

## Chemical Sensitivity and the Environment

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### **Controversies in Allergy**

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The rapidly accelerating rate of growth of modern technology has been accompanied by a proliferation of chemical entities that supports the view that ours is a chemical environment. Whether isolated from natural products or synthesized for commercial usage, the ubiquitous nature of the chemical agent is widely appreciated; it has been estimated that as many as 2,000 new compounds are introduced annually. The growing realization of the widespread presence of hazardous chemicals in our environment has rendered critical the problem of chemical susceptibility originally described by Randolph almost 30 years ago.<sup>1</sup> While celebrated instances of gross contamination through industrial waste have long been the object of professional attention, it is only recently that literally thousands of chemical products heretofore believed innocuous have been incriminated as agents of homeostatic dysfunction. With the discovery that the chemical incitant may trigger a maladaptation response in virtually any of the four smooth muscle systems (cardiovascular, respiratory, gastrointestinal, genitourinary) or the skin, has come the realization of the gravity of chemical sensitivity.<sup>2</sup> Moreover, current research identifies disease onset with incitant sensitization and not with the end stage process, as has been done previously. Over the past three years, some 700 reports have isolated instances of chemical sensitivity to commonly encountered environmental incitants. An attempt will be made in the discussion which follows to present the problem of chemical susceptibility as it is encountered in three major components of our environment: air, food, and water.

In the past two years, hundreds of reports have testified to the dangers of chemical agents, and the problems in isolating these incitants. This matter is complicated by the fact that sensitivity to one chemical often triggers a host of other sensitivities to both chemicals and foods. As Zschunke<sup>3</sup> observes, the rate of technological growth has greatly complicated the already difficult job of tracing environmental chemical incitants. Nevertheless, countless reports continue to emerge which affirm previous findings and define an increasing number of new sensitivities to chemical agents long considered harmless.

Current data affirm the view that conventional methods for the isolation of chemical incitants may no longer be effective. With the findings that sensitivities occur in association with subthreshold and picomolar quantities of chemical agents,<sup>4</sup> has come the discovery that standard procedures such as skin tests often fail to demonstrate positive reactions which are clinically verifiable.<sup>5</sup>

Recent literature verifies previous findings regarding the harmful effects of certain chemical incitants, such as formaldehyde,<sup>6</sup> phenol,<sup>7</sup> chlorine, and petroleum alcohol.<sup>8</sup> Commonly encountered chemicals such as glycine,<sup>9</sup> chlorophenothane, toluene and turpentine,<sup>10</sup> have been associated with the triggering of a plethora of vascular alterations, and some chemicals, such as hydralazine have been found to induce advanced-stage disease processes.<sup>11</sup>

The growing awareness of the significant chemical contamination of our air and water supplies is illustrated by the increasing body of research which has attempted to isolate environmental incitants. Water contaminants have been shown to trigger vascular alterations,<sup>12</sup> while air pollutants such as suspended particulates, formaldehyde, and ozone have been associated with dysfunctions ranging from mild respiratory distress to severe central nervous system disorders.<sup>13</sup>

A number of familiar metals have been incriminated, among them nickel, cobalt, chromium,<sup>14</sup> aluminum,<sup>15</sup> mercury,<sup>16</sup> and platinum.<sup>17</sup> Other common environmental chemical incitants include xylene,<sup>18</sup> various acylates,<sup>19</sup> and acrylated prepolymers,<sup>20</sup> benzoyl peroxide, carbon tetrachloride,<sup>21</sup> sulfates,<sup>22</sup> dithiocarbamates,<sup>23</sup> and isocyanates.<sup>24</sup>

While the list of potential chemical incitants is far too extensive to explore in detail, an attempt will be made to elucidate the hazards present for the chemically sensitive individual in a variety of circumstances.

## Chemical Contamination in Foods

The widespread contamination of our urban water and food supplies is witnessed by the increasing use of food additives, preservatives, and dyes in the manufacturing and processing of commercially available food products. Recent research has made it increasingly apparent that many chemicals in products which we consume must be viewed as incitants capable of triggering a wide variety of disease processes.

The literature on the dangerous effects of alcohol and tobacco has long been well documented and accepted. Nevertheless, research continues to elucidate the role played by both substances in the mediation of an ever-increasing number of symptoms. Gong<sup>25</sup> presents evidence of ethanol-induced bronchospasm, and reports of chemical sensitivity to tobacco glycoproteins,<sup>26</sup> of tobacco dermatitis,<sup>27</sup> and of tobacco-induced Raynaud= phenomenon<sup>28</sup> are not uncommon.

The literature abounds with reports of chemical sensitivities<sup>29,30</sup> to many food and water contaminants in the form of additives. The notion of food allergy has become immensely complicated with the discovery of food-contaminant sensitivity, forcing researchers to define more clearly the nature of the incitant, not only as it is encountered in foods, but in the air and water as well. Bell<sup>31</sup> has reported urticarial reactions and immunological changes as a function of exposure to a number of food additives. Condemi<sup>32</sup> and Bell both suggest that food dyes may trigger reactions in sensitive individuals; such reactions may even include psychiatric conditions commonly thought to be psychogenic, such as certain forms of hyperactivity. Lindemayer<sup>33</sup> has presented data which associate urticarial reactions with several additives, such as p-hydroxybenzoic acid methylester, p-hydroxybenzoic acid propylester, benzoic acid, sodium benzoate, ponceau rouge, and indigo carmine. Monroe=s<sup>34</sup> data indicate a causal role played by tartrazine azo dyes and salicylates in the provocation of vascular alterations. Other additives, including sodium nitrite and sodium glutamate, have been found to trigger migraine phenomena in susceptible patients.<sup>35</sup>

The ability of food preservatives such as sulfur dioxide and sodium salicylate to provoke asthmatic reactions continues to receive documentation<sup>36,37</sup> and some data incriminate aspirin additives and aspirin-like food contaminants and dyes in the triggering of symptoms ranging from urticaria and angioedema to bronchoconstriction and purpura.<sup>38</sup> An even wider variety of symptoms, including severe gastrointestinal disorders, has been associated with sensitivities to aniline, commonly found in rapeseed oil.<sup>39</sup>

Current research is expanding awareness of the role of chemical incitants in mediating what have long been considered food allergies. Data reported by Bell suggest that the study of chemicals which are the digestive by-products of common foods such as wheat and milk may provide a greater understanding of this interface between food and chemical sensitivities.

## Chemical Incitants in the Home Environment

Recent attention focused on the analysis of indoor air pollution has led to the discovery of a multitude of sensitivities to chemicals confronted in the home environment. Over the past few years articles of personal hygiene, clothing, furnishings, and countless commonly used household products have been incriminated as triggering agents of homeostatic dysfunction.

Time and space limitations allow only a cursory review of the numerous hygienic products which have been revealed as noxious for the chemically susceptible individual. Among these are a wide variety of cosmetics,<sup>40,41</sup> particularly those containing glycerin, propylene glycol, or butylene glycol,<sup>42</sup> perfumes,<sup>43,44</sup> and hair products such as dyes,<sup>45,46</sup> creams,<sup>47</sup> sprays,<sup>48</sup> and shampoos.<sup>49</sup> Moreover, sensitivities have been demonstrated to occur in association with lip salve,<sup>50</sup> fingernail preparations,<sup>51</sup> soaps,<sup>52</sup> sanitary napkins,<sup>53</sup> mouthwash,<sup>54</sup> antiperspirants,<sup>55</sup> contact lenses,<sup>56</sup> contact lens solutions,<sup>57</sup> and suntan lotions.<sup>58</sup>

Reports of sensitivities to textiles and to those chemicals used in the processing of clothing continue to appear. ElSaad<sup>59</sup> reports sensitivities to synthetic acrylic fibers, and Burrows= data indicate the existence of contact dermatitis secondary to polyester spin finishes.<sup>60</sup> Recently, the epoxy resins used in manufacturing many trousers have been isolated as triggering agents, and reports on synthetic clothing as environmental antigens are widespread.<sup>61</sup> Products such as spray starch used in the maintenance of fabrics may also be considered toxic for

the chemically sensitive individual,<sup>62</sup> for whom, as Larsen's interesting study suggests, even the metallic buttons on blue jeans may trigger reactions to nickel.<sup>63</sup>

Many household cleaning products, particularly those containing formaldehyde, have been shown to be hazardous for many. Several laundry products and detergents may be identified as household irritants,<sup>64</sup> as well as a number of products used to clean and polish furniture.<sup>65</sup>

It is increasingly apparent that the very construction of many homes may prove dangerous for the chemically sensitive patient. A considerable amount of data suggests that chemicals contained in wood preservatives are environmental irritants capable of triggering a variety of symptoms.<sup>66-68</sup> Frigas<sup>69</sup> has reported asthma secondary to household insulation containing urea formaldehyde foam, and scattered reports suggest that petrochemical contaminants in construction products such as plaster<sup>70</sup> and cement<sup>71</sup> may also trigger chemically induced reactions.

Other products commonly encountered in the home have been identified as environmental irritants. Current data support earlier findings regarding the hazards of pesticides<sup>72</sup> such as 2,4 DNP and fungicides.<sup>73</sup> Moreover, research increasingly suggests the possibility of sensitivities to apparently innocuous items such as rubber bands,<sup>74</sup> coins,<sup>75</sup> epoxy,<sup>76</sup> and countless paper products.<sup>77,78</sup>

The current emphasis on indoor air pollution has sparked research on other apparently benign features of the home environment. Thus, numerous house plants,<sup>79,80</sup> and common insects<sup>81</sup> are now viewed as environmental irritants of homeostatic dysfunction. In addition, sensitivities to cold and heat,<sup>82</sup> and to contaminants in household water supplies have been associated with symptoms ranging from urticaria to severe respiratory distress. It is now clear that, in the face of increasing amounts of data which point to previously unsuspected household irritants, a more cautious attitude should be adopted regarding the issue of environmental safety in the home.

## Chemical Irritants in the Occupational Environment

For years, the hazards of occupational exposure to chemicals have been studied by researchers from various fields; however, until recently, attention has been focused primarily on a small number of extremely dangerous products encountered in work places generally acknowledged to be hazardous. In the past few years, however, research has exposed the dangers inherent in an ever-widening circle of work environments including numerous settings commonly thought to be safe. Many workers' symptoms are improved during evening hours and weekends,<sup>83</sup> hence the conviction that heretofore safe occupations must be re-evaluated for their potential hazards.

The manufacturing industry is replete with examples of chemical contamination. Car factory workers exposed to polyurethane foam have been shown to be at significant risk,<sup>84</sup> and this industry is loaded with chemicals capable of triggering sensitivities, such as chrome, rubber, nickel and isocyanates in spray paints.<sup>85-86</sup> Numerous other industries, including electronics,<sup>87</sup> textiles,<sup>88</sup> and food processing<sup>89</sup> burgeon with irritants which threaten the susceptible individual.

But dangers are not confined to the metropolitan industrial setting; recent reports suggest that occupationally-related respiratory diseases are common among grain elevator workers<sup>90</sup> and farm workers who evidence symptoms ranging from rhinitis to asthma.<sup>91</sup>

A number of familiar trades have come to be associated with chemical risks in recent years, among them carpentry<sup>92</sup> (in which contact sensitivities to woods are reported widely), painting, identified with severe respiratory symptoms,<sup>93</sup> and bricklaying, where sensitivities to chemicals such as cobalt are now extensively described.<sup>94</sup>

There are increasing reports of chemically induced reactions among beauticians,<sup>95</sup> and researchers have now incriminated a vast number of chemicals to which such workers are exposed on a daily basis, among them nickel sulfate, pellidol, and cobalt chloride.<sup>96</sup> Bakery work has come to be identified with risks in the form of chromium exposure through contact with a chromium compound in flour,<sup>97</sup> as well as exposure to gas from the ovens; photographers and those responsible for developing photographs now appear at high risk for chemically induced respiratory disease,<sup>98</sup> as well as cerebral and vascular dysfunction.

The list of occupations in which exposures to potentially hazardous chemicals may occur seems endless. It is now clear that physicians, laboratory technicians,<sup>99</sup> nurses<sup>100</sup> and others in direct contact with numerous drugs and chemicals face potential dangers. What is remarkable, however, is the extent to which seemingly safe occupations are fraught with risks; witness Fisher's<sup>101</sup> report of a chemically-triggered reaction in a concert violinist caused by contact with his rosin.

It would, of course, be impossible to discuss here all of the chemical agents encountered in the occupational environment to which reactions have been observed; the spectrum of incitants ranges from organic chemicals<sup>102</sup> and inhalants<sup>103</sup> to natural dyes<sup>104</sup> and synthetic compounds.<sup>105</sup> Symptoms have been found to be provoked by natural metals such as zinc and cobalt,<sup>106</sup> as well as industrial chemicals, among them chloramine,<sup>107</sup> formalin,<sup>108</sup> paraformaldehyde, zylene,<sup>109</sup> and the persulfates.<sup>110</sup> Moreover, an array of reactions has been reported in association with common industrial agents such as the diisocyanates<sup>111</sup> and toluenes.<sup>112</sup> It is of critical importance to consider the chemicals confronted in occupational products which are apparently benign: recent reports have isolated chemical contaminants in cement,<sup>113</sup> printing paper,<sup>114</sup> and even latex surgical gloves.<sup>115</sup>

The spectrum of disease processes secondary to occupational incitant exposure is a broad one. Over the past three years, some 60 reports have associated dermatitis with chemical sensitivity in the work environment. It has been observed that occupational dermatitis may range from mild discomfort to permanent incapacity; such reactions have been found in association with a multitude of occupations: physician, dentist,<sup>116</sup> medical technician,<sup>117</sup> metalworker,<sup>118</sup> musician,<sup>119</sup> florist,<sup>120</sup> caterer,<sup>121</sup> office worker,<sup>122</sup> and retail salesperson.<sup>123</sup> Against the backdrop of present research it seems clear that a virtually infinite number of occupational milieus contain dangers for the susceptible patient. Data clearly reveal the necessity of environmental control for the evaluation and treatment of such occupational sensitivities.

Other disease processes that may assume the dimensions of an occupational illness include erythema and vesiculation,<sup>124</sup> thrombocytopenic purpura,<sup>125</sup> Raynaud=s phenomenon,<sup>126</sup> and coronary artery spasm.<sup>127</sup> A number of environmentally-triggered respiratory symptoms have been noted, among them bronchoconstriction,<sup>128</sup> airway obstruction,<sup>129</sup> pneumonitis,<sup>130</sup> dyspnea,<sup>131</sup> alveolitis,<sup>132</sup> and asthma.<sup>133</sup> Recent data also suggest that CNS dysfunctions, including depression, fatigue, and sleep disturbances,<sup>134</sup> and even some forms of carcinoma<sup>135</sup> may exist secondary to occupational chemical exposure.

## Chemical Hazards in Drugs and Medical Procedures

Current data are replete with reports of sensitivities to the chemicals contained in a multitude of drugs. The histamine-releasing properties of numerous drugs used in anesthesia and surgery have been known for some time, but only recently have marked sensitivities been shown to a rapidly increasing number of medications, among them neomycin, ethylenediamine, benzocaine,<sup>136</sup> betanol,<sup>137</sup> alpha-methyl dopa,<sup>138</sup> potassium iodide<sup>139</sup> and succinylcholine.<sup>140</sup> Such sensitivities assume a multitude of forms, ranging from dermatitis and edema to asthma.

Of all commonly used medications, aspirin has, more than any other in recent years, been associated with a wide variety of homeostatic reactions. Among the chemically induced reactions to aspirin are asthma,<sup>141,142</sup> chronic rhinitis,<sup>143</sup> urticaria,<sup>144</sup> angioedema,<sup>145</sup> and angina.<sup>146</sup> Anderson reports sensitivities to a number of common drugs used topically,<sup>147</sup> and data burgeon with reports of dermatitis secondary to commonly used health aids, such as medicated bandages<sup>148</sup> and hearing aids.<sup>149</sup>

Numerous reports over the past two years have described the causal roles played by drugs in the mediation of migraine phenomena. Oral contraceptives,<sup>150</sup> vasoconstrictors,<sup>151</sup> and a host of monoamines and opiates<sup>152</sup> have been incriminated. Purpura and petechiae have been demonstrated to occur secondary to exposures to anticoagulants<sup>153</sup> and vaccines,<sup>154</sup> while urticaria and advanced stage vascular alterations have been associated with many drugs, among them antibiotics, sedatives, tranquilizers, laxatives, diuretics,<sup>155</sup> cancer therapeutic drugs,<sup>156</sup> and hallucinogens.<sup>157</sup> The role of oral contraceptives in provoking venous thromboembolism has been known for sometime. Recently, cloxacillin,<sup>158</sup> diazepam, penicillamine,<sup>159</sup> nitroprusside and dopamine<sup>160</sup> have been shown to exhibit phlebotogenic properties. Coronary artery spasm may be provoked by epinephrine, methacholine and imipramine,<sup>161</sup> and Raynaud=s phenomeon may exist secondary to chemicals contained in vinblastine, bleomycine,<sup>162</sup> and sulphasalazine,<sup>163</sup> among others.

A number of medical and surgical procedures have now been associated with chemically triggered reactions. Nickel sensitivity has been reported secondary to the use of skin clips,<sup>164</sup> and hemodialysis has been associated with necrotizing dermatitis, a function of exposure to the epoxy resin in the needles,<sup>165</sup> and to the polyvinyl-chloride tubing.<sup>166</sup> Countless dental procedures have also come to be identified as triggering agents of chemical sensitivities.<sup>167,168</sup> Procedures involving implants<sup>169,170</sup> and prostheses appear riddled with difficulties for the chemically sensitive individual; metal sensitivities are widely reported and are incriminated in the failure of joint prostheses.<sup>171</sup>

This paper attempts to present the implications of environmental contamination for the chemically susceptible individual. It is hoped that this review will lead to a fuller comprehension of the potential hazards represented by the ever increasing number of chemical entities in our environment; the need for environmental control becomes apparent as this comprehension is broadened. The clinician=s use, both in the office and in the hospital, of a controlled environment in which to diagnose and treat susceptible patients greatly simplifies the process of isolating the incitant. Modern technology has afforded the practitioner access to procedures such as mass

spectrometry and gas chromatography which greatly facilitate the process of assessing environmental contamination. The efficacy of such control is illustrated in the operation of an environmental control unit within the hospital. Such a facility promotes symptom clearance by allowing patients to avoid contact with virtually all incitants. Rooms in the unit are constructed of inert materials, and chemically less contaminated foods, purified air, and purified waters are constantly monitored to insure their relative freedom from chemical contaminants.

By establishing such a control, the clinician affords himself a baseline in relation to which reactions to environmental incitants may be judged; chemical challenge under such conditions allows the establishment of a cause-effect relationship between incitant and homeostatic response. The elegance of environmental control lies in the fact that the diagnostic procedures which develop out of it also serve as treatment strategies. Avoidance of the incitant and the construction of a chemically safe home environment represent the primary intervention procedures which are critical to the treatment of chemical sensitivity.

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