Curing Cancer – Dustin Diamond dies of lung cancer

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TV actor Dustin Diamond, age 44, died of widely disseminated (stage 4) small cell lung cancer only one month after diagnosis (**NBC News**). This essay discusses, in a relatively nontechnical manner, important aspects of this disease and prospects for future curative treatment (**MedPage Today**).

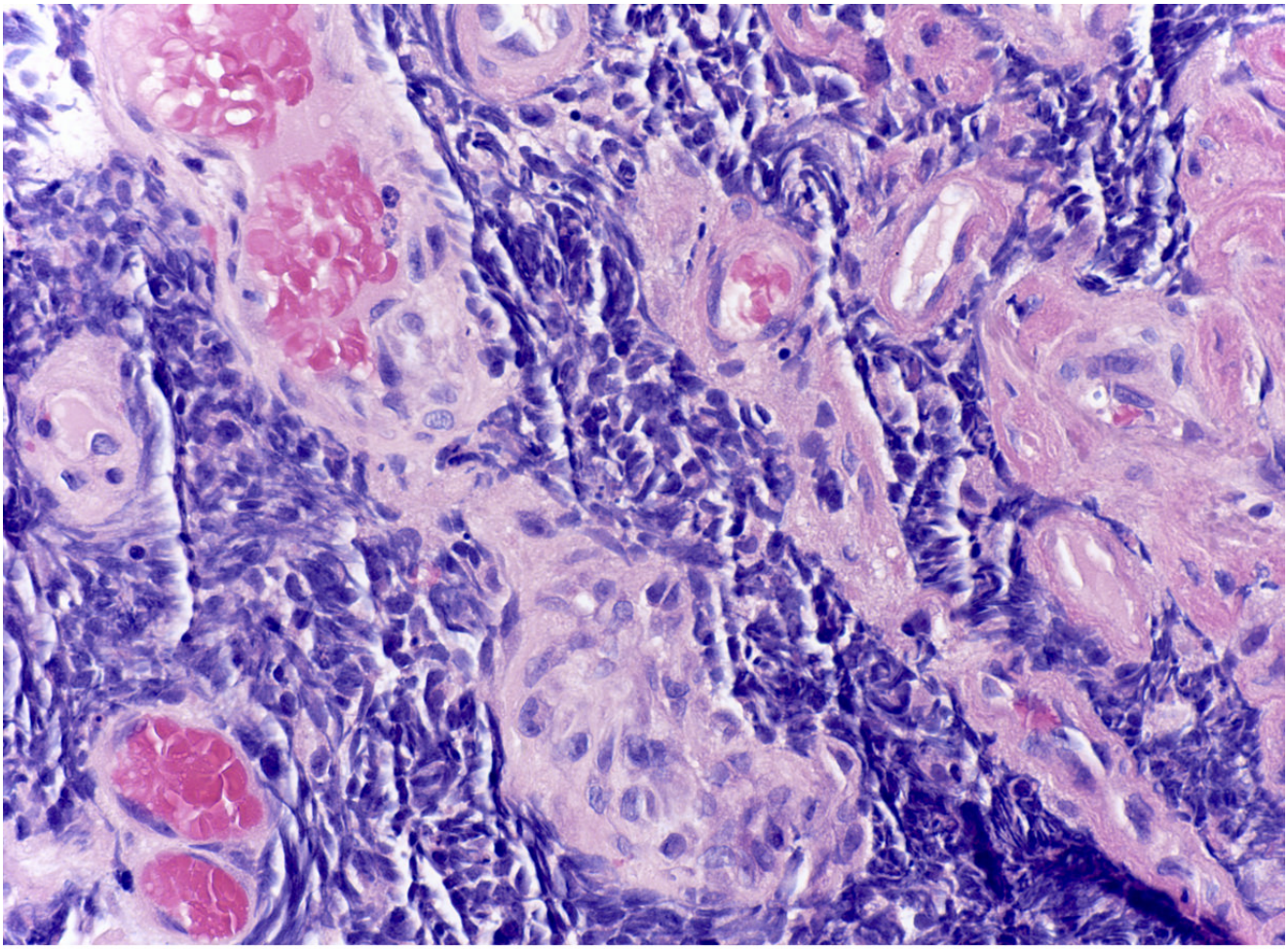
What is cancer?

Cancer is a group of diseases characterized by the uncontrolled growth and spread of abnormal cells. It is classified based on the origin of the cells that becomes malignant: carcinoma (from cells that line or cover internal organs or are in the skin), sarcoma (from bone or soft tissue / connective tissue), lymphoma (from lymphocytes, a type of white blood cell) and some less common types.

What is small cell lung cancer?

Lung cancer is the leading cause of US cancer death and is predicted to cause 21.7% of the 608,570 projected US cancer deaths in 2021 (**Cancer Facts & Figures 2021**). Lung cancer is subclassified into nonsmall cell carcinoma (primarily squamous cell carcinoma and adenocarcinoma) and small cell carcinoma. These categories have distinct differences in behavior and treatment.

Small cell carcinoma of the lung arises from rare neuroendocrine cells in the respiratory tract which receive input from nerves and produce hormones. As in Dustin's case, it is typically aggressive, with a poor prognosis and no curative treatment (**PathologyOutlines.com-Small cell carcinoma**). Microscopically, the tumor is composed of relatively small (compared to other cells) blue cells, which are mostly nuclei with little cytoplasm. The cells are fragile and often appear smudged on biopsy.



Small cell lung carcinoma is a fragile tumor and often crushed during biopsy, as shown; however, the small size of the tumor cells and lack of nucleoli can still be appreciated; the high nuclear to cytoplasm ratio is also demonstrated

What causes lung cancer?

Over 80% of lung cancer cases are caused by cigarette smoking, which exposes cells throughout the respiratory tract to its 7,000 chemicals, including 60+ carcinogens. Other common causes are secondhand smoke, radon exposure and occupational exposure to hazardous substances. The table below indicates what percentage of lung cancer in the US is caused by various risk factors (note: since risk factors overlap, the totals add up to more than 100%):

Table 2 - Population Attributable Fraction of Lung Cancer

	Smokers and Never Smokers	Never Smokers
Tobacco (smoking)	80%	Not applicable
Secondhand smoke	5%	North America: men, 8.2%, women, 5.6%
Random chronic stress / bad luck	Not available	50-70%
Radon	10%	Men: 18.9 - 25.8% Women: 19.7 - 26.9%
Occupational	10%	Not available
Outdoor air pollution	1-2%	Not available
Tuberculosis	Not available	North America: 1.1% Europe: 2.4% China: 12.7%
Germline / family history	Not available	North America: 2.0% Europe: 1.2% China: 2.9%
Chronic obstructive lung disease	Not available	North America: 0.4% China: 0.6%
Pneumonia	Not available	North America: 0.2%
Indoor air pollution (women)	Not available	China: 19.9% (household use of coal)

Unspecified attributable risk: aging, diet, HIV, HPV, abdominal obesity, cannabis / marijuana smoking.

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Pernick 2020: How Lung Cancer Arises (PDF)

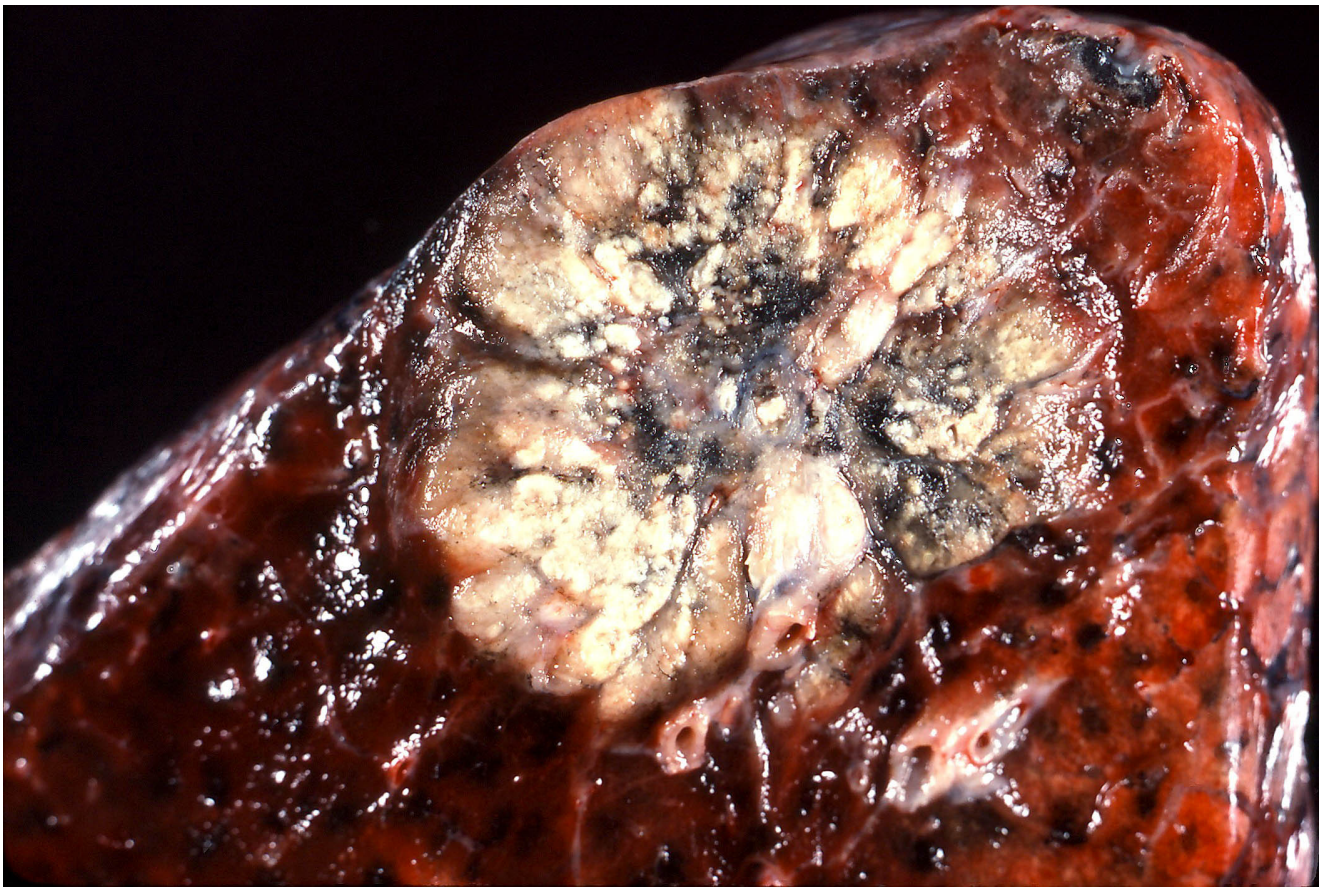
There is also a baseline rate of lung cancer, estimated at 2 cases per 100,000 population per year in the US, which occurs without any risk factors, which I attribute to "random chronic stress" or cellular accidents (**Curing Cancer Blog-Part 7**).

On the cellular level, life is considered to follow the principles of self-organized criticality. This means that our cells, tissues and organs are relatively stable but a small change can rarely set off an avalanche of other changes leading to a catastrophic condition. For lung cancer, the carcinogens in cigarette smoke alter the DNA of cells in the lung and also induce a

chronic inflammatory reaction that, over time, produces an environment that makes the catastrophe of malignancy more likely to arise. Typically, it takes decades between the initial changes and a clinically obvious tumor.

How does cancer kill people?

Human life requires functioning, interdependent organs. Malignant tumors (tumor just means a growth) destroy cells so these organs cannot function. For example, this tumor (an adenocarcinoma) has destroyed much of the lung:



Over time, cancer spreads to neighboring tissue and may enter blood vessels or lymphatic vessels to disseminate throughout the body with similar destructive effects.

Aggressive cancers, including most lung and pancreatic cancers, appear to have “hijacked” cellular programs used during embryogenesis, when rapid cell division and migration of cells serve a useful purpose. As the embryo matures, this programming is turned off. However, the presence of chronic inflammation, carcinogen exposure, hormones (for some cancers), immune system dysfunction and cellular accidents, over years to decades, may create an environment that reactivates this programming. Unfortunately, the adult cellular environment, unlike that in the embryo, has no mechanism to turn it off (**Curing Cancer Blog-Part 6**).

Cancer also arises due to activation of an evolutionarily ancient "toolkit" that was active in the single cell precursors of human beings but is typically suppressed by additional controls that evolved in multicellular organisms. This is called the atavism theory of cancer (**Davies 2011**).

How to cure these aggressive cancers?

Dustin's rapid death resembles that of children with childhood leukemia before the 1950s, when most died within weeks to months of diagnosis (**The Emperor of All Maladies**). Curative treatment today for childhood leukemia is based on a combination of drugs which individually kill a large proportion of tumor cells or facilitate the action of other drugs to do so. Extensive clinical trials have determined that there are actually dozens of different leukemic diseases, each with different optimal treatments (see Table of Contents of **PathologyOutlines.com-Bone marrow neoplastic chapter**).

For aggressive adult tumors, we need to develop more effective single treatments and combinations of treatments to kill tumor cells or make them less destructive (**Curing Cancer Blog-Part 5**) . We also need to treat and monitor systemic changes that nurture the tumor (**Curing Cancer Blog-Part 6**). Enlisting as many patients as possible in clinical trials will facilitate these efforts. Long term, we need to reduce or counter patient risk factors that continue to produce new tumors.

Prevention is also treatment. Strong public health programs are needed to give professionally crafted messages about smoking, excess weight, radon, healthy eating, exercise and vaccinations (**European Code Against Cancer**). It is important to create a culture of being healthy so that everyone is encouraged to make their own health a priority. We also need to develop better screening tests for aggressive cancers, analogous to high blood pressure or cholesterol for heart disease and strokes. Testing for chronic inflammation may be useful, but we must determine what specifically to test for.

Together, these strategies will reduce the shock and devastation of cancer death that are all too common today.