Chapter 9
Respiratory Disorders

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Firefighting involves inhalation of products of combustion, toxic materials that happen to be on site, and particles generated by debris from disintegrating structures. Obviously the lung is the organ of first contact and plays a role both as the route of entry for systemically toxic agents, such as carbon monoxide and cyanide, and as target organ for these various insults, either acute or chronic. The first has been obvious and well accepted. Acute effects on the lung itself have now been well characterized. However, chronic effects on the lung itself have been difficult to prove until suitable longitudinal studies of pulmonary function became available. It is still remarkable how little non-cancer lung disease is associated with firefighting considering the extent and severity of the hazards. Nonetheless, chronic lung disease clearly does exist as a risk of firefighting,

One reason for the difficulty in demonstrating chronic effects was that early population studies focused on the question of whether mortality was elevated from chronic obstructive pulmonary disease (COPD) rather than using functional, measurable endpoints as outcomes. Another reason is that the extant literature for years did not appreciate the time course of acute effects. When functional endpoints were examined, the results were not always interpreted as they would be today. Even in retrospect, however, there was not much to suggest a relationship. One of the few studies of that era to use an index of exposure also did not show an exposure-response relationship, after an initial period likely to represent a subpopulation of recent hires who did not make it through probation [1].

Chronic respiratory disease other than lung cancer has not been prominent in population-based studies of firefighters and cohort mortality studies have generally not shown an effect. One apparent exception is a cohort followed in the US Pacific Northwest up to 1980 that was reanalyzed and found to show a healthy worker effect for overall mortality (SMR 82), which had been absent in most studies of that

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era, and no elevation in mortality from non-malignant respiratory disease (81; 71–89) when compared to the US general male population. On the other hand, firefighters were reported to show an excess risk of respiratory disease deaths (SMR 141; 86–294) when compared to police. However, in this study police had an unusually low mortality from non-malignant respiratory disease (SMR 48; 25–84), compared to the general US population [2]. Thus, it seems more likely that the study was actually uninformative, because of an anomaly in the police, rather than being the strong evidence for an effect among firefighters that the authors suggested.

A more nuanced way of thinking about lung effects was to consider acute and chronic on a continuum of effects [3]. Earlier investigators were not remiss in neglecting this obvious natural history. However, the evidence compiled to test this line of thinking was initially misleading.

Acute lung injury, as with other toxic effects, should be proportional to exposure, both in terms of peak concentration (which would be expected to correlate with provocation of bronchospasm, and cumulative exposure, or dose, which would be expected to correlate with inflammation and chronic effects. In one particular bad office building fire in Los Angeles burning polyvinyl chloride released clouds of thick black smoke (such fires also produce hydrochloric acid) and 19 firefighters demonstrated transient hypoxemia and two who were also involved in fire suppression did not. When they were retested a month later and compared to matched controls, they had returned to baseline lung function, which was within predicted limits for all but four who smoked. This study suggested that the acute lung injury of smoke inhalation was transient and did not lead to immediate de-compensation of baseline function. The authors concluded that acute smoke inhalation did not appear to predispose to the development of chronic respiratory symptoms or chronic functional respiratory impairment." [4] However, in retrospect this is an over-interpretation of the data in what is a small study, based on an exposure that is not representative of fire smoke in general. The study could not rule out a contribution to cumulative damage and risk of accelerated loss of function over time. Indeed, those are precisely the predominant concerns today.

The paucity of evidence for a benign (non-cancer) respiratory effect left the field in some turmoil. It seemed obvious that firefighters should be at risk for lung disease, both malignant and non-malignant. However the empirical evidence in the 1908s and 1990s was not supporting these conjectures. In the end, it was the wrong type of evidence.

Acute Effects

The lung is a structurally simple but vulnerable organ, intimately linked physiologically as well as physically to the heart and circulation, and continuous with the upper respiratory tract, which is the site of many important host defenses that protect it, which shares many responses with the lower respiratory tract (such as airways reactivity) and the digestive system, to which it is related embryologically.

Because of its structure simplicity and functional limitations, the lung has only a limited number of possible responses to toxic injury and the immune or inflammatory reaction to that injury, which can be categorized in general terms as airways responses (reactivity and inflammation), alveolar and vascular responses (pulmonary edema and pneumonia-like inflammatory infiltrate), interstitial responses (most obviously pneumoconioses, of which asbestosis is most commonly cited by firefighters as a risk. (Although asbestosis itself is not observed, the risk of asbestos exposure relevant to cancer has now been indirectly confirmed by the demonstration of high rates of mesothelioma (an asbestos-associated disease) among firefighters [5].) Studies of the prevalence (usually) or incidence of lung disease, symptoms, and loss of pulmonary function among firefighters are relatively few and in the early years mostly cross-sectional rather than longitudinal. The latter is much more useful, both in determining both causation and disease risk and because decrement in lung function over time has high predictive value for individual prognosis as well as group risk.

Studies of lung disorders or of lung function are well-recognized to be subject to bias, most obviously confounding from smoking. Smoking rates appear to be less among firefighters than in the general population, so that there is a built-in overcorrection in mortality studies where the reference is the general population but when firefighters are studied alone or with a highly-selected comparison group (such as police), attribution becomes difficult. Survivor bias is a major problem in firefighters, because the well-known "healthy-worker effect" appears to be much less strong, historically, for firefighters than for other occupations of comparable socio-economic status (SES) but has also improved in recent years, creating a temporal discontinuity. (There is also a temporal variation in exposures due to changes in composition of housing and building materials.) Misclassification bias becomes a serious problem in studies of firefighters when attempting to make associations with particular disease categories, such as isolating risk among airways disorders (asthma, bronchitis and bronchiolitis, emphysema and their combinations, in the form of COPD).

Further, knowledge of the respiratory outcomes associated with firefighting has changed in recent years due to intensive studies of the New York Fire Department (FDNY) members who responded to the World Trade Center (WTC) tragedy in 2001, and for which anomalous types of airways disease have been reported (in particular, forms of bronchiolitis previously under-appreciated). These findings support the impression that WTC responders are experiencing different health care outcomes from other municipal firefighters without WTC-related exposures.

Acute Effects on Lung Function

That firefighters may experience short-term drops in blood oxygen (hypoxemia) following smoke exposure has been known for many years and was quantified in the early studies of firefighters at a time when synthetic materials were already installed in residences and office buildings.

In the pioneering Boston studies, acute inhalation to fire smoke in a relatively unremarkable series of fires was noted to be associated with decreases in FEV_1% of 0.050 l on average, a reduction that is significant for a pre-/post-exposure change but not likely to be noticed by the firefighter, and 0.10 l in 30 % of subjects suggesting a subset with increased susceptibility (although only one subject in 39 gave a history of asthma). The loss of pulmonary function was transient but was proportional to intensity of exposure. Of interest is that second exposures within hours resulted in greater acute reductions in flow, proportional to the previous exposure. Cough and eye irritation were frequent but not severe [6]. Not commented on was the observation that in a small fraction of observations (roughly a third), flow not only did not decline but increased, greatly so in a few subjects, suggesting some unrecognized mechanism of bronchodilation.

The susceptibility of a subset of firefighters was further underlined with a small case series of prolonged reactive airways disease following exposure to fire smoke containing pyrolysis products of polyvinyl chloride (PVC), which consist principally of vinyl chloride and hydrochloric acid [7]. These cases, two of which would today be considered irritant-induced asthma and the other a severe organizing bronchitis modified by steroids, were used by the authors to highlight the dangers of PVC pyrolysis and combustion products. However, it can also be interpreted as highlighting the paradox that whether from exposure or susceptibility characteristics, relatively few firefighters show such dramatic changes.

Firefighters are not immune to the effects of cigarette smoking and evaluation of baseline function must therefore take smoking into account. Comparing smokers and non-smokers, most smoking firefighters had preserved the major ventilatory measures of pulmonary function (FVC, FEV_1) although they tended to have symptoms of productive cough, but a minority showed decreased FEV_1, FEV_1% ($\leq$70), or dV_{max}, while nonsmoking firefighters did not. (Such results are entirely to be expected among smoking populations.) More interesting, while as expected small airways disease (by the He dilution method) was present in firefighters in 35 % of smoking firefighters, without restriction by age, small airways disease was also present in 13 % of nonsmoking firefighters, but only among the nonsmoking firefighters with $\geq$25 years of fire service. The degree of small airways disease was not enough to cause respiratory impairment to be clinically significant. A small subset of these firefighters were engaged in one particular fire but did not show marked changes in their baseline lung function after the fire. The authors commented that their results were relatively benign in part because the fire was not especially severe, as indicated by relatively low carboxyhemoglobin measurements. Even so one of their cases, who had exhausted his SCBA air supply while in the basement of a building and had to breathe smoke on the way out, required hospitalization and had a profound chronic respiratory impairment and ultimately had to leave the fire service [8]. This relatively early study established that smoking played a role in respiratory impairment equal to or more likely greater than fire smoke inhalation under normal firefighting operations, but that under abnormal conditions acute and severe respiratory effects were possible, even in fires that did not involve exceptionally toxic inhalation (such as the combustion and pyrolysis products of polyvinyl chlorine mentioned above).

The issue of susceptibility naturally arises first in the context of airways reactivity and prior history of asthma. Therefore it was natural, in the subsequent groundbreaking study, to evaluate the acute response to fire smoke among firefighters in light of their baseline airways responsiveness to methacholine, the provocative test for airways reactivity. In a series of determinations following otherwise unremarkable fires, it was found that 24 % of firefighter subjects transiently lost more than 2 standard deviations in FEV_1, although as much as 10 % in only two (about 7 %) of cases, both of which showed increased methacholine responsiveness. Contrary to expectations, however, the degree of loss was not proportional to the initial degree of airways reactivity [9]. This led the authors to conclude that fire smoke acted by means other and in addition to simple airways irritation. However, three of the five subjects with greatest pre-/post-fire changes in flow had histories of childhood asthma. The study did not factor in smoking history, in part because the design of the study was grounded on physiological rather than toxicological principles and did not take into account possible tolerance effects. It was also impractical, given the study design requiring multiple measures, to recruit a reference population. Unfortunately, the study could not be repeated with a larger population and with a reference group.

Understanding of the acute effects of smoke inhalation has required studies conducted under controlled circumstances. The previous approach of studying firefighters following uncontrolled events proved to be misleading (see above). In practice, this has meant studying lung function, inflammatory responses, and physiological responses following controlled burns or in smoke chambers. In one such study using smoke chambers, in Singapore, an ethnically homogeneous group of firefighters (Malay) without airways reactivity (by histamine challenge) at baseline showed transient, acquired airways reactivity following smoke exposure, and a subset that had prolonged duration of reactivity showed persistence of flow reductions even after reactivity came back to normal after 24 h.

Similarly, a panel of Seattle firefighters, none of whom had documented asthma, showed exposure duration-related acutely decreased airflows (FEV_1, $FEF_{25–75\,\%}$) and airway responsiveness to methacholine from their baseline within hours after firefighting, with associated reduction in specific airway conductance. The findings were unrelated to smoking [10].

Less physiologically-grounded, more clinically-relevant studies also demonstrated that although most firefighters show a relatively small reduction in lung function, principally in FEV_1 and $FEV_{25–75\,\%}$ (indicative of small airways abnormality), a small subset showed more profound changes that could interfere with function [11]. These changes were independent of lung function.

Further studies during the overhaul phase of firefighting identified it as associated with acute decline in ventilator measures and increased measures of inflammation (CC16 and SP-A, described in the next subsection), and correlated with carboxyhemoglobin levels [12]. This strengthened the growing impression that overhaul involved significant exposure and could be as risky as knockdown. However, at the same time, an anomaly was identified in that similar changes were seen in firefighters who used cartridge (air-filtering) respirators, suggesting that the cartridges were not completely effective protection. This evidence argued strongly

for using SCBA during overhaul, rather than relying on air-filtering devices. However, practical considerations make this difficult on the ground.

Acute onset of respiratory symptoms, including shortness of breath, mucosal irritation and sinusitis were also documented, in addition to transient lung function changes [13].

At the same time, a parallel series of studies demonstrated that the same effect was observed among wildland firefighters. (Not reviewed here.) This was important in establishing that synthetic materials were not the only cause of acute lung function change, as wildfire smoke is predominantly of lignocellulose origin and less irrigating than smoke from burning synthetic materials. It was unclear which combustion products were responsible. However the wildland firefighter population also demonstrated an anomaly: not showing the expected response to increased concentrations of smoke-derived irritants [14]. Rather they were behaving as if exposure to wood fire smoke triggered a limited, maximum reaction.

Acute Inflammation

Concomitant with acute changes in pulmonary function are changes in the expression and release of various acute response and inflammatory markers following exposure to fire smoke, at least in studies unconfounded by smoking. Not surprisingly, exposure to fire smoke provokes an acute inflammatory response in the lung, release of neutrophils and their accumulation in sputum, and release within a few hours of biomarkers such as IL-6, IL-8 and TNF-α, accompanied by a rapid decline in IL-10 (cytokines) [15, 16]. Similar effects were seen in wildland firefighters [17]. The lung response evolves to lymphocyte proliferation and elevation of fibronectin in lavage fluid [18]. (Novel biomarkers, including chitotriosidase, have been studied as a predictor of chronic effects in the World Trade Center population [19] but not as yet among firefighters in general.) None of this is surprising or out of keeping with what is known of the inflammatory response in the lung.

A more specific indicator that may be of value in structural firefighters is elevation in high-sensitivity C-reactive protein (CRP) levels. The elevation in CRP levels predicts reduced levels of airflow, although longitudinal data have not been conducted to assess causation [20]. In addition to suggesting a candidate for an inexpensive, readily available clinical marker, the finding is also consistent with the view that acute inflammation changes functional capacity and that effects might be cumulative.

Acute oxidant and irritant gas exposure may result in deep lung injury and capillary leak (also known, in the terminology of pathology, as “diffuse alveolar damage” and in the clinical literature as “toxic inhalation”), which progresses over time (usually hours) to first interstitial and then alveolar pulmonary edema, which carries a high mortality [21]. Fortunately, this outcome is rare in firefighters, despite the potential for it. The probable reason is that exposure to common fire smoke does not include the one combustion product most likely to do this: nitrogen dioxides.

The oxides of nitrogen can be formed from combustion but require high heat or pressure to produce in quantity. Rather toxic inhalation and pulmonary edema are more likely to occur in burning hazardous materials, or "hazmat" situations, where the combustion source and substrate produces highly reactive chemical products that are relatively water-insoluble and so penetrate to the deep lung, such as phosgene and paraoxons. These situations are not common, fortunately.

Transition from Acute to Chronic Effects

Baseline circulating surfactant-associated protein and Clara cell protein (CC16) levels were lower for firefighters than police, in a cross-sectional study [22]. However, this should not be over-interpreted as suggesting that police have a higher level of response by inflammation in the lungs. More likely, inflammation in the lungs of firefighters may be low between incidents of exposure levels or conceivably tolerant or even downregulated in response to multiple acute inflammatory responses, whereas in police there may be more frequent low-level provocation of inflammation due to air pollution or vehicle exhaust.

It now seems clear that most of the acute effects of fire smoke resulting in lung responses are reversible and correct over a relatively short period, under normal circumstances. However, an individual firefighter may reach a tipping point in response to unusually severe exposure or because of personal susceptibility. In those exceptional cases, the acute effect results in subacute or chronic injury of such magnitude that it leads to impairment or prolonged recovery.

Chronic Effects

Since 2001, the literature on chronic pulmonary health effects in firefighting has featured two areas of emphasis: the experience of undifferentiated municipal firefighters and that of respondents to the World Trade Center (WTC) tragedy. As noted earlier in Chap. 1, the exposure regime and the pattern of health outcomes are different for WTC responders and this is reflected in the compensation criteria for surviving FDNY responders, which is handled separately from claims from other firefighters and which has its own presumption criteria. While some lessons from the WTC responders are obviously generalizable, much is not. One example of a seemingly unique WTC-related phenomenon is the frequency of progression of what initially appears to be restrictive disease in a subset of WTC responders but which in fact represents air trapping [23], a finding that is suspected to be associated with the pathology of constrictive bronchiolitis [24]. This is not a feature of the literature on firefighters in general. Thus, this section will mention WTC responders only sparingly and where the issue is narrow and clearly relevant to all municipal firefighters.

Pulmonary Function

One of the seminal studies on firefighters was significant not only because it proved an effect but because it provided the explanation as to why other studies did not. This early observation was then largely overlooked or forgotten by other investigators.

The pioneering studies on lung function among firefighters were conducted in Boston in the 1970s [6, 25–30]. Measurement of lung function by spirometry at baseline was repeated at one year and subsequently at an average interval of three and one-half years. The study revealed that lung function declined over time but not in a steady way and that the decline was not associated with the frequency of fires attended or, oddly, with smoking history. However, the study had many anomalies. Cigarette consumption was inversely proportional to the number of fires fought. (This is consistent with a firefighter having had enough of smoke of any kind, but also introduces a counter-trend that may have confounded the result.) Firefighters who had fought no fires had a higher rate of decline in ventilator measures, both FVC and FEV_1. (This suggests that there was a reason they were being kept away from fires, not that other duties affected their lung function.) Firefighters who had been involved in knockdowns or who had experienced "shellackings" or "pastings" (colloquial terms for being overwhelmed by smoke) did not show disproportionate decrements in pulmonary function. Excluding firefighters on the sick roll or with known illness did not affect the result. However, 21 % of subjects were lost to follow up, a very high number for a longitudinal study spanning only 3 years, and those who left the fire service had shown greater than average decrements in lung function on the first round of testing, after 1 year. Faced with these contradictions, the authors concluded that there were major confounding factors of selection that resulted in affected firefighters being excluded from service [28]. A second study, conducted on retirees, showed that selection factors within the fire service resulted in protection of firefighters in that era through transfers, administrative promotions, and especially retirement [29]. A third study at 6 years showed no accelerated loss of lung function, which was attributed to success in encouraging adherence to SCBA usage but may have been an artifact of the strong selection pressure that operated on firefighters who were symptomatic or even possibly subclinical but less robust in their performance. In the 6-month study, the authors recognized the earlier pattern of out-migration and internal accommodation within the fire service in their data [27].

The expected association between firefighting and accelerated decline in lung function was finally demonstrated unequivocally in a cohort of Boston firefighters studied by a different group. They determined that firefighters had a greater loss of pulmonary function than a non-firefighter male reference group followed in a normative aging study, together with larger variation (as measured by standard error, SE) and that the effect was not explained by age alone, initial function, or smoking, although smoking was associated with clinical symptoms (such as cough). For FEV_1, nonsmoking firefighters showed an average annual decline of 81 ± 19

(SE) ml/y compared to 64 ± 3.9 for nonsmoking subjects of the aging study. Initial function was higher for firefighters than for the reference population, which the authors credited to selection bias due to employment standards [31]. This study, by Sparrow et al., established that exposure to fire smoke is associated with accelerated decline in lung function in firefighters, as it is in other occupations with respiratory hazards.

However, this apparently clear demonstration of an association was then made not so clear, by a series of unrelated studies suggesting that cigarette smoking was a clear risk factor for decline in lung function but that firefighting, as a risk factor, showed primarily short-term effects and little evidence for chronic impairment in the long-term [32, 33, 8]. Even so, there were exceptions among these studies, in two of which firefighters demonstrated chronic changes that were associated with respiratory symptoms [11, 13] and one which suggested that cigarette smoking, in a population of high-prevalence (43 %) smoking Polish firefighters, played a minor role and that the effect of firefighting predominated.

Finally, an important study of professional firefighters in Seattle demonstrated that while ventilatory measures were indeed preserved in a stable population of volunteer subjects (implying the possibility of self-selection bias), the firefighters showed a decline in diffusing capacity ($D_{L\blacksquare CO}$) after adjustment for relevant factors such as age and smoking. The decline appeared to have two components: a general trend of decline associated with year and a much smaller decline associated with number of fires fought [12].

$D_{L\blacksquare CO}$ is routinely obtained in diagnostic pulmonary function testing but is not a screening test. $D_{L\blacksquare CO}$ correlates empirically with many disorders that affect the opportunity for gas transfer, but as a clinical study it is primarily useful for diseases that have less relevance for firefighting, such as interstitial lung disease. For other lung disorders, the $D_{L\blacksquare CO}$ has substantial drawbacks as a physiological measure, related as it is to blood volume, perfusion, and diffusing time, and so its use as a screening test for firefighters was not recommended.

Not surprisingly, among premorbid risk factors, firefighters with α_1- antitrypsin deficiency lung function showed accelerated loss of lung function, even in phenotypically PiZ heterozygous firefighters who have a moderate serum level of circulating protease inhibitor [34]. Although empirically demonstrated for World Trade Center respondents, this particular finding of susceptibility is almost certainly generalizable to normal fire smoke and is observed in other situations of occupational exposure, and so is mentioned here. Homozygous PiZZ persons are unlikely to qualify or be retained as firefighters because their defect is likely to result in impairment that would disqualify them based on employment standards.

By far the most important susceptibility state across the range of pulmonary outcomes, however, is asthma or atopy, the hereditary predisposition to allergy characterized by asthma, sinusitis, childhood eczema, and allergic rhinitis and marked by an increase in serum immunoglobulin E and accompanied by airways hyperreactivity (the degree of which is quantified by responsiveness to inhaled methacholine). People with atopy are also variably predisposed to other lung conditions which are associated with decline in lung function. (The “Dutch hypothesis”, which links this

"allergic diathesis" with lung cancer and COPD remains to be proven definitively but is widely accepted.) For firefighting subjects with allergy or asthma, the primary problem is apportioning their decline in lung function among three drivers: atopic predisposition (hereditary), firefighting (acquired and occupational), and smoking (acquired and non-occupational). The problem is complicated in that, as described above, fire smoke can induce airways reactivity acutely. Dutch investigators (no relation) attempted to do so by examining firefighters who had not been exposed to fire smoke for at least 7 days. They found that increased airways responsiveness to methacholine was significantly associated with the number of fires fought in the previous 12 months, after adjustment for smoking (which had an independent effect) and for history of atopy, and that this effect was unaffected by age or gender. There was a strong interaction between atopy and the number of fires fought. The principal conclusion of the study was that firefighters, especially those with asthma or atopy, needed to adhere to respiratory protection [35]. However, the major contribution of this study to new knowledge was to elegantly unpack the relative contributions of the three drivers.

Bringing some confusion back into the order that had been emerging, a study from South Australia of longitudinal pulmonary function among municipal firefighters found multiple influences [36]. The reference population was a probabilistic sample of the adult (male) population of South Australia, monitored in a longitudinal health survey. The great majority of participants had either quit smoking or never smoked; depending on whether the first or second round of testing was used to define the "cohort", smoking prevalence rates were 5 % or 10 %. The methodology was somewhat unusual, in that an extreme case definition of accelerated decline in lung function was used to define the outcome: > 50 ml/y, reported to be the average annual decline for heavy smokers in Australia (the average for the general population is about 30). By comparison, most such studies are based on measured airflow or difference from previous measurement [37]. This study demonstrated that there was more than one trend playing out, which is another way of saying that there were probably multiple confounders obscuring the main trend of association between decline in lung function and fire smoke exposure. One trend was that younger generations of firefighters showed better pulmonary function at the time of entry into the fire service than their elders, so the population effect overall was clearly confounded by differences in the subcohorts. Another trend was that lung function did decline over time at an accelerated rate in older firefighters (>45 years), but stayed the same or even increased in younger firefighters (a highly improbable result, which will be discussed in detail below); the control population showed the expected slow longitudinal decline. The third trend was that preservation of lung function was associated with active use of respiratory protection. Firefighters gained more weight (although this finding was not statistically significant) than reference subjects. They did not report more asthma but did report a lower prevalence of chronic bronchitis and emphysema (6 %) compared to reference subjects (27 %), as would be expected among nonsmokers. Yet another trend, acknowledged by the authors, is the healthy worker effect [36].

This study has many issues, which the authors recognized. One is that the follow-up time was very short, less than 3 years on average, possibly too short to establish

a stable trend against a background of some variability. There were probably too few smokers to study interactions with smoking. Because of this, the proper comparison might have been between firefighters and nonsmokers in the reference group, which was not reported, although it should have been taken into account in the regression model.

On the face of it, the finding of a greater trend toward loss of lung function among firefighters who do not reliably use respiratory protection, which suggests that fire smoke has an effect, is inconsistent with no loss or an increase in lungfunction among firefighters compared to non-firefighters. Of course, an actual increase in lung capacity is not strictly possible but might appear to be the case with the reversal of reversible airways disease in a substantial number of subjects. The prevalence of asthma in a very large percentage of this population was not reported but was ruled out either, so this remains a possible explanation. It may also be that the case definition approach turned a continuous function (airflow) into a binary or step function and so distorted the regression analysis. There was a difference in the methodology of spirometry, with a stricter protocol for the firefighters, but a systematic error would not explain why firefighters' lung function appeared to increase. One possibility is that if there were significant error in the measurement, in which case there may have been a statistical regression to the mean after the initial measurement gave a skewed response. In short, this study is essentially uninterpretable on the basis of longitudinal trends, probably because of multiple confounding and dissimilarity in smoking prevalence, although it is suggestive that respiratory protection is a successful means of preserving lung function. As follow-up lengthens, the meaning of these trends may become clearer.

What is required, clearly, is a longitudinal study of firefighters without exceptional exposures large enough to have sufficient power to resolve trends due to occupation, smoking, atopic diathesis (including asthmahistory), and aging. Such as study is currently underway in the FDNY, where established protocols and identical equipment and technical staff ensured consistency. The FDNY team is following 940 new firefighter hires since the WTC tragedy, and using a much smaller number (97) of EMT personnel as a reference group; firefighters have more stringent employment standards. The prevalence of smoking overall was 3.5 %. Data from the first 5 years has now just become available, separated by overall rates and those for nonsmokers. The firefighters were significantly taller and had higher initial ventilator function; turnover was very low and the few firefighters who separated were individually documented not to have left for respiratory disability. Perhaps surprisingly, the study demonstrated an average loss of ventilatory function as FEV_1 of 45 ml/y for both groups, with essentially no difference (there was slightly greater decline in FEV_1%, which is a calculated rather than a primary indicator). There was no difference observed between nonsmoking and smoking firefighters, probably because the period of follow-up was too short for this to become apparent in the relatively young population of new firefighters; weight gain was the only factor observed to affect the trend in both occupational groups. The authors pointed out that in addition to being much larger than previous studies and having a much lower smoking prevalence to contend with, this was the first study to document longitudinal trends in a firefighter population with mandated and high levels of SCBA compliance [38].

Thus, the most defensible conclusion at present is that the current generation of firefighters is not demonstrating accelerated decline in ventilatory function, at least at this early time in their careers, probably because of enforced adherence to policies requiring use of respiratory protection. Older cohorts, however, may demonstrate some accelerated loss of airflow but the situation is complicated by cohort effects and is highly multifactorial, with ample room for confounding. Taking into account the important role of SCBA as effective protection, it can finally be concluded that fire smoke is indeed associated with accelerated decline in ventilatory function but that the contemporary firefighting profession is protected to the extent that firefighters adhere to appropriate respiratory protection.

Clinical Outcomes

Pulmonary function reflects physiological changes. Clinical outcomes involve the appearance of distinct symptoms (which for lung disease emphasize cough, shortness of breath, and wheezing) or the diagnosis of specific diseases. The two main diagnoses of concern are asthma and obstructive airways disease, not to be confused with COPD (which implies the characteristic lung disorder due to smoking). Bronchitis, as has been shown, clearly occurs as an acute response and a chronic form of bronchial inflammation (as opposed to the characteristic lung disorder of chronic bronchitis) may contribute to asthma and obstructive airways disease in firefighting. Interstitial disease due to pneumoconiosis does not seem to occur in firefighters, although exposure to asbestos is confirmed and some mineral dust exposure may occur incidentally in the course of duties. (Mineral dust exposure is much more likely to be a factor in the WTC responders.) Sarcoidosis is discussed in Chapter 7, lung cancer in Chapter 6.

Asthma

By definition, asthma is a disorder of reversible airways obstruction. Because it is defined by a nonspecific functional change and not by pathology or etiology, asthma is not really a single disease, although the respiratory disorder that children get and often outgrow probably is a coherent diagnosis. There are many other types of asthma but two are of most concern to firefighters. One is the importance of a history of asthma, either current or in childhood, as a marker for atopy and reactive airways, which may render a firefighter more susceptible to the effects of fire smoke. The other is irritant-induced asthma, which is a form of new-onset asthma in the adult that occurs when inflammation is induced in the airway by exposure to chemical irritants, as occur in abundance in fire smoke. It is suggested (see Chap. 5) but not proven that fire smoke is probably more irritating than cigarette smoke because the latter contains some agents that tend to damp down inflammation, including nicotine. This means that for a given exposure, fire smoke is likely to induce more inflammation

acutely and ultimately induce greater chronic effects than the same exposure to cigarette smoke. Of course, exposure to cigarette smoke is usually much higher because it is inhaled intentionally and repetitively into the respiratory tract as a nicotine-delivery device. Fire smoke is likely to cause chronic irritant-induced occupational asthma, whereas cigarette smoke induces its characteristic deep lung lesions resulting in emphysema in part because the smoke is more tolerable in the short term.

Given the acute changes in airflow and the known susceptibility of the airway to irritant-induced inflammation and bronchospasm, it is rational to expect that asthma rates would be elevated in firefighters. Surveillance data, which inevitably are biased by gross underreporting, suggest that firefighters had the second-highest reported rates of work-related asthma among all occupations in California, after janitors, in the mid-1990s [39]. Because of extreme and often systematic biases in reporting, which amplify the effects of small errors and distortions, reported rates are untrustworthy and the remainder of the list (which included bus drivers and "eligibility clerks" among high-risk occupations) is not so plausible.

Prevalence studies of asthma among firefighters, using a battery of diagnostic techniques with bronchoprovocation being the gold standard, confirms that asthma is under-diagnosed by community physicians among firefighters, at about 6 % for Swiss firefighters; a prevalence of 14 % was suggested as closer to the true value [40]. Brazilian municipal firefighters had a prevalence of symptoms leading to clinical diagnosis of asthma (without the gold standard) that was about 9.3 % and higher than police [41]. It would appear, then, that Swiss physicians are relatively conservative in making the diagnosis. However, these prevalence rates of asthma are still not far from reported asthma prevalence in most developed countries.

It should be noted that the default diagnosis of many uncritical clinicians for any variable lung disease is often "asthma", especially in a non-smoker. (In a smoker, it would be "COPD".) Some of the WTC responders have carried the diagnosis of asthma from their local physicians without confirmation or specialist evaluation. They are now being reevaluated through the efforts of monitoring programs, often receiving more nuanced diagnoses.

In short, given the combination or accelerated decline in ventilator function (see earlier discussion in this section) and induction or irritant airways inflammation, some individual firefighters may be pushed into respiratory impairment or insufficiency, particularly following poor recovery from unusually intense exposure situations. Thus, reversible airways obstruction in the form of irritant-induced asthma cannot be ruled out for firefighters but it must be very uncommon, especially with adequate respiratory protection. The picture is undoubtedly confused by inconsistency in the diagnosis of asthma.

Chronic Obstructive Airways Disease

Chronic obstructive airways disease is used here as a descriptive term for acquired fixed airflow obstruction with or without airways reactivity, in order to emphasize the functional changes and to avoid the term "COPD". "COPD" is sometimes used

casually in medicine and epidemiology as a generic term for fixed airways obstruction, but in occupational and pulmonary medicine it has a well-understood and accepted definition as the name of a particular disease associated with smoking.

Chronic obstructive pulmonary disease (COPD) is a clinical entity, associated with a smoking habit, that involves individually variable contributions of three specific processes. (1) Emphysema is a general term for simplification (destruction) of the lung architecture. In smoking-related emphysema, it starts at the level of alveoli and shows a specific pathology (peribronchiolar alveolitis). As it progresses, it results in fixed airways obstruction and a rapid decline in ventilatory function over the long term. (2) Chronic bronchitis, an inflammation of the airway wall, can be a primary diagnosis but is most often minor or absent in COPD. 3) Variable degrees of reversible airways obstruction and hyperreactivity, which may or may not present clinically as asthma but is mostly responsible for short-term changes in lung function and is responsive to the same treatment. COPD may have all three elements or proportions of each, with fixed airways obstruction predominating but reversible airflow obstruction being the major target of treatment. There are other emphysemas, asthmas, and bronchitides besides those associated with smoking. They are not "COPD" in the true sense.

The population mortality studies discussed earlier (in great detail for cancer outcomes) are consistent in not showing elevated mortality from what would be recorded (and routinely misclassified) on a death certificate and compiled in vital statistics as "COPD", asthma, or total respiratory disease. Much as in asthma among firefighters, the search for the crime in the form of chronic obstructive airways disease associated with firefighting has not turned up either a victim or a smoking gun.

Firefighters can develop COPD if they smoke. However, fixed airways obstruction among firefighters, in the absence of smoking, would not be true COPD. It would be a form of chronic obstructive airways disease with its own features, characterized by accelerated decline in ventilatory function (see above). It would lack or modify the characteristic pathology of peribronchiolar inflammation and would probably have more regular features of bronchitis, with changes in the airway epithelium characteristic of chronic inflammation. To date, evidence for a novel type of chronic airways obstruction has been difficult to find. Even at the accelerated loss of function documented in older firefighters, they may escape respiratory impairment in their lifetime if their smoking habit is not extreme.

One reason for this paradox is that firefighters are under so much selection pressure. Individuals with a susceptibility to lung disease, either known or inapparent (see the reference above to the "Dutch hypothesis") may be self-selected to be more resistant to the irritating effects of fire smoke. This is speculation, because there is no biological marker for the effect other than rate of decline in lung function over time.

Individual cases of emphysema, respiratory disability, and respiratory failure are documented, such as the PVC-related cases noted above. Unfortunately, the few older case reports lack essential exposure information and clinico-pathological correlation and have been silent on degree of airway inflammation and presence or absence of obliterative bronchiolitis. These features would be considered essential to a contemporary case report. There have also been clear cases of misdiagnosis and misclassification in the literature, including asthma that was demonstrated without question to be advanced emphysema but was still misidentified as asthma in the title of the article [42].

In short, given the probability that accelerated decline in ventilator function (see earlier discussion in this section) could push some individuals into respiratory insufficiency, particularly following unusually intense exposure situations, fixed airways obstruction and chronic obstructive airways disease cannot be ruled out as a risk for nonsmoking firefighters but it must be rare.

Conclusion

The weight of evidence at present supports the conclusion that individual firefighters may be at risk for disabling lung disease following specific, acute events associated with extreme exposure, which may interact with individual susceptibility. Individuals who have experienced these catastrophic events will have a compatible history.

The weight of evidence at present supports the conclusion that firefighters are at general risk for lung symptoms and decline in function in any form, probably highly variable. When it appears, this condition is typically diagnosed in the community as asthma. It may clinically resemble adult-onset, intrinsic asthma (which is actually often a form of chronic bronchitis) but in fact may consist of the inexorable accelerated decline of pulmonary function into clinical impairment, combined with a superimposed irritant-induced bronchitis. However, the condition is more complicated than conventional intrinsic asthma and is not well characterized.

The clinical picture in firefighters is confused in part because of intense selection pressure frequently resulting in high or supranormal lung function on entry and preservation of lung function over many years despite inhalation of irritants that would normally be associated with accelerated decline. The picture that results appears to feature unusually stable lung function at baseline on which is superimposed multiple episodes of short-term, acute changes from which the lung recovers easily, until an exceptional exposure reaches a tipping point.

The weight of evidence at present does not support the conclusion that firefighters in general are at risk for chronic fixed obstructive airways disease as a direct result of firefighting in unexceptional situations. It is well known that unusually intense and toxic exposures (for example, to oxidant gases) may induce different types of obstructive airways disorders (such as bronchiolitis obliterans) but such cases are fortunately unusual and demonstrate compatible histories. Firefighters are of course not immune to smoking-related COPD if they smoke. Older firefighters who smoke and who have documented histories of participation in many knockdowns might experience an accelerated decline in lung function that "catches up with them" during their lifetime and presents as the onset of "COPD" after retirement, since clinicians would not be able to distinguish COPD from other forms of fixed airflow obstruction. Across the board, however, fixed airways obstruction does not appear to be a general or common problem among firefighters, contrary to expectation. This conclusion cannot be held too dogmatically, however, because all studies necessary to resolve the complicated issues have not been done and there is a strong healthy worker effect.

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