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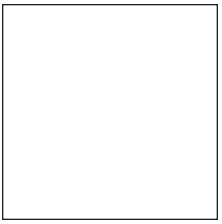

"Clearing the Smoke"

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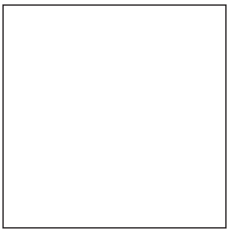

In 1994, through the generosity of the Bannan Institute for Jesuit Education and Christian Values, the Department of Religious Studies of Santa Clara University inaugurated the Santa Clara Lectures. This series brings to campus leading scholars in theology, offering the University community and the general public an ongoing exposure to debate on the most significant issues of our times. Santa Clara University will publish these lectures and distribute them throughout the United States and internationally.

Upcoming Lecture:

"The Common Good in a Divided Society"
David Hollenbach, S.J.
Sunday, April 18, 1999
7:30 p.m., Recital Hall in the Performing Arts Center

Dear readers:
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Previous Lecturers

John Meier

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Clearing the Smoke

Klaus J. Porzig, M.D.

When Denise Carmody asked me some time ago to give the Santa Clara lecture, she enticed me by adding that it was a chance to use the bully pulpit. The one topic that an oncologist would not pass up to talk about in the bully pulpit is smoking, and more importantly, smoking among children and teenagers. It is clear that this age group is critically important in the pathophysiology of the disease as well as to the tobacco industry, since without teenage smokers, there will be few adult smokers, given current trends.

Tobacco was introduced into Europe from the Americas in the mid-1550s. From 1600 to 1900, tobacco was smoked in pipes and cigars, or used as snuff, or as chewing tobacco. It wasn't until the industrial revolution and the invention of the cigarette-making machine in the 1880s that cigarettes were mass produced and increased in popularity. In 1913, R.J. Reynolds started to mass produce and mass market Camel cigarettes. At the turn of the century, lung cancer was rare in this country. There was a sharp rise in the incidence of lung cancer in men 20 to 25 years after the mass marketing of Camels began. In 1954, the first major studies linking cigarette smoking and lung cancer were published in this country. Ten years later, the first report on smoking and disease was released by the surgeon general. Based on the strength of 7,000 published studies, it was concluded that smoking caused lung cancer, laryngeal cancer, and chronic bronchitis. This spawned efforts by government and non-governmental organizations to limit the prevalence of smoking. By 1970, a gradual decline in smoking began. In 1965, 42 percent of adults over 18 smoked, while the number decreased to 25 percent in 1993.

Currently, about 46 million Americans smoke. Annually, 400,000 die due to smoking-related disease. Of these, 140,000 will die of lung cancer, 180,000 will die of cardiovascular disease caused by smoking, and the remainder will die of other types of cancer or other diseases such as chronic obstructive lung disease or emphysema. While there has been a significant overall decline in cigarette consumption, there has been an alarming increase in smoking among children and teenagers. In 1991, 27 percent of high school students smoked. In 1997, that number increased to 36.4 percent. Every day in this country, 3,000 children and teenagers begin to smoke, amounting to more than 1 million new smokers per year. These are the tobacco industry's "replacement smokers" to take the ranks of those who died or managed to quit.

In this talk, I will try to show that this increase in child and teenage smoking is alarming for two very important reasons. The first has to do

with the biology of lung cancer. The genetic damage that occurs in the cells of lung epithelium begins early on and may be irreversible, leading to lung cancer 20 to 25 years later. The second has to do with the epidemiology of smoking. It is very clear that this age group is crucial to the tobacco industry's efforts to keep the ranks of smokers filled, and that the advertising and promotional activities target this age group, despite repeated industry denials that they are doing that.

We have known for a long time that tobacco can cause cancer. In 1759, John Hill described an association between the heavy use of snuff and oral cancers. In 1918, animal experiments showed that skin cancers could be induced on the backs of animals by painting them with coal tar. In 1941, Isaac Berenblum carried out classic experiments which established that the etiology of cancer was a multi-step process. He showed that in order to induce a cancer in the skin on the back of an animal, one had to initiate the process with one chemical and then promote the malignancy by applying a second chemical at a later time. Exactly how a cell becomes a cancer cell remained hidden, as if in a black box, until the discovery 10 to 15 years ago of oncogenes, tumor suppressor genes, and other regulatory genes of cell proliferation. Before I continue with that part of the story, I need to digress briefly to review in whirlwind fashion the basics of molecular biology. My apologies to those of you for whom this is too basic, but it is important for the rest of the talk for everyone to understand them.

The unit of information storage of a cell is deoxyribonucleic acid or DNA. It is made up of a double helix of repeated sequences of four molecules, two purine and two pyrimidine nucleotides. The sequence of these molecules in the DNA strand is the genetic code. Long stretches of DNA made up of thousands of nucleotides comprise a gene. In turn, thousands of genes make up each of the 46 chromosomes contained in each cell, and these 46 chromosomes govern the structure and function of the cell. The genetic information in DNA is the blueprint for the most important molecules in the cell, and these are proteins. The cell uses ribonucleic acid or RNA to translate the information contained in a gene into the structure of various proteins.

Of the thousands of genes in each cell, there are a number that govern the growth and multiplication of cells. There are genes that stimulate cell growth and division, others that inhibit cell growth and division, others that regulate growth, and still others that repair damaged genes. When there are errors in the DNA nucleotide sequence in a gene, a number of consequences can ensue. There can be a change in the structure of its protein such that it doesn't function properly, or such that its function can't be turned off. With certain kinds of gene sequence errors, the protein

can't be made at all, and there is total loss of that protein. In still other errors, there is excessive production of a protein. All of these errors combine to cause havoc in the regulation of cell growth and multiplication.

Errors in the genetic code can occur spontaneously, and these spontaneous errors occur at a very low rate. Carcinogens are mutagens that are chemicals that damage a strand of DNA, causing errors in the code of a gene. These errors increase the damage to genes and cause the rate of damage to increase from the normally low spontaneous rate to a much faster rate.

As I mentioned before, the transformation of a normal cell into a cancer cell is a multi-step process. We know now that each one of these steps involves an abnormality in a growth-controlling gene and its protein product. An abnormality in a single, growth-controlling gene cannot cause a cell to become cancerous nor can two abnormalities do that. As the number of growth-controlling genes becomes abnormal, though, there appear visible abnormalities in the growth pattern of these cells. However, these cells are not frankly cancerous until five to nine critically important growth-controlling genes become abnormal. Once a gene is damaged, it can be repaired by repair enzymes. However, sometimes the gene cannot be repaired, and certainly not if the repair enzyme mechanism itself is damaged. As I mentioned, genetic damage can occur spontaneously, and the requisite number of five to nine abnormalities can thus accumulate, but that happens over many years. Carcinogens, on the other hand, significantly increase the rate at which this damage occurs, causing the abnormal cell to be a cancer cell decades earlier. Thus, someone who might normally never get cancer instead develops the disease at a relatively early age when he or she is exposed to carcinogens.

Overall, 85 to 90 percent of lung cancers are due to smoking. Cigarette smoke contains tar, which contains over 4,000 chemicals, 43 of which are known to be potent carcinogens. These include nitrosamines, benzene, formaldehyde, aromatic amines, and many others. The epithelial cells that line the bronchi or air passages of the lung are the cells in the lung that are at risk for becoming malignant and causing a cancer to grow. Cigarette smoke acutely damages these epithelial cells. Acutely injured cells die, causing them to be replaced by the division of other cells. Dividing cells are much more susceptible to being damaged by carcinogens than are non-dividing cells.

When one or two growth-controlling genes become abnormal in a cell, one initially sees hyperplasia, or abnormal growth, of these otherwise normal-appearing cells. When additional growth-controlling genes become abnormal, then dysplasia occurs, which is characterized by slightly abnormal growth pattern and slightly abnormal appearing cells. With additional

abnormalities, carcinoma in situ develops. This is characterized by cells that grow independent of other growth control mechanisms but that do not yet have the ability to invade into surrounding tissues. Additional mutations would have to occur for cells to have the ability to invade surrounding tissues. After a total of between five to nine growth-controlling genes becomes abnormal, the cell is frankly malignant, growing uncontrollably, able to metastasize by invading surrounding tissues, and eventually invading blood vessels to travel elsewhere in the body.

Repair mechanisms often can repair the damage or end the life of abnormal cells—but not always, particularly if the repair mechanisms themselves are damaged. An example is p53, which is a protein that can sense when growth-controlling genes have been damaged. The protein p53 directs repair enzymes to repair the gene. If the repair was successful, p53 allows the cell to continue through the cell life cycle and divide. If the repair was not successful, p53 directs the cell to undergo programmed cell death, called apoptosis. If p53 itself is damaged and either absent or not functioning, the damage to the growth-controlling gene is not repaired, and the abnormal cell is allowed to divide, giving rise to more abnormal progeny cells. Thus, when a young smoker says that he will smoke only a few years and then give up the habit before irreversible damage has occurred, he is playing Russian roulette. While it is recognized that when a person stops smoking, after only a few years many of the damaging health effects (particularly those related to heart disease) may be reversed, the damage that occurs early on may be irreversible (particularly if the damage involves growth-controlling genes). That early genetic damage is silent and not clinically expressed until years later when lung cancer develops. More importantly, perhaps, once a person starts smoking, it is unlikely that he or she can stop because of the addictive nature of nicotine.

The multi-step nature of carcinogenesis implies that the risk of smoking-related cancer is strongly dependent on the duration and intensity of smoking. The risk of developing lung cancer increases exponentially as both the duration and intensity of smoking increase. Epidemiologic and experimental evidence suggest that the risk of developing lung cancer varies more strongly with the duration of cigarette smoking than with the number of cigarettes smoked. Lung cancer incidence varies with the fourth power of duration of smoking, but only the second power of the number of cigarettes smoked. Thus, the risk of developing lung cancer by age 50 is 350 percent greater if a person begins smoking at age 13 than if he begins at age 23. Early-onset smokers are more likely to develop a long-term addiction to nicotine than late-onset smokers, and early-onset smoking is associated with heavier smoking.

Thus far I have tried to explain why, from a pathophysiologic basis,

the onset of smoking in adolescence is particularly critical. I would like now to turn to the reasons young people are a particular target of cigarette promotion. I will first examine the factors related to the establishment of smoking in teenagers. There is no single factor that causes teenagers to smoke. In the 1994 surgeon general's report on *Preventing Tobacco Use Among Young People,* five stages are described in the initiation and development of tobacco use among children and adolescents:

forming attitudes and beliefs about tobacco
trying tobacco
experimenting with tobacco
regular use of tobacco
addiction to tobacco.

A number of factors combine to influence a teenager to progress through these stages. These include sociodemographic, environmental, behavioral, and personal factors.

Peer influence, including that of siblings, is particularly potent in establishing early attitudes toward smoking and may be important in initiating experimentation with smoking. Parental tobacco use is generally felt not to be very important, but a report in the *Journal of the American Medical Association* (*JAMA)* in 1997 surveyed 504 preschoolers ages three to five. The report found that children of mothers who smoke are six times more likely to report that they intended to smoke in the future than children of nonsmoking mothers. Children whose fathers smoke are three times more likely to say they would smoke in the future. Children from families with lower socioeconomic status are at increased risk of initiating smoking. Children with lower levels of academic achievement, and less involvement in organized school activities and in sports, are more likely to be influenced to smoke.

Adolescents with a lower self-image and self-esteem are less likely to resist peer pressure and more likely to be influenced by tobacco promotion that glamorizes smoking. In reading interviews of teens who smoke, they repeatedly express the notion that smoking is "cool," and that their smoking will help them achieve that. This is described in a model outlined in the surgeon general's report. Cigarette advertisement and promotion in print media, in movies, at sports events, and through a myriad of promotional gimmicks create an idealized image of smokers. This image has an effect on the shaping of the adolescents' idealized self-image. If the actual self-image is strong and close to their ideal, they will not seek to change it, and they are at less risk of starting to smoke. If, on the other hand, the actual self-image is low, they will alter behavior to be more like the idealized version and are at greater risk of smoking.

Availability and accessibility are important factors in teenage smok-

ing. Although state laws prohibit tobacco sales to minors, teenagers frequently have no difficulty buying cigarettes. Several reports in 1989 and 1991 revealed that in communities across the country, including Santa Clara, Solano County, Woodbridge, Ill., and Buffalo, N.Y., about 75 percent of convenience stores were found to sell tobacco products to minors. After initiation of community education programs and stiffening of local laws, the percentage decreased significantly. There is one hopeful note. In an article in the *San Francisco Chronicle,* Jan. 30, 1999, a sting operation in Mountain View was reported. Teenagers participating in the sting were able to buy cigarettes in only two out of several dozen stores.

The most important influences, and the ones most easily changed if the political will were there to do it, are advertisement and promotion by the tobacco industry of its products. Since the late 1960s, tobacco consumption in this country began to decline. In 1965, 40 percent of adults smoked, and by 1987 that fraction declined to 26 percent. Presently, about one million adults stop smoking per year. More than 400,000 adults die of smoking-related illnesses. Thus, each year the tobacco industry must replace about 1.5 million smokers who have died or were able to quit. Teen smoking decreased until the late 1970s. Since 1991, there has been a significant increase in teen smoking. In 1991, 27 percent of high school students considered themselves smokers. In 1997, that number increased to 36.4 percent. Three thousand children and teenagers begin smoking each day, amounting to one million new smokers per year. Among current adult smokers, 89 percent started smoking by age 18. The majority of teen smokers under age 18 who are experimenting with cigarettes claim they do not intend to be smoking five years later, yet 76 percent still are, attesting to the highly addictive nature of nicotine and the likelihood of addiction with only experimental exposure. Virtually no adult smokers started smoking after age 25. Once smokers begin steady smoking, there is very little brand switching, and the brand that they start with is the brand they will die with. Thus, when the tobacco industry claims that their advertisement is aimed only at adults to get them to switch brands, it is not true.

It is a clear fact that the industry continues to target children, based on studies of the types of advertisements and promotions of tobacco products, on comments and testimony of advertising executives, and on evidence in internal documents of the tobacco companies, released in recent trials and settlements between the industry and the government. Advertisements of Camel and Marlboro brands is ubiquitous in youth-oriented magazines and in promotions of sporting events, car races, and logo-festooned give-aways such as tee shirts, baseball hats, backpacks, and CDs. These brand logos appear on video arcade games, children's toys,

and candy products. In one survey of 12- to 17-year-olds, 34 percent admitted owning a tobacco promotional item. To purchase many of these items, coupons obtainable only in cigarette packs are required.

The two brands most heavily advertised in teen-oriented magazines and through promotional items are Marlboro and Camel. The most successful ad campaign for both adolescents and adults under 25 has been the one centered around the Marlboro Man, and later, Marlboro Country. As most people will recognize, the Marlboro Man is depicted as a cowboy who epitomizes the stereotype of American independence. He is usually featured alone, he interacts with no one; he is strikingly free of interference from authority figures such as parents, older siblings, or bosses. In the words of Phillip Morris CEO R.W. Murray, "The cowboy has appeal to people as a personality; there are elements of adventure, freedom, being in charge of your destiny."

No advertising campaign and promotion, however, has been as successful among adolescents as that of Old Joe Camel. In the 1980s, R.J. Reynolds launched a new advertising campaign featuring a cartoon dromedary which had been very successful in a French ad campaign for the company in the 1970s. The American version was molded after James Bond and Don Johnson of "Miami Vice." Described as a cool and smooth character popular with women, Joe Camel is depicted in a variety of settings including gambling, racing, at sports events, and in other action scenarios. In a study by DiFranza in *JAMA* in 1991, 1,060 high school students ranging in age from 12 to 19, and 345 adults older than 21, were interviewed. Students were more likely to recognize Old Joe—98 percent vs. 72 percent. Nearly twice as many students as adults described him as "cool," and nearly three times as many teens said they would want a person like Old Joe to be their friend. In 1988, when Joe Camel was launched, the Camel cigarette brand accounted for 0.5 percent of the illegal adolescent market. In 1991, that number increased to an astounding 33 percent. Given the 1991 average price of a pack of Camels, the illegal revenues increased from $6 million in 1988 to $476 million in the children's market segment. The statistics that I cited earlier would indicate that most adults are not impressed by Joe Camel. But it is astounding how pervasive Joe Camel imagery is and how effective it is at making an impression on children. In a study by Fisher and others, three- to six-year-olds were surveyed as to their ability to identify various brand logos. This study showed that 30 percent of three-year-olds recognized Joe Camel and could correctly match him with a separate picture of a cigarette, while the recognition rate for six-year-olds was 91 percent. Six-year-olds identified Joe Camel as often as the Mickey Mouse logo of the Disney Channel. In another study of teenage smokers, 34 percent indicted cigarette advertisement as the

principal influence causing them to smoke.

Smoking is not intrinsically pleasurable and is instead quite unpleasant. The combination of psychosocial and environmental factors of peer pressure and advertisement creates the conditions through which beginning smokers overcome the initial noxious effects and continue to smoke. It is, however, nicotine that keeps them smoking. Nicotine is highly addictive. Once cigarette smoke is inhaled, nicotine reaches the brain within 10 seconds. Nicotine has effects on the brain, heart, and adrenal glands. In the brain, it binds to nicotine receptors and is involved in the mesolimbic dopaminergic reward system, which also mediates the addicting actions of cocaine. Nicotine is involved in the modulation of hormones such as epinephrine and cortisol. Animal research shows that repeated exposure to nicotine results in the up regulation of nicotine receptors; that is, an increase in number of these receptors. This increase may be involved in the physiologic basis of addiction. After a period of exposure to nicotine, physical dependence on nicotine develops. The dependent person then appears to be functioning normally when under the influence of nicotine but when deprived of nicotine will feel abnormal or not right. The withdrawal from nicotine causes craving for nicotine, irritability, frustration or anger, anxiety, difficulty concentrating, restlessness, decreased heart rate, and increased appetite. In recently released internal tobacco industry documents, their own research led them to believe that nicotine was addictive. In one study in the early 1960s, psychologic and cognitive tests and skill tests were performed on nonsmokers and smokers. Nonsmokers and smokers who had recently had a cigarette scored equally well in cognition and coordination. However, the performance of smokers who were deprived of cigarettes was significantly inferior. Without nicotine, there is no reason to smoke. In the early 1970s, one tobacco company tried to market a nicotine-free cigarette. It was a resounding failure. Without the addicting drug, there is no reinforcement and no physical demand to inhale noxious smoke. In the absence of addiction and physical dependence, there is no pleasurable benefit from smoking. Smoking makes a smoker feel better, calmer, sharper, and more relaxed only because the withdrawal from nicotine makes him feel terrible.

The tobacco industry has consistently denied that there are adverse consequences to smoking, and that smoking causes a number of diseases including cancer, heart disease, and chronic obstructive lung disease, among others. The industry has consistently denied that nicotine is an addictive drug, and that they are manipulating the level of nicotine in cigarettes. They are also strenuously denying that they target children and adolescents in their advertisements. Ever since the early 1950s, when numerous studies became available describing the health consequences of

smoking, the tobacco industry has sought to conceal their own research and obfuscate and distort other scientific research. Since 1994, thousands of pages of internal tobacco company documents have become available and are published on the Internet in a variety of forms on a number of Web sites. These incriminating documents clearly show that the companies have consistently lied to the public and to government agencies. At a hearing before Representative Henry Waxman's Subcommittee on Health, on April 14, 1994, chief executives of the seven major tobacco companies swore under oath that nicotine was not addictive and that they were not manipulating nicotine levels in cigarettes to ensure that addiction. In this era of truth seeking, none of these executives has yet been indicted for perjury.

Tobacco industry executives have known since the early 1960s that smoking causes cancer, heart disease, and chronic lung disease. They have known that nicotine is addictive. Illustrative is a memo written by Addison Yeaman, general counsel for Brown and Williamson, on July 17, 1963. In it he states: "Moreover, nicotine is addictive. We are then in the business of selling nicotine, an addictive drug, effecting the release of stress mechanisms. But cigarettes, despite the beneficent effect of nicotine, have certain unattractive side effects: 1) they cause or predispose to lung cancer, 2) they contribute to certain cardiovascular disorders, and 3) they may well be truly causative in emphysema, etc." In another document, an executive states, "We are a drug company, not a cigarette company." On Jan. 23, 1998, DNA Plant Technology Corporation settled with the government for $200,000, and their agreement to cooperate in the government's case against Brown and Williamson Tobacco Co., with whom they were accused of genetically engineering tobacco plants to consistently produce higher levels of nicotine and then illegally smuggling the seeds to Brazil. Internal documents repeatedly reveal industry attempts at manipulating levels of nicotine in cigarettes.

The tobacco industry has consistently targeted children and adolescents in their advertisements and promotions. In a 1981 memo, a Brown and Williamson vice president described habits of 12- to 18-year-olds, euphemistically termed "young adult smokers." He warned that smoking rates were on the decline since 1976-77, which meant that the company would "no longer be able to rely on a rapidly increasing pool of teenagers from which to replace smokers lost through normal attrition." In a presentation to the R.J. Reynolds board of directors in September 1974, the company vice president for marketing, C.A. Tucker wrote, "They represent tomorrow's cigarette business. As this 14 to 24 age group matures, they will account for a key share of the total cigarette volume for at least the next 25 years.... Our strategy becomes clear...[we should pursue a] direct advertising appeal to the younger smokers."

The industry has tried to distort legitimate scientific inquiry. One example is a 15-year-long research project at Harvard University, funded and directed by a tobacco law firm, that was nothing but a public relations ploy.

Once the industry realized that their product killed people, they hired legions of lawyers to protect this knowledge from discovery and to protect the industry from liability. They accomplished this through the establishment of a number of tobacco industry research committees and institutes. The most recent device to accomplish this is the Committee of Counsel, a mechanism by which the lawyers of the various tobacco companies cooperate and share information. By involving lawyers in virtually every internal study, the industry attempts to make the studies part of attorney-client privilege, and thus not discoverable in liability cases.

Until recently, the tobacco companies have been invincible in their defense against product liability suits and efforts to regulate nicotine as a drug. Since the publication of incriminating internal documents from a number of these companies since 1994, this defensive wall has been breached. The companies have been forced to settle a number of suits from states and insurance companies seeking to recover costs of treating illnesses caused by this industry. They are beginning to lose individual product liability suits which they had consistently won in the last 40 years. Because tobacco industry profits are so huge, these developments don't have them worried. As long as they can continue to addict a million teenage replacement smokers to nicotine each year, their continued profits will be assured even if they have to pay out billions in settlements.

However, this past year there seemed to be a realistic chance that there would be federal regulations to regulate the industry to reduce smoking among teenagers. Key among the provisions were restrictions on advertisement and the imposition of even bigger fines if the rate of teenage smoking did not drop on a yearly basis. But again the tobacco companies had little to worry about. As they had done time and time again in the last 40 years, key senators and congressmen came to the rescue of this industry. As reported in the *Washington Post* on June 18, 1998, "Though the bill had a majority of votes in its favor, it failed…to overcome the Senate's standard parliamentary hurdle of 60 votes for contested bills. The end came after the central player in the debate, Majority Leader Trent Lott, moved to end the marathon," thus killing the bill.

In the July 19, 1995, *JAMA,* there is an interview with Victor L. Crawford. Mr. Crawford was a lawyer and Tobacco Institute lobbyist, making his living defending the industry against all comers in the Maryland legislature. He was a smoker and at the time of the interview was dying of metastatic cancer of the tongue caused by his smoking. He had come forward to cooperate with anti-smoking groups to provide what

he knew about tobacco industry activities and tactics. Toward the end of the interview he was asked if he had qualms when he was working for the Tobacco Institute. He replied, "I knew in my heart it was wrong, but it wasn't going to happen to me. What I didn't know was what suffering it really does cause, and nobody knows that until they go through it." Later when he was asked if he could reach people currently working for the tobacco companies he replied, "They know. In their hearts they know. But they don't know how bad it is until it happens to them. The money is good and you can make a similar argument about liquor. But liquor at least has some redeeming values. Tobacco has none. None. But all I can tell them is they've got to follow their own conscience. They don't realize the suffering that they're causing until it happens to them and the suffering that they're causing is beyond words."

The tobacco company executives, their boards of directors, and their lawyers know. Trent Lott and others like him in power know. They know that a million teenagers a year in this country are newly addicted to cigarettes, and that 400,000 per year will ultimately die because of smoking. They all know. But the money is too good and the greed is too overpowering.

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