of employment. He was admitted to a hospital about three months after his first exposure to the solvent complaining of weakness, weight loss, icterus, and vomiting. A skin sensitization test with Stoddard solvent was "highly positive." The diagnosis was made of obstructive jaundice originating in the liver parenchyma, with subacute yellow atrophy of the liver.

In 1958, Kegels (221) reported the effects of white spirits on a 36 year old man who, after four months of cleaning floors with large amounts of the solvent, was diagnosed as having aplastic anemia with thrombocytopenia and leukopenia. Kegels indicated that this man probably had a sensitivity to white spirits, since coworkers with similar exposures did not develop aplastic anemia.

The clinical histories of three fatalities from among four cases reported to have aplastic anemia as a result of exposure to Stoddard or Stoddard type commercial solvents were discussed by Scott et al. (164) in 1959. In the first fatality, a housewife used a Stoddard type solvent as well as CCl_4 for spot cleaning household rugs two or three times a month for two years before excessive uterine bleeding and purpura appeared. A bone marrow smear was classified as hypocellular, and a sternal bone marrow biopsy showed moderate hypoplasia.

The second fatal case was a high school student who had cleaned his hands in Stoddard solvent four or five times per week during a six month course in automotive mechanics. A sternal bone marrow biopsy showed marked hypoplasia and severe hypocellularity with a predominance of lymphoid elements. The autopsy report indicated moderate bone marrow hypoplasia with all normal elements present.

The third fatal case was a man who periodically used Stoddard solvent to remove paint from his hands for two years. The patient denied using other potentially myelotoxic agents. An episode of purpura, pallor, and fatigue occurred one year before his illness was first recognized and apparently subsided spontaneously. There was no clear chronologic relationship between his intermittent symptoms and periods of exposures to the solvent. The bone marrow aspirate smear was classified as slightly hypocellular. Autopsy findings showed marked hypoplasia of the bone marrow with alternating areas of aplasia and hypercellularity resulting from an increase in lymphoreticular elements.

The fourth patient was a housewife who had used a Stoddard type solvent as a dry cleaning agent for 20 years. Once every year she immersed the family clothing in a large open tub containing the solvent, usually working indoors. The patient's bone marrow smear was classified as normal in cell number. The sternal bone marrow biopsy showed normal bone development with an increase in the lymphoid elements. After splenectomy, this patient's condition improved. The authors concluded that these four cases implicated Stoddard type solvents as possible myelotoxic agents capable of producing aplastic anemia. However, they gave no information on the specific composition of the solvent(s) and were thus not able to address the possible role of myelotoxic compounds such as benzene.

In 1970, Prager and Peters (165) described a 41 year old man who had been frequently exposed to "Solvasol #5," a Stoddard type solvent, for 16 years in the course of his employment as a heavy equipment mechanic. The patient had felt progressively more tired, light-headed and bruised easily. A sample of sternal bone marrow showed no marrow particles. Bone marrow taken from the ilium showed a marked decrease in the number of marrow cells and in all cellular elements. The patient was diagnosed as having aplastic anemia and died 11 months later. The authors suggested that Stoddard type solvents might contain a myelotoxic agent which remained unidentified.

Grant (157), in 1974, reported that Stoddard solvent was essentially innocuous to the human cornea. No specific details were given.

In 1983, Churchhill et al. (166) reviewed nine published case reports and six case-control studies relating to the association between hydrocarbon exposure and glomerulonephritis. The nine publications classified as case reports describe a possible association between hydrocarbon exposures and a) Goodpasture's syndrome or antiglomerular basement membrane disease in 14 adults (167-172), b) epimembranous glomerulonephritis in five adults (173, 174), and c) subacute proliferative glomerulonephritis in one adult (175). The hydrocarbon exposures were for "solvents" in 12 cases (170, 172, 175), gasoline in four cases (167, 168, 171), and gasoline based spray paint (169), jet fuel (170), mineral turpentine (171), and unspecified (174) in one case each.

Case-control studies

Churchhill et al. (166) reviewed six case-control studies which have been published relating to the association between hydrocarbon exposures and glomerulonephritis. Five of the studies referenced (176-180) have reported a significantly greater prior exposure to hydrocarbons for patients with glomerulonephritis compared to control groups. The authors pointed out major methodologic deficiencies present in four of these studies (176-179) which they considered to seriously weaken these associations. The major methodologic weaknesses were a) the use of inappropriate control groups, b) the use of unblinded interviewers, c) failure to consider recall bias (181), and d) failure to define a credible measure of hydrocarbon exposure.

In 1979, Ravnskov et al. (180) reported an odds ratio of 3.9 (95% CL 1.9 - 8.1, p = 0.0003) for hydrocarbon exposure when 50 patients, admitted with a diagnosis of glomerulonephritis, were compared with two age and sex matched groups of hospital controls.

van der Lann (182) failed to find a significant difference in organic solvent exposure between newly diagnosed cases of glomerulonephritis and hospital outpatient controls matched for age and sex.

In 1966, Tuttle et al. (183) reported on the neurological status and behavioral performance of nine PCE exposed males, nine PCE exposed females, and nine unexposed controls, working in laundry and dry cleaning plants. Neurological status ratings were based on scores from a) reported symptoms, b) physical examination by a neurologist, and c) motor latency and conduction velocity testing by electromyography. Neurological status was shown to be significantly different ($p < 0.10$) for PCE exposed workers when compared to unexposed controls. Multiple regression analyses suggested that the neurological deficits were significantly related ($p < 0.02$) to workers' prior exposures to Stoddard solvent, not PCE.

In 1983 Stemhagan, et al. (184) reported on a case-control study of 265 persons with primary liver cancer, diagnosed between 1975 and 1980 in New Jersey, and measured occupational risk factors. They reported the relative risk estimate for gasoline service station operators to be 2.88 (95% CL 1.20 - 6.88). Among laundry and dry cleaning workers they found a relative risk estimate of 2.50 (95% CL 1.02 - 6.14) with liver cancer cases concentrated among plant operators who actually processed the clothing and were more likely to have had chemical exposures, although the specific solvent exposures were unspecified.

A case-control study of primary liver cancer and solvent exposure was reported by Hernburg et al. (185) in 1984 in which 126 cases (64 males and 62 females) and 175 hospital controls were studied with regard to solvent exposures commencing greater than ten years before diagnosis. Six female cases and no controls were exposed to dry cleaning solvents. One of the six cases was exposed only to synthetic solvents, two others used both CCl_4 and petroleum solvents, and three were exposed to petroleum solvents only. The male cases and controls showed no significant differences in solvent exposure history.

An unpublished case-control study by Bryan (186) of 197 renal cell carcinoma cases in Oklahoma showed males reporting a history of being a laundry or dry cleaning worker to have a significantly elevated relative risk estimate of 17.05 ($p = 0.0474$) when compared to hospital and population controls, while females reporting laundry and dry cleaning employment had a nonsignificantly elevated relative risk estimate of 4.32. Asal _et al._ (187) have recently completed a three year on-going case-control study of renal cell carcinoma (RCC). Potential risk factors in RCC were studied in 315 RCC cases, 313 hospital controls, and 336 population controls. Risk factors included history of employment for greater than one year in "high risk" industries such as petroleum refining and distributing, and the dry cleaning industry. The results of univariate analyses of these occupational risk factors were adjusted for age, smoking and weight, and are shown in Table 9 for both population and hospital control comparisons. Using Cox's linear logistic

TABLE 9

ODDS RATIOS (OR) AND 95% CL FOR MALE AND FEMALE RCC CASES COMPARED TO POPULATION AND HOSPITAL CONTROLS, BY OCCUPATIONAL RISK FACTOR

Occupational Risk Factor	Population Controls			
	Male		Female	
	OR	95% CL	OR	95% CL
Petroleum refining & distributing	4.3	1.7-10.9	1.6	0.4-6.5
Dry cleaning	0.7	0.2- 2.3	2.8	0.8-9.8
	Hospital Controls			
	Male		Female	
	OR	95% CL	OR	95% CL
Petroleum refining & distributing	1.3	0.7- 2.6	1.0	1.0-
Dry cleaning	2.0	0.7- 8.8	2.3	0.7-16.6

regression analyses for male cases and population controls, work in a petroleum related industry was reported as significantly associated with risk of RCC (OR = 9.4, 95% CL = 1.1 - 82.2). Neither of these associations were significant however, when male or female cases were compared to hospital controls. No significant association between RCC and history of dry cleaning employment was found by the univariate analyses of male or female cases when compared to population or hospital controls. Using multivariate techniques, no significant associations were found when male or female cases were compared to hospital controls, when male cases were compared to population controls, or when female cases were compared to population controls. Only when comparing female cases to population controls using an 11 variable model was a statistically significant association between RCC and history of dry cleaning employment noted. History of employment in the dry cleaning industry was used as a proxy for exposure to dry cleaning solvents. The detailed lifetime occupational histories collected have been linked to the solvent use characteristics of specific dry cleaning plants in Oklahoma to estimate, when possible, the actual solvent exposures and durations of exposure experienced by male and female cases and controls, and are presented in Appendix H. Of the eight female cases of RCC, three were found to have had no solvent exposures. Three others had unknown exposures; two were pressers with 2 and

11.5 years of employment respectively, and the third had an unknown dry cleaning job title for 8.5 years. One female case was exposed to PCE for two years, and one female was exposed to petroleum solvents while employed as a presser for four years, and was also exposed to an unknown solvent in an unknown dry cleaning job title for 8.5 years. The elevated odds ratio for female dry cleaners in this case-control study is consistent with the Oklahoma dry cleaner cohort mortality data previously reported by Duh and Asal (22) in which the SMOR for kidney cancer for all sex and race groups was 3.9 (95% CL = 1.9 - 7.6). This increased risk among female, but not male Oklahoma dry cleaners is not consistent with a sex-specific reanalysis of this cohort mortality data in which the PMR for kidney cancer among 181 white male Oklahoma dry cleaners was 6.86, (95% CL = 2.51 - 14.93) but only 1.20 (95% CL =0.03-6.69) among 220 white females. No kidney cancer deaths were found among 17 black males or the 22 black females in the study.

In 1981, McLaughlin et al. (188) reported on the results of a population-based case-control study of RCC involving 495 cases and 697 controls and noted that a significant association was found for exposure to petroleum, tar, and pitch products. In 1985, McLaughlin et al. (188a) reported on the reanalysis of the relationship between petroleum related employment and RCC using the males from the previously reported case-control study (188). They reported 37 per cent of cases and 36 per cent of controls held jobs with potential petroleum exposures (odds ratio = 1.0). The risk of RCC was not related to length of employment in petroleum related occupations. For employment as a gasoline station attendant, a slight overall association with RCC (odds ratio = 1.2) was observed, with six per cent of the cases and five per cent of the controls having worked in this capacity. The risk increased with the number of years employed in gasoline service stations, but the trend was not statistically significant.

In 1981, Chapman et al. (189) found a larger than expected proportion of male controls that had been laundry and dry cleaning workers in an occupational bladder cancer case-control study. Smith et al. (190) reported bladder cancer risk among laundry workers, dry cleaners, and others in chemically related occupations. The exposed groups included 103 cases who reported having ever worked in a laundry or dry cleaning occupation as operatives for at least six months, and a chemically related exposure group of 5,766 bladder cancer cases which included those who either worked in other occupations or industries that might expose them to similar chemicals or indicated exposure to chemicals found in the laundry and dry cleaning business. These groups were compared to 1,869 population based controls. Little excess risk was found to be associated with either occupational exposure group, based on relative risks in the exposed or chemically related exposed nonsmokers. No significant interaction between occupation and other potential risk factors, such as cigarette smoking, was found. The authors concluded that the chemicals to which laundry workers and dry cleaners are exposed do not appear to increase the risk of bladder cancer.

Pitha et al. (197) have reported on a blinded, retrospective study of the histopathologic features present in the apparently normal kidney parenchyma removed with the tumor from ten hydrocarbon exposed and twenty unexposed nephrectomized renal cell carcinoma cases previously identified by Asal et al. (187). The objectives of the study were to correlate the histopathologic findings observed among the ten exposed cases in relation to their occupational hydrocarbon exposure, and to compare the differences in renal pathology between each exposed case and its two matched unexposed cases. Hydrocarbon exposure indices were developed and criteria established for matching exposed and unexposed cases and for scoring the histological sections. Slides from each of ten exposed/unexposed sets of three cases were independently reviewed and reported by a panel of three consulting pathologists. Analyses of the data indicated no correlation between the indices of exposure and pathology scores among exposed cases and no significant differences in renal pathology within matched exposed/unexposed sets.

Cohort studies

In 1962, Kaplan and Zeligman (191) found that the use of kerosene or mineral spirits for cleaning caused dermatitis in 10 of 98 railroad maintenance workers. The extent or duration of vapor exposure or liquid contact was not reported.

In 1973, Ramos and Shama (192) reported that exposure to petroleum distillate (naphtha) caused dry throats, burning or tearing of eyes, mild headaches, dizziness, respiratory irritation, and, in some cases, dermatitis in workers of an electric company. They determined that the TWA exposures to the distillate vapors ranged from about 25 to 274 mg/m^3. There was no apparent relationship between solvent concentration and symptomatology. The dermatitis was believed to be caused by direct contact with the petroleum distillate, and ranged from mild redness of the skin to fissuring and blister formation.

Markel and Shmunes (193), in 1974, described the health hazard evaluation of a Stoddard solvent exposure at a greeting card company. Twelve workers were exposed to a concentration of Stoddard solvent of 99 to 1,906 mg/m^3 (average, 438 mg/m^3) in their working environment. The authors concluded that, under the conditions found at the time of the survey, Stoddard solvent did not constitute a hazard to the health of the workers on the basis of pulmonary function tests (forced expiration volume, and forced vital capacity) and a serologic antigen test.

In 1974, Larsen and Shmunes (194) reported that Stoddard solvent used to clean polishing machines were probably the cause of dermatitis in several industrial workers. The workers also complained of headaches and eye and nose irritation. Although the detectable concentrations of Stoddard solvent were less than 115 mg/m^3 (20 ppm), the authors felt that higher concentrations could have occurred immediately after the polishing machines were cleaned with Stoddard solvent, which could have caused the headache and eye and throat irritation.

Dry cleaner mortality studies

A review of all published mortality studies of dry cleaners can be found at Table 10a.

Blair et al. (21) reported, as the preliminary results of a cohort study of 10,000 laundry and dry cleaning workers, a proportionate mortality analysis of 330 of the workers who had died during the period 1957 to 1977. Deaths were identified from the mortality records of two union locals in St. Louis, Missouri. The distribution by cause of death among the 330 was compared to that expected based on the proportionate mortality experience of the United States. Only 279 of the 330 had worked exclusively in dry cleaning establishments; however, the authors did not analyze the proportionate mortality of these 279 separately. The dry cleaning solvent(s) used by the dry cleaners in this study

TABLE 10a

REVIEW OF DRY CLEANER MORTALITY RATIOS, BY STUDY AND CANCER SITE

Study	Years	Sex	Race	Study Type	Total Deaths	Cancer Deaths
Blair (21)	1957-77	All	All	PMR	87	1.28*
Katz (23)	1963-77	Female	White	PMR	141	0.96
Duh & Asal[a] (22)	1975-81	Male	White	PMR	181	1.46**
	1975-81	Female	White	PMR	220	0.62**
Washington (26)	1950-79	Male	White	PMR	1268	1.09
	1974-79	Female	White	PMR	398	0.83
Massachusetts (24)	1971-73	Male	White	MOR	52	0.94
Nakamura (27)	1971-80	Male	Japanese	SPCMR	297	1.00
	1971-80	Female	Japanese	SPCMR	133	1.00
Brown & Kaplan (25)	1960-82	Male	White	SMR	33	1.07
	1960-82	Female	White	SMR	39	1.07
	1960-82	Male	Black	SMR	37	1.45*
	1960-82	Female	Black	SMR	33	1.10

*$p < 0.05$, **$p < 0.01$, [a]using a sex-specific PMR reanalysis of the data

TABLE 10a (Continued)

Study	Sex	Race	Buccal Cavity	Biliary & Liver	Pancreas	Lung
Blair (21)	All	All	-	2.35	1.29	1.70*
Katz (23)	Female	White	-	0.89	1.17	0.98
Duh & Asal[a] (22)	Male	White	-	1.64	0.95	2.22**
	Female	White	-	-	0.35	0.77
Washington (26)	Male	White	2.24**	1.98*	0.99	1.02
	Female	White	1.18	0.50	0.71	0.69
Massachusetts (24)	Male	White	0.88	-	1.39	1.15
Nakamura (27)	Male	Japanese	0.83	1.04	0.62	0.92
	Female	Japanese	0.91	0.67	0.48	1.55
Brown & Kaplan (25)	Male	White	1.11	-	1.11	1.00
	Female	White	2.00	-	1.67	1.03
	Male	Black	1.00	-	1.43	1.76
	Female	Black	-	-	2.86	-

*$p < 0.05$, **$p < 0.01$, [a]using a sex-specific PMR reanalysis of the data

TABLE 10a (Continued)

Study	Sex	Race	Breast	Kidney	Bladder	Stomach
Blair (21)	All	All	0.69	2.00	0.83	1.47
Katz (23)	Female	White	0.72	2.57*	1.89	0.34
Duh & Asal[a] (22)	Male	White	-	6.86**	0.70	0.63
	Female	White	0.10**	1.20	-	0.61
Washington (26)	Male	White	-	0.74	1.19	-
	Female	White	0.90	1.45	1.51	-
Massachusetts (24)	Male	White	-	4.46**	-	0.32
Nakamura (27)	Male	Japanese	-	0.89	1.36	0.97
	Female	Japanese	0.28*	2.50	-	0.86
Brown & Kaplan (25)	Male	White	-	1.43	2.73	-
	Female	White	0.89	3.33	4.00	-
	Male	Black	-	-	5.00*	-
	Female	Black	0.88	3.33	-	-

*p < 0.05, **p < 0.01, [a]using a sex-specific PMR reanalysis of the data

TABLE 10a (Continued)

Study	Sex	Race	Intestine	Uteri	Skin	Lymphoma
Blair (21)	All	All	-	2.08	4.29**	-
Katz (23)	Female	White	-	1.95*	2.07	1.79
Duh & Asal^a (22)	Male	White	-	-	1.67	-
	Female	White	-	1.67	1.54	1.92
Washington (26)	Male	White	-	-	1.11	0.48
	Female	White	-	1.46	-	0.73
Massachusetts (24)	Male	White	-	-	-	1.58
Nakamura (27)	Male	Japanese	1.70*	-	1.43	-
	Female	Japanese	0.15*	0.96	-	-
Brown & Kaplan (25)	Male	White	-	-	-	-
	Female	White	-	-	-	-
	Male	Black	-	-	-	-
	Female	Black	-	-	-	-

*p < 0.05, **p < 0.01, ^{a}using a sex-specific PMR reanalysis of the data was unknown. Among the 330 deaths, cancer of the lung, cervix, and skin contributed to the finding of a significant excess of deaths from cancer at all sites ($p < 0.05$). For lung cancer, there were 17 deaths observed versus ten expected; for cervical cancer, ten observed deaths versus 4.8 expected; and for skin cancer, three observed deaths versus 0.7 expected. A significant deficit of deaths occurred in the cause of death category identified as "all circulatory diseases," with 100 observed versus 125.9 expected ($p < 0.005$), a finding that could account for the excess proportion of cancers observed.

In 1981, Katz and Jowett (23) analyzed the death certificate records of 671 white female laundry and dry cleaning workers who had died during the period 1963 to 1977. The records of dry cleaning workers were not studied separately from those of laundry workers, since both groups of workers shared the same occupational code. Furthermore, the actual solvent to which the dry cleaners were possibly exposed was not known. In this study, cause-specific proportionate mortality for the 671 deceased female laundry and dry cleaning workers was compared to that for the deaths of all other working females in Wisconsin during the same period, and to deaths of females in "lower-wage occupations" in Wisconsin during the same period. Significantly elevated proportionate mortality ratios were found for deaths from cancer of the genitals (unspecified) (PMR = 4.67 to

4.95,p < 0.01) and for deaths from cancer of the kidney (PMR = 2.53 to 2.57,p < 0.05) when deaths among women of all occupations and deaths among women of "lower wage occupations" were used as the comparison groups.

Duh and Asal (22) analyzed the death certificates of 440 laundry and dry cleaning workers who had died in Oklahoma during the period 1975 to 1981. Occupations were identified from the death certificates, therefore laundry workers could not be separated from dry cleaning workers because they shared the same occupational codes. Age, sex, race, and cause distribution of deaths in the United States in 1978 were used as the standards of comparison. An analysis was done using the standardized mortality odds ratio (SMOR) (195). The SMOR differs from the more traditional PMR in that it compares the number of deaths from the cause of interest to the number of deaths from "auxiliary" causes in the exposed population, the odds to the expected odds derived from a comparison population, taking into account covariates such as age, sex, and race. The SMOR for homicide was the only SMOR in the study group that was significantly elevated for noncancer causes of death (SMOR = 3.8, 95% CL = 1.4 - 10.6; observed deaths = 7, expected deaths = 2.9). Deaths from ischemic heart disease were significantly decreased (SMOR = 0.8, 95% CL = 0.7 - 1.0; observed = 134, expected = 153.7). Among deaths from cancer, the SMORs for cancer of the respiratory system

(SMOR = 1.8, 95% CL = 1.3 - 2.5; observed = 39, expected = 23.9); cancer of the lung (SMOR = 1.7, 95% CL = 1.2 - 2.5; observed = 37, expected = 22.6); and cancer of the kidney (SMOR = 3.8, 95% CL = 1.9 - 7.6; observed = 7, expected = 1.9) were significantly elevated. Deaths from cancer of the breast were significantly decreased (SMOR = 0.1, 95% CL = 0.0 - 0.4; observed = 1, expected = 10.5). Since, as the authors noted, wage levels in the laundry and dry cleaning industry are not high, the excess of homicide and the deficit of breast cancer and ischemic heart disease may have resulted from the inverse correlation with socioeconomic status. Smoking histories were not available. Because both lung and kidney cancer have been associated with smoking, it is difficult to evaluate the study's elevated SMORs for those diseases with respect to dry cleaning solvent exposures. The authors did note, however, that mortality from other smoking related diseases such as emphysema, ischemic heart disease, cancer of the buccal cavity, and pharyngeal cancer were slightly less than expected. The occupational code that identified the study group included both laundry and dry cleaning workers and would tend to weaken any association that might have been present by adding to the group at potential risk a number of individuals that would not otherwise have been considered exposed.

Nakamura (27) studied the age-standardized proportionate mortality occurring among 1,711 members of the All Japan Laundry and Dry Cleaning Association (AJLDA) who died between 1971 and 1980. Additional data on smoking and drinking habits and exposure history were obtained from the families of 294 AJLDA members who died between 1979 and 1981. No excesses of overall cancer were noted for either male (SPMR = 100) or female (SPMR = 104) laundry and dry cleaning workers. For both males and females, a statistically significant excess occurred for "other forms of heart disease," such as cardiac insufficiency, congestive heart failure and cor pulmonale and "other diseases of the liver," which included hepatic coma, hepatitis, acute and fulminant hepatitis, acute liver failure and liver failure.

Using a method of standardized proportional cancer mortality, a significant increase in mortality was noted due to cancer of the small intestine, including duodenum (18 observed vs. 10.6 expected, $p < 0.05$) for males and for bone cancer (5 observed vs. 0.5 expected, $p < 0.01$) for females. Of the 294 deaths occurring between 1979 and 1981, 272 can were analysed by selected cause of death, and by laundry or dry cleaning worker status. Only 143 (52.6%) of 272 were reported to be dry cleaners.

Cancer mortality among oil refinery workers

It has been estimated that there are more than 100,000 workers in 300 operating refineries in the United States (198). These workers are exposed to a great variety of crude and refined petroleum products, solvents, petrochemicals and fuel additives. There have been at least eight epidemiologic studies that directly assessed cancer risks among refinery workers (199-206) as well as early surveys (207, 208) and subsequently updated studies (209, 210). Reviews of these studies have been published by Savitz and Moure (211) and Futagaki (212) for all cancer sites, and by Raabe (213) and Enterline and Viren (214) for kidney cancer. Increased risk has been reported for cancer of the esophagus (200), stomach (200, 204, 209), pancreas (204, 205, 209), leukemia (204, 209), multiple myeloma (209), nasal cavity and sinuses (202), and the skin (202).

Wen (206) postulated that the divergent and inconsistent findings from these studies may be due to:
variations in study design and study subjects; differences in sample size, lengths of observation and exposure experience; variations in quality and completeness of data collected; and different methods of analysis, such as the standardized mortality ratio versus the proportionate mortality ratio.

Savitz and Moure (211) identified three major methodological concerns which applied to refinery worker mortality studies. First and foremost, exposure definition was very weak, failing to identify which chemicals were involved, and having few details regarding exposure intensity or duration. A second major concern in this literature is with latency and the failure to examine cancer risk in the appropriate time period. The third issue concerns potential confounding influences which includes the absence of data on cigarette smoking and ethnicity.

If the positive findings in refinery worker mortality are restricted to those with statistical significance, no consistent positive results were found for any cancer site. Given the methodological concerns outlined above, excess risk may have been overlooked and attention should be focused on those cancers for which some evidence of an occupational excess exists, notably melanoma, leukemia, and cancers of the stomach, brain, kidney, and pancreas.

Experimental human studies

Drinker et al. (97) noted that gasoline vapor at concentrations of 1,000 ppm caused slight dizziness, nausea, and headache in several volunteers exposed for one hour. Sayers et al. (96) had previously reported, in 1927, similar symptoms in humans exposed to concentrations of ethyl gasoline ranging from 700 to 2,800 ppm for 14.5 to 50 minutes. In 1943, Nelson et al. (215) described the eye, nose, and throat irritation experienced by ten men and women exposed to Stoddard solvent at varying concentrations for three to five minutes. The authors had observed that solvent concentrations greater than 400 ppm were irritating to the eyes, nose, and throat of most subjects, and that concentrations less than 400 ppm would be satisfactory (presumably in terms of comfort) for an 8-hour exposure.

Nau et al. (156) reported in 1966 that an "aromatic-rich" mixture of C_9-C_{10} fractions produced by catalytic reforming, distilled at 311 to 392 ^{o}F and having an average molecular weight of 125, had a minimum identifiable odor level of 11 mg/m^3 (2 ppm). The minimum concentration which produced lacrimation and/or irritation of the eyes, skin, and mucous membranes was found to be 138 mg/m^3 (25 ppm).

In 1975, Carpenter et al. (113) used six volunteers, ages 25 to 48, to determine the odor threshold for Stoddard solvent. The volunteers were exposed to graded concentrations ranging from 0 to 50 mg/m^3 (0 to 9 ppm) based on a mean molecular weight of 144. The odor threshold was between 0.5 mg/m^3 (0.09 ppm) and 5 mg/m^3 (0.9 ppm). The sensory threshold to vapors of Stoddard solvent was determined for six volunteers, ages 25 to 59 who were subjected to the solvent at concentrations of 140, 850, and 2,700 mg/m^3 (24, 150, and 470 ppm) for 15 minutes. No eye irritation was noted at 140 mg/m^3, but slight and transitory eye irritation occurred in one of six volunteers at 850 mg/m^3 (150 ppm). At 2,700 mg/m^3 (470 ppm), all six experienced eye irritation, three with tearing. Slight dizziness also was reported by two subjects at the 2,700 mg/m^3 concentration (470 ppm). Olfactory fatigue occurred at all concentrations tested. Volunteers who experienced olfactory fatigue recovered full acuity within ten minutes after they were removed from exposure.

In 1975, Astrand et al. (216) reported the effects of exposure to white spirits on alveolar air and blood solvent concentrations during rest and exercise. Fifteen men ages 20 to 34, were exposed to 1,250 and 2,500 mg/m^3 for 30 minutes during rest and for 20 minutes at each of three work intensities corresponding to light industrial work, manual labor, and heavy manual labor. One man developed premature atrial beats in conjunction with solvent exposure. No differences were noted in heart rate, alveolar ventilation, or oxygen uptake either at rest or during exercise due to solvent exposure, nor was the blood lactate content affected. A linear relationship between the arterial and alveolar concentrations of the aliphatic and aromatic fractions was noted, but the aliphatic components were not very soluble in blood. The authors concluded that the solvent content of the exhaled or alveolar air was less reliable than measuring the blood concentration of aliphatic and aromatic fractions when assessing uptake. As expected, more solvent was absorbed during exercise than during rest, confirming that work intensity may influence solvent vapor toxicity.

In 1975, Gamberale et al. (217) studied the effects of white spirit exposure on perceptual speed, reaction time, short-term memory, numerical ability, and manual dexterity. Fourteen men, age 18 to 34 were exposed to concentrations of

625, 1,250, 1,875, and 2,500 mg/m^3 for four consecutive 30 minute periods. The authors concluded that exposures to white spirits at these concentrations probably did not affect the performance tests. Eight men were exposed to 4,000 mg/m^3 of white spirits for 50 minutes with no effect on perceptual speed, numerical ability or manual dexterity. There was, however, a definate prolongation of reaction time and a possible impairment of short-term memory as a result of the higher exposure level.

In 1984, Pedersen and Cohr (218) reported the effect of a six hour single exposure of 12 volunteers to 100 ppm of white spirit containing 99 per cent paraffins, 52 per cent paraffins and 48 per cent naphthenes, and 18 per cent aromatics. The serum concentrations of alpha-amylase, cholesterol, triglyceride, sodium, potassium, creatine kinase, orosomucoid, urate, and glucose were measured in 12 volunteers 6 and 48 hours after the start of exposure. The only significant changes reported were a decrease in serum alpha-amylase and potassium levels 48 hours after exposure to the white spirit high in napthenes. In a subsequent study (219) seven subjects were exposed to 100 ppm of white spirit containing 99 per cent paraffins six hours per day for five days. The baseline plasma concentrations of IgG, IgA, IgM, orosomucoid, and serum concentrations of creatine kinase and follicle stimulating hormone (FSH) were compared to the values obtained 24 hours, 96 hours, and 158 hours after the start of the exposure. A dose related significant increase in serum creatine kinase concentration, and decrease in serum FSH were observed. The peak increase in serum creatine kinase took place 168 hours after the initial exposure and was 76 per cent above the baseline. The peak decrease in serum FSH concentration occurred 24 hours after the initial exposure and was 11 per cent below the base line.

In 1985, Pfaffli (220) reported that the mean excretion rates of urinary dimethylbenzoic acid isomers, a trimethylbenzene metabolite, were linearly correlated to the total hydrocarbon exposure experienced by a group of white spirit exposed car washers.