

Natelson

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Mr. Stan Perry
Haynes and Boone, L.L.P.
1221 McKinney Street, Suite 2100
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Re: Cause No. 04-CV-00347 (GPM); *Chester Lambert, et al vs. B.P. Products, et al*,
In, The United States District Court For The Southern District of Illinois.

Dear Mr. Perry,

Thank you for allowing me to review the material you provided concerning the above numbered action. As you are aware, I am a board-certified hematologist in private practice at Christus St. Joseph Hospital, in Houston, Texas, where I also serve as Academic Chief of Medicine and Director of the Transitional Internship Program. I am a member of the Board of Directors of the Stehlin Foundation for Cancer Research, at Christus St. Joseph Hospital, and of the Gulf Coast Regional Blood Center where I chair the Education and Research Committee. I am the current and a past President of the Gulf Coast Hematology Society. I have more than 35 years experience in clinical hematology and am familiar with the disorders classified as leukemias and lymphoproliferative diseases and, specifically, with what is known concerning the etiology, diagnosis, clinical course and therapy of chronic lymphocytic leukemia (CLL) and non-Hodgkin's lymphoma (NHL). My medical license is current and on file with the appropriate authorities. You have a copy of my current curriculum vitae. My testimony has never been excluded by any court.

This action concerns Mr. Chester Gene Lambert (DOB 02-04-50, SSN 292-48-0395) who is described in the medical records as an analyst. It is alleged in the pleadings that he developed chronic lymphocytic leukemia (CLL) as a consequence of exposures to jet fuel, for example, JP-4 fuel, during the interval from 1973-1989.

The records indicate that his clinical diagnosis of CLL was first made in May of 2003, when he was admitted to the hospital for evaluation of fever and pain on urination. Routine laboratory studies showed a markedly elevated white blood cell count of 124,000/cu mm (normal value, 4,500-10,000/cu mm) with greatly increased numbers of lymphocytes. Further studies indicated that he had hypogammaglobulinemia, with reduced levels of both IGG and IGM globulins. A bone marrow examination was consistent with infiltration by CLL. Radiographic scanning techniques demonstrated extensive retroperitoneal lymphadenopathy. Flow cytometry studies showed the abnormal lymphoid population to manifest positive CD markers for 5, 19, 20, 22, 23

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and 38 with negative markers for CD 10. The cells were kappa chain positive. These findings confirmed a diagnosis of CLL. Chromosome studies on the bone marrow cells gave normal results.

During the 2003 hospital admission he described smoking for 25 years and was continuing to smoke. However, medical records from 1988 indicate that he then claimed to have smoked 1.5 packs per day for 22 years. Thus, he would have in excess of a 50-pack-year history of smoking. He is variously described in the records as having COPD or asthma. At some point, he had undergone a cholecystectomy and also surgery on his clavicle. He described no family history of hematological disease. He had spent time in the military service but not in Vietnam. A blood count done in 1988, indicated an increased percentage of lymphocytes.

He initially received treatment with Rituxan and, later, fludarabine. These treatments resulted in both improved blood counts and a disappearance of lymphadenopathy, as confirmed by a negative PET scan. Nevertheless, he has continued to require therapy to control the illness. The last notes I received, date from around January of 2005. Based upon his positive CD-38 marker, his general prognosis for long-term control of CLL remains poor (1).

In some instances and, in part, because both CLL and non-Hodgkin's lymphoma (NHL) are typically B-Cell neoplasms, questions are occasionally raised as to whether a particular individual's illness is properly classified as an example of CLL or of NHL. The malignant B-cells of CLL circulate throughout the blood, bone marrow, lymph nodes and spleen. In many affected individuals, large numbers of these tumor cells tend to remain in the circulation, and peripheral white blood counts may exceed 300,000/cu mm with only minimal enlargement of lymph nodes or spleen. In others, the peripheral white blood cell count may be near normal, but there is major enlargement of lymph nodes and spleen along with heavy bone marrow infiltration consequent to preferential tumor cell deposition in these sites. The routine histology of a lymph node biopsy, in both groups, shows the same pattern of diffuse infiltration by small non-cleaved lymphoid cells, which is also morphologically consistent with the small lymphocytic lymphoma (SLL) variant of NHL (2-3).

With the introduction of flow cytometry, a technique by which millions of cells can be rapidly processed and accurately analyzed to identify and classify relatively small numbers of clonal malignant cells, we are now able to diagnose CLL accurately, even with a minimal elevation in the peripheral blood total leukocyte count, and separate it from several distinct forms of NHL which have a similar light microscopic cellular appearance in blood and tissue. The exception is with SLL, which has an immunological phenotype identical to CLL. Thus, in the two different clinical presentations described in the preceding paragraph, the separation between CLL versus SLL becomes somewhat arbitrary. Current convention, as described by the World Health Organization, distinguishes between these two diagnoses with the following statement, "**The term SLL (*small lymphocytic lymphoma*), consistent with CLL, is restricted to cases with the tissue morphology and immunophenotype of CLL, but which are non-leukemic.**" (2). Thus, one might encounter an individual with a normal white blood cell (and lymphocyte) count at diagnosis and the flow cytometry pattern of CLL/SLL on bone marrow or lymph node cells.

That patient would be classified as having SLL. In most instances, with this characteristic flow cytometry panel, there is an elevation of the white cell count and lymphocytes (leukemic phase) at diagnosis, and for the purposes of epidemiologic studies, statistical studies, clinical trials, ICD-9 coding, and the REAL B-cell neoplasm classification, these individuals, such as Mr. Lambert, the subject of this action, have CLL. About 90% of the patients characterized by this CD marker pattern will have CLL and about 10%, SLL. The clinical syndromes and prognosis of SLL and CLL are similar, but not identical (4). The treatment of the two entities is also quite similar.

During the course of the disease, forms of both low-grade NHL and of CLL (as well as Hodgkin's disease) may transform into a more aggressive histological pattern and clinical course. We sometimes refer to this "new" illness as a transformed lymphoma or transformation of CLL. In patients with low-grade small cell follicular NHL this process may occur in as many as 40% of patients during the course of their illness with the "new" lymph node histology resembling that of a diffuse large cell lymphoma (5). Such a transformation also occurs in CLL, although much less frequently (about 3-5% of cases), where it is often referred to as Richter's syndrome. Here the lymph node histology now may also resemble a diffuse large cell lymphoma, or even Hodgkin's disease, although the CD markers for CLL often remain unchanged. Even patients with Hodgkin's disease may undergo this transformation process as part of the natural history of their illness and with relapses of disease. Modern studies show that this transformation process is typically initiated by viral activation with Epstein-Barr or Herpes viruses and may occur more frequently after use of fludarabine therapy, which may cause extreme immunosuppression (6-7). This would be similar to viral-induced post-transplantation lymphoma and the NHL seen in HIV disease. Transformed NHL and CLL typically require intensive therapy to control the illness and, in the case of CLL, the disease process often becomes rapidly fatal. Typically, we consider a patient with a transformed NHL, Hodgkin's disease or CLL to continue to be counted as an example of the initial disease process, for epidemiological purposes, regardless of the disease outcome.

Importantly, and practically, and for the purposes of legal actions such as this one, it is immaterial and non-productive to argue as to whether one chooses to call a particular individual's lymphoproliferative illness CLL or NHL. This is because, as I will discuss (*vide infra*), neither of these two categories of illness has been proven to have a basis of chemical causation, including benzene, solvent, and fuel exposure. I will begin by commenting about what is known concerning the etiology of NHL.

NHL is a common illness that appears to have been steadily increasing in incidence for more than 15 years, currently with around 55,000 new cases being diagnosed each year, in the United States. There are many distinct sub-groups within the spectrum of this disorder, with the most common types being the diffuse large cell B-cell type and the follicular lymphomas (5). In the majority of patients with NHL, no specific etiology is typically confirmed, although in recent years, an ever-increasing spectrum of infectious disorders, primarily viral and, occasionally, bacterial, have been thought responsible, making infectious agents the most common known cause of NHL (8-19). The notion that exposure to noxious chemicals may cause these diseases

has faded, based upon numerous modern reports with long-term follow-up of cohorts of industrial workers (*vide infra*) with known chemical exposures. As stated in two recent articles, "Fifty years ago, the idea that infectious agents caused lymphoma would have seemed heretical...viruses...were not considered a cause of disease in humans - that simply was not what infections did. Rather, tumors were considered to be the consequence of environmental exposures and of inherited genetic abnormalities...In the past 15 years, we have moved a long way from that position. Today, a variety of infectious agents have been identified as either linked to or truly causative of lymphoma." (17). And, "Almost half of all lymphomas contain one or more viruses that have been linked to the development of the disease." (9).

Clinically, with few exceptions such as the malt lymphomas caused by *Helicobacter species*, treatments with anti-infective agents are currently not helpful in the specific treatment of NHL, regardless of causation issues. Thus, the general workup for a patient with NHL does not currently mandate attempts to establish the presence of particular viral sequences in lymph node DNA for example, although modern laboratory techniques may allow this to be accomplished. Thus, current review articles on NHL typically describe the causation of most examples of NHL to be considered unknown, even though we recognize the aforementioned major associations with various infective agents. Examples of such statements appearing in two recent comprehensive reviews of NHL are, "In most cases of non-Hodgkin lymphoma, cause is unknown. Some subtypes are associated with infection..." And, "... the etiology of the most common types of lymphoma remains elusive." (5, 18).

There are familial patterns of disease in many forms of lymphoproliferative disorders including Hodgkin's disease, NHL and CLL (20-22). With modern flow cytometry studies, the familial tendency for CLL can be identified and studied long before any clinical disease is evident, by identifying even tiny populations of monoclonal lymphoid cells (21). We also recognize that NHL may appear after intensive immunosuppression, such as that given with organ transplantation (23). Lupus erythematosus, both systemic and discoid, and forms of rheumatoid arthritis, have also been associated with an increase in the incidence of NHL (which is 40 times that of the general population in patients with Sjögren's syndrome), even prior to administration of immunosuppressive therapy (24-25). The incidence of NHL is greatly increased in people with HIV infection and, specifically, the Epstein-Barr virus is thought to be a particularly prominent cause of NHL in this patient group (15). The Epstein-Barr virus is also a well-established cause of both Hodgkin's disease and NHL in non-HIV infected individuals. NHL is also thought to occasionally result from hepatitis C virus infection (5, 14-18).

Epidemiological studies have attempted to evaluate a possible association between NHL and exposure to diverse chemicals such as pesticides, chemotherapy drugs such as methotrexate, petrochemicals such as benzene and butadiene in the synthetic rubber industry, paint and aromatic paint solvents, gasoline and diesel fuels, polymer production such as vinyl chloride and other chlorinated hydrocarbons such as trichlorethylene, and even to Agent Orange. Many of these studies are large cohort-based observations that span over 25-50 years with an enormous subject/year exposure data base and recurrent updates. In particular, these reports have failed to

support a relationship between the appearance of NHL and occupational exposure to benzene and any of the aforementioned chemicals (26-48). Longitudinal studies following petrochemical workers with significant potential for benzene and other aromatic hydrocarbons and employees in plants with documented massive pure benzene exposure, such as the Pliofilm industry experience, have shown no statistically significant increased incidence of NHL (49-51). The authors of a large study on factory workers in China, predominantly indoor painters exposed to benzene and other chemicals, have claimed a statistically non-significant increase in NHL among these individuals (52). This study has been widely criticized for inaccurate data on the amount of benzene present, inaccurate figures separating NHL from Hodgkin's disease, non-availability of slides or even pathology reports for review in more than a third of the alleged NHL cases, and for many other reasons including a questionable control group (53-55). Importantly, its authors comment on all prior large studies which have examined the association of benzene exposure and subsequent risk of the development of NHL, thus including all such studies done on workers in developed countries, stating, **"We agree that, on balance, the earlier studies did not demonstrate an elevation in NHL risk..."** (56). The massive pollution in China, which provides potential exposure to many toxins, and the endemic presence of viral infections linked to NHL, such as hepatitis C, and the increased presence of gastric *Helicobacter pylori* infection, because of poor hygienic conditions, make conclusions from this study difficult to interpret and also to apply to workers in the United States (57-58).

The United States Government agencies, such as the EPA and OSHA, continue to list acute myeloid leukemia (AML) as the sole hematological malignancy proven to be potentially linked to benzene exposure and propose the longitudinal studies of the Pliofilm cohort of benzene exposed workers as the benchmark for confirming this link (49-51). Thus, in a review concerning benzene exposures in the Pliofilm worker cohort, **"... there is a general consensus among scientists and regulators that acute myeloid leukemia (AML) is the only cancer type that has been observed consistently across various studies."** (51). And, in another recently published long-term follow-up of a United Kingdom benzene-exposed worker cohort, the authors find, consistent with the United States Pliofilm experience, **"...this study does not support claims that exposure to benzene affects risks for lymphohaematopoietic malignancies other than ANLL [ANLL is acute non-lymphocytic leukemia and a synonym for AML]."** (48).

Cigarette smoke, which is the most potent chemical carcinogenic mixture known, has also not been shown to be a cause of NHL, Hodgkin's disease, or CLL (59-62). Thus, there has been no consistent evidence, either clinically or from an epidemiological standpoint, to implicate any specific chemical or group of chemicals in the causation of NHL or, for that matter, in causation of Hodgkin's disease (61-62). As stated in a recent review of Hodgkin's disease, the author writes, unequivocally, **"It has no defined associations with any occupational exposures, any chemical exposures, cigarette smoking, other lifestyle issues or ionizing irradiation."** (62). I will next comment specifically concerning CLL, the illness affecting Mr. Lambert.

CLL is the most common form of leukemia in Western nations, accounting for approximately 25-30% of the total of all types of leukemia, with about 14,000 cases diagnosed

each year in the United States. Although the incidence increases with age, about one third of affected individuals are younger than 60 years at diagnosis. As discussed earlier in this report, the diagnosis of CLL is currently established by the finding of a proliferation of mature-appearing lymphoid cells in the peripheral blood and bone marrow, which are positive for the CD-5, CD-19, CD-20 and CD-23 markers, along with the presence of monoclonal surface immunoglobulin, and negative for the CD-10 marker, as demonstrated in Mr. Lambert. As discussed earlier, these specific markers may also be present in lymph node tissue from the SLL variant of NHL, but since Mr. Lambert had a leukemic phase (markedly increased numbers of circulating lymphocytes in the peripheral blood) at the time of his diagnosis, he had CLL. The presence of additional markers, such as CD-38 (identified in Mr. Lambert) and/or Zap-70, separate those patients with aggressive forms of CLL from those with negative CD-38/Zap-70 markers who have a more indolent course that may extend more than 20 years, even without specific therapy (1).

The medical literature including text books, educational materials and journal articles concerning CLL continues to provide a uniform and unambiguous opinion that no specific environmental factors, including chemicals such as benzene or radiation, play any role in its causation (3, 62-76). The etiology is generally stated to be unknown, aside from the strong familial incidence patterns (20-22). For example, in two very recent reviews, **"CLL does not have a readily identifiable causative agent and is absent in studies of leukemia secondary to radiation or chemotherapy."**, and, **"no single environmental risk factor has been found to be predictive for CLL....a definitive cause for CLL is still not known, however, a genetic aetiology may offer the best explanation."** (58, 76).

Tumor cells of many types may exhibit chromosomal aberrations. Patients with acute myeloid leukemia (AML) or CLL are no exception. However, there are differences in the frequency and in the general patterns of chromosomal abnormalities seen in *de novo* AML, versus *secondary* forms of AML, which follow exposures to environmental toxins such as benzene, chemotherapy drugs, or radiation. In all types of the latter cases, loss of parts of chromosomes 5 and 7 are common. By contrast, in *de novo* AML, chromosome trisomy and balanced translocations, for example involving 11q23, are the most frequently described aberrations (77-78). The most recent studies in CLL show the most common chromosomal abnormalities in that illness to include trisomy 12 and deletions of 11q22, but not abnormalities of chromosomes 5 and 7 (79). I believe these observations would tend to further support the mass of evidence against the notion that potential environmental toxins such as benzene may cause CLL.

As previously discussed here, long-term longitudinal and comprehensive epidemiological reports summarizing many years of follow-up on petrochemical and gasoline workers and others with the potential for extensive exposure to many chemicals, including benzene and other solvents, as previously referenced in the discussion of NHL, have also failed to identify any definitive association with the development of CLL. The cohort of workers heavily exposed to benzene from the Pliofilm industry, which has been studied intensively for many years, and is the reference standard cited by OSHA and the EPA for malignancies induced by benzene, shows

only an increase in cases of AML, and no increase in CLL or NHL. Similarly, the large "Chinese" study of more than 74,000 workers exposed to disputed, but probably massive levels of benzene and other solvents, shows no increased incidence of CLL (48). A recent longitudinal study of workers exposed to an average cumulative benzene level of nearly 40 ppm years, working with specific benzene-related chemical processes shows no increase in the incidence of CLL (47). Another recently published long-term cohort study of benzene-exposed workers from the United Kingdom, somewhat similar in scope to the United States Pliofilm study, also finds no increased incidence of CLL (48). Similarly, the 2005 analysis of the Australian petroleum surveillance program reports no evidence for an increase in CLL among this cohort of petroleum workers (80). As commented on in another modern report, **"There are no clearly established relations between CLL and work in the petroleum industry"** (33). And, as previously mentioned, smokers who are exposed to a large number of carcinogenic compounds, including 10 times the amount of benzene non-smokers experience, and who have an increased incidence of lung cancer as well as many other neoplasms including AML, also have no increased incidence of either NHL or CLL.

Although the cause of CLL remains unproven, a 2005 New England Journal of Medicine comprehensive review on the illness follows the lead of modern studies on NHL causation and speculates, **"...it is possible that latent viruses or commensal bacteria repetitively activate particular B-cell clones through the B-cell receptor. CLL would result, directly or indirectly, from specific infections and would be perpetuated by them - in a manner similar to the gastric lymphomas that evolve in response to *Helicobacter pylori*... this immune-stimulation mechanism is in keeping with the view that the basis for CLL is autoimmunization."** (3).

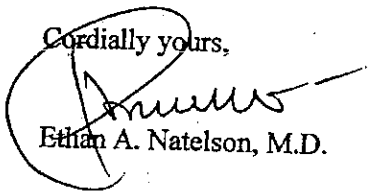
CLL is a neoplasm that can be easily suspected clinically and specifically defined and separated from other B-cell neoplasms by its characteristic immunophenotypic markers, as was accomplished in Mr. Lambert's case. In searching for etiologic factors in patients with this type of illness, it is becoming increasingly clear that epidemiological analysis by broad and heterogenous categories such as "leukemia" or "myelodysplasia" or "lymphohematopoietic neoplasms" as has been done in years past, does not yield useful and meaningful data. Just as an epidemiological analysis of the leukemias must be cell-specific, so must analysis of the many types of NHL. As commented on in a 2006, article, **"...differences in incidence patterns by histologic subtype strongly suggest that there is etiologic heterogeneity among lymphoid neoplasms and support the pursuit of epidemiologic analysis by subtype. The established specificity of certain infections and increasing evidence suggesting that certain risk factors and host susceptibility may be related to specific subtypes further support this conclusion...Research within large consortium efforts such as InterLymph, the International Lymphoma Epidemiology Consortium, will likely contribute to identifying the elusive etiologic causes of lymphoid neoplasms."** (81).

In summary, as in all epidemiological studies or other types of observations used to support a claim of disease causation, we look not only for statistical significance in any individual report,

but uniform, consistent and reproducible findings of causation among multiple study populations examined by different techniques. Moreover, we should expect to find a threshold and/or dose-response curve for an alleged chemical or toxin, which might be causative. Addressed in terms of "specific" causation, there is no test that would allow one to prove that any particular patient with NHL or CLL contracted his/her disease from any particular chemical. In terms of "general" causation, there are no consistent epidemiological studies that have shown NHL or CLL to be a consequence of exposure to any particular chemical, or combination of chemicals, or at any particular threshold of chemical exposure. Rather, the contrary is true as shown with many long-term cohort studies.

Thus, in my opinion, and in all medical probability, the etiology of CLL in Mr. Lambert remains unknown, as it commonly appears in the general population, and there is no reason to suppose it was caused by any workplace chemical exposure. Please let me know if you require any additional information.

Cordially yours,


Ethan A. Natelson, M.D.

REFERENCES:

1. Ghia, P, et al The pattern of CD38 expression defines a distinct subset of chronic lymphocytic leukemia (CLL) patients at risk of disease progression. *Blood* 101:1262-1269, 2003.
2. Muller-Hermelink, et al Chronic lymphocytic leukemia/small lymphocytic lymphoma. In World Health Classification of Tumors. Pathology and Genetics of Tumors of Haematopoietic and Lymphoid Tissues, Eds Jaffe, ES, et al IARC Press, Lyon, France 2001, pp 127-130.
3. Chiorazzi, N, et al Chronic lymphocytic leukemia. *New Eng J Med* 352:804-815, 2005.
4. Tsimberidou, A-M, et al Comparison of small lymphocytic lymphoma with chronic lymphocytic lymphoma, the M.D. Anderson Cancer Center experience. *Blood* 106:270a, 2005.
5. Evans, LS, et al Non-Hodgkin Lymphoma. *Lancet* 362:139-146, 2003.
6. Thornton, PO, et al Richter's transformation of chronic lymphocytic leukemia. The possible role of fludarabine and the Epstein-Barr virus in its pathogenesis. *Leuk Res* 29:389-395, 2005.

7. Fong, E, et al Hodgkin's disease variant of Richter's syndrome in chronic lymphocytic leukaemia patients previously treated with fludarabine. *Brit J Haematol* 129:199-205, 2005.
8. Ambinder, R, Infection and lymphoma. *New Eng J Med* 349: 1309-1311, 2003
9. Samaniego, F, The viral origins of lymphomas. *OncoLog* 47(4):8, 2002.
10. Matias, KP, Studies of the viral origins of some cancers lead to new prevention, treatment strategies. *OncoLog* 49(1)3-6, 2004.
11. Pagano, JS, Viruses and lymphoma. *New Eng J Med* 347:78-79, 2002.
12. Pagano, JS, et al Infectious agents and cancer: criteria for a causal relation. *Sem Cancer Biol* 14:453-457, 2004.
13. Vilchez, RA, et al Association between simian virus 40 and non-Hodgkin lymphoma. *Lancet* 359:817-823, 2002.
14. Malkin, D, Simian virus 40 and non-Hodgkin lymphoma. *Lancet* 359:812-813, 2002.
15. Goedert, JJ, et al Spectrum of AIDS-associated malignant disorders. *Lancet* 351:1833-1839, 1998.
16. Mele, A, et al Hepatitis C virus and B-cell non Hodgkin lymphoma: An Italian multi-center case-control study. *Blood* 102:996-999, 2003.
17. Parsonnet, J, Isaacson, PG, Bacterial infection and MALT lymphoma. *New Eng J Med* 350:213-215, 2004.
18. Fisher, SO and Fisher, RI, The Epidemiology of non-Hodgkin's lymphoma. *Oncogene* 23:6524-6534, 2004.
19. Lecuit, M, et al Immunoproliferative small intestinal disease associated with *Campylobacter jejuni*. *New Eng J Med* 350:239-248, 2004.
20. Zhu, K, et al Non-Hodgkin's lymphoma and family history of malignant tumors in a case control study (United States). *Cancer Causes & Control* 9:77-82, 1998.
21. Houlston, RS, et al Causation of chronic lymphocytic leukemia-insights from familial disease. *Leuk Res* 27:871-876, 2003.
22. Rawstron, AC, et al Inherited predisposition to CLL is detectable as a sub-clinical monoclonal B-lymphocyte expansion. *Blood* 100:2289-2291, 2002.
23. Andreone, P, et al Posttransplantation lymphoproliferative disorders. *Arch Int Med* 163:1997-2004, 2003.

24. Fox, RJ, Sjögren's syndrome. *Lancet* 356:321-331, 2005.
25. Mellemkjoier, L, et al Non-Hodgkin's Lymphoma and other cancers among a cohort of patients with systemic lupus erythematosus. *Arth Rheum* 40:761-768, 1997.
26. Wong, O, et al Non-Hodgkin's lymphoma and exposure to benzene in a multinational cohort of more than 308,000 petroleum workers, 1937-1996. *J Environ Occup Med* 42:554-568, 2000.
27. Wong, O, et al An updated mortality study of workers at a petroleum refinery in Beaumont, Texas, 1945-1996. *J Occup Environ Med* 43:384-401, 2001.
28. Lynge, E, et al Risk of cancer and exposure to gasoline vapors. *Amer J Epidemiol* 145:449-458, 1997.
29. Satin, KP, et al A 50 year mortality follow-up of a large cohort of oil refinery workers in Texas. *J Occup Environ Med* 38:492-506, 1996.
30. Satin, KP, et al Updated epidemiological study of workers at two California petroleum refineries 1950-95. *Occup Env Med* 59:248-256, 2002.
31. Divine, BJ, et al Update of the Texaco mortality study 1947-93: Part II., Analyses of specific cause of death for white men employed in refining, research, and petrochemicals. *Occup Environ Med* 56:174-180, 1999.
32. Rushton, L, et al A case-control study to investigate the risk of leukaemia associated with exposure to benzene in petroleum marketing and distribution workers in the United Kingdom. *Occup Environ Med* 54:152-166, 1997.
33. Huebner, WW, et al Incidence of lymphohematopoietic malignancies in a petrochemical industry cohort: 1983-94 follow up. *Occup Environ Med* 57:605-614, 2000.
34. Bosetti, C, et al Occupational exposure to vinyl chloride and cancer risk: A review of the epidemiologic literature. *Eur J Cancer Prev* 5:427-430, 2003.
35. Sathiakumar, N, et al Mortality from cancer and other causes of death among synthetic rubber workers. *Occup Environ Med* 55:230-235, 1998.
36. Tsai, SP, et al A mortality, morbidity and hematology study of petrochemical employees potentially exposed to 1, 3-butadiene monomer. *Chemico Biological Interactions* 135-136:555-567, 2001.
37. Ruder, AM, et al Mortality patterns among workers exposed to styrene in the reinforced plastic boatbuilding industry: An update. *Am J Ind Med* 45:165-176, 2004.

38. Boice, JD Jr, et al Mortality among aircraft manufacturing workers. *Occup Environ Med* 56:581-597, 1999.
39. Blair, A, et al Mortality and cancer incidence of aircraft maintenance workers exposed to trichloroethylene and other organic solvents and chemicals: extended follow up. *Occup Environ Med* 55:161-171, 1998.
40. Wong, O, Carcinogenicity of trichloroethylene: an epidemiologic assessment. *Clin Occup Environ Med* 4:557-589, 2004.
41. Chang, YM, et al A cohort mortality study of workers exposed to chlorinated organic solvents in Taiwan. *Ann Epidemiol* 13:652-660, 2003.
42. Brown, LM, et al Exposures in the painting trades and paint manufacturing industry and risk of cancer among men and women in Sweden. *J Occup Environ Med* 44:258-264, 2002.
43. Boffetta, P, et al Meta-analysis of studies of occupational exposure to vinyl chloride in relation to cancer mortality. *Scand J Work Environ Health* 29:220-229, 2003.
44. Mariettae, X, et al Lymphomas in rheumatoid arthritis patients treated with methotrexate: A 3-year prospective study in France. *Blood* 99:3909-3915, 2002.
45. Selected Cancers Cooperative Study Group, The association of selected cancers with service in the US military in Vietnam. 1. Non-Hodgkin's lymphoma. *Arch Int Med* 150:2473-2483, 1990.
46. Garabrant, DH, Review of 2,4-dichlorophenoxyacetic acid (2,4D). *Epidemiology and toxicology. Crit Rev Toxicol* 32:233-257, 2002.
47. Bloemen, LJ, et al Lymphohaematopoietic cancer risk among chemical workers exposed to benzene. *Occup Environ Med* 61:270-274, 2004.
48. Sorahan, T, et al Cancer risks in a historical UK cohort of benzene exposed workers. *Occup Environ Med* 62:231-236, 2005.
49. Paxton, MB, et al Leukemic risk associated with benzene exposure in the Pliofilm cohort. I. Mortality update and exposure distribution. *Risk Anal* 14:147-154, 1994.
50. Bayliss, DL, et al Carcinogenic effects of benzene: An update. *Nat Cent Environ Assess, Washington Office EPA/600/P-97/001G* pp 1-57, April 1998.
51. Williams, PD, et al Reconstruction of benzene exposure for the Pliofilm cohort (1936-1976) using Monte Carlo techniques. *J Tox Environ Health* 66:677-781, 2003.

52. Hayes, RB, et al Benzene and the dose response incidence of hematologic neoplasms. *J Natl Can Instit* 89:1065-1071, 1997.
53. Wong, O, Investigation of benzene exposures, benzene poisoning and malignancies in China. *Reg Toxicol Pharm* 35:126-135, 2002.
54. Budinsky, RA, et al An evaluation of modeled benzene exposure and dose estimates published in the Chinese-National Cancer Institute collaborative epidemiology studies. *Reg Tox Pharm* 30:244-258, 1999.
55. Linet, MS, et al Clinical features of hematopoietic malignancies and related disorders among benzene-exposed workers in China. *Environ Health Perspect* 104:1353-1364, 1996.
56. Hayes, RD, et al Re: Benzene and the dose-related incidence of hematologic neoplasms in China. *J Natl Can Instit* 90:469-471, 1998.
57. Beach, M, China: Millions choke while stoves burn. *Lancet* 354:137, 1999.
58. Pyatt, D, Benzene and hematopoietic malignancies. *Clin Occup Environ Med* 4:529-555, 2004.
59. Adami, J, et al Smoking and the risk of leukemia, lymphoma and multiple myeloma. *Cancer Causes Control* 9:94, 1998.
60. Schöllkopf, C, et al Cigarette smoking and risk of non-Hodgkin's lymphoma- A population-based case-control study. *Cancer Epidemiol Biomarkers Prev* 14:1791-1796, 2005.
61. McCunney, RT, Hodgkin's disease, work, and the environment. A review. *J Occup Environ Med* 41:36-46, 1999.
62. Cartwright, RA and Watkins, G, Epidemiology of Hodgkin's disease. A review. *Hematol Oncol* 22:11-26, 2004.
63. Sgambati, MT, et al Chronic Lymphocytic Leukemia, Epidemiological, Familial and Genetic Aspects, Chap 3 in Chronic Lymphocytic Leukemias, 2nd Edition, Cheson, BD, Editor, Marcel Dekker, Inc. New York, pp 33-62, 2001.
64. Kipps, TJ, Chronic lymphocytic leukemia and related diseases. Chapter 98 in William's Hematology, 6th Edition. Beutler, E., et al Eds. McGraw-Hill Medical Publishing Division, New York, pp 1163-1194, 2001.
65. Fayad, L, et al Chronic lymphocytic leukemia and associated disorders. In Medical Oncology, 2nd Edition. Pazdur, R., Ed. MD Anderson Cancer Center and PRR Huntington, New York, pp 37-56, 1995.

66. Rai, KR, et al Chronic Lymphocytic Leukemia, Chapter 72 In Hematology, Basic Principles and Practice. 3rd Edition. Hoffman, R, et al Eds. Churchill Livingstone, New York, pp 1350-1363, 2000.
67. Cheson, B., The chronic lymphocytic leukemias, Chapter 46.3 In Cancer Principles and Practice of Oncology, 6th Edition, Devita, VT, Jr., et al Editors, Lippincott, Williams & Wilkins, Philadelphia, pp 2447-2465, 2001.
68. Keating, M, The Chronic Leukemias, Chapter 176 in Cecil Textbook of Medicine, 21st Edition. Bennett, JC, et al Eds., WB Saunders Co., Philadelphia, pp 944-953, 2000.
69. Hussein, MA, Chronic lymphocytic leukemia, Chapter 12-25 in Medicine for the Practicing Physician, 4th Edition. Hurst, JW, Editor, Appleton & Lange, Stanford, Conn pg 877-879, 1996.
70. Armitage, JO, Longo DL, Malignancies of lymphoid cells. Chapter 112 in Harrison's Principles of Internal Medicine, 15th Edition, Ed. Braunwald, E, et al McGraw-Hill, New York pp 715-716, 2001.
71. Rai, KR, et al Chronic Lymphocytic Leukemia. In American Society of Hematology Education Program Booklet, pp 313-318, 1998.
72. Caligaris-Cappio, F, New insights into the biology of B-cell chronic lymphocytic leukemia. In American Society of Hematology Education Program Booklet, pp 249, 1999.
73. Hisada, M, et al Solid tumors after chronic lymphocytic leukemia. Blood 98:1979-1981, 2001.
74. Morrison, VA, Chronic Leukemias. In CA, 1 Amer Cancer Soc 44:pg 353, 1994.
75. Rozman, C, Montserrat, E, Chronic lymphocytic leukemia. New Eng J Med 333:1052-1057, 1995.
76. Redaelli, A, et al The clinical and epidemiological burden of chronic lymphocytic leukaemia. Europ J of Cancer Care 13:279-287, 2004.
77. Leone, G, et al The incidence of secondary leukemias. Haematologica 84:937-945, 1999.
78. Smith, MA, et al The secondary leukemias: Challenges and research directions. J Natl Can Inst 88:407-418, 1996.
79. Sindelarova, L, et al Incidence of chromosomal anomalies detected with FISH and their clinical correlations in B-chronic lymphocytic leukemia. Can Genet Cytogen 160:27-34, 2005.

80. Gun, R, et al Health Watch: The Australian Institute of Petroleum Health Surveillance Program. Twelfth Report, Dept Pub Health, Univ of Adelaide, South Australia, ISBN 0-646-44545-6 (2005).
81. Morton, LM, et al Lymphoma incidence patterns by WHO subtype in the United States, 1992-2001. Blood 107:265-276, 2006.

