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1. INTRODUCTION

This project which I have been working on, called “Lung cancer and antioxidants” , is about this disease which has been in our life for ages, Ebert Papyrus in Ancient Egypt already provided documentation about tumours; and unfortunately it will may remain for ages too, due to the wide variety of its cases, as nowadays it is said that everybody is more and more stressed and smoking can be a way of scaping from their own problems, and pollution will always exist. Otherwise, medicine has improved a lot, and investigation purpose is to prevent and control it. Recently researches are mainly on steam cells and biomedicine discoveries have an important role.

My work is divided into two different parts:

The first one consists of presenting cancer, both as a general introduction and specifically lung cancer. I have explained what cancer is, its causes, symptoms and evolution, possible treatments and side effects … To complete this theorical part, I have interviewed Dr. Salvador Macip, a well-known researcher, who had been in SINAI hospital in New York for some years, and now he is working at Leicester University. I have also been able to obtain some information from a lung cancer patient, which has demonstrated the theory about lung cancer, despite this patient died before he could receive all the possible treatments.

Secondly, after having presented it, there is the practical part where I have found the link between antioxidant substances and cancer, and I have proved it in the school science laboratory. There, I experimented with yeast culturing, hydroxide peroxide (H_2O_2), and some antioxidant samples. I expected to obtain different reactions and different results. It was a very well aim achieved. Another motivating experience was visiting the Hospital Clínic Laboratory in Barcelona where I could work with a lung tissue.

After doing everything, I have summed up the results obtained and I come to the final conclusions.

2. DEFINITION OF CANCER

2.1 DISEASE OF CANCER

2.1.1 CANCER IN A FEW WORDS

Cancer is a disease caused by some cells which have reproduced uncontrollably. *(fig.1)*

The cells form different groups or tumours which are called benign tumours, (they are not cancer, they can be removed, and they rarely appear again), and those invading other tissues are known as malignant tumours or metastasis -the true cancer-, and it is spread to the different parts of the body through blood and the lymphatic system.

There is a wide variety of cancers; therefore, we can confirm that it is more or less a family of 100 diseases related by the fact that it is an uncontrolled reproduction in all cases.
All cancers stem from body cells.

The process of normal cells turning into cancer cells: The body is composed of many sorts of cells. These cells grow and divide in a controlled manner and are continuously producing more cells needed for the body to remain healthy. As the cells age are damaged, they die and are substituted by new cells. The process in which cells die is called apoptosis. *(Fig.2)*

However, this orderly process sometimes does not go on the right way. The DNA of a cell can become damaged or modified, which can produce mutations that affect how a normal cell can grow and develop. The result of these mutations is that cells do not die when they are supposed to and therefore, extra cells develop unnecessarily. These extra cells might cause a mass of tissue known as a tumour. *(Fig.3)*

2.1.2 CANCER AND CELLULAR CYCLE

Cancer formation means several mutations that genes may control during a cellular cycle. The cells' cycle is the process in which one cell is formed by mitosis until it is divided again.

This process consists of two parts, the first one called interphase and the second one, mitosis. During the first one, the cell grows and has big bio synthesizer activity (G2), it duplicates its DNA and gets ready to divide (G3).

Mitosis (phase M) is when the first cell creates two cells identically the same as the one they come from. In a non cancerous cell all this process is regulated by some molecules which are called points of control, and they act as traffic lights, stopping or accelerating the process. So after G1, comes G0, in a stopping phase where the cells are active but they neither grow, nor divide. Now, until G1 finishes, is when the size of the cell and DNA damages are controlled.

These points of control are where proteins as cyclins, and CDK (Cyclin Dependent Kinases), have their importance with the other molecules which stimulate the mitosis as growing factors or hormones. When some mutations affect those genes which codify these proteins, then the cell looses control and it can cause cancer.

2.1.3 LUNG CANCER

This investigation will focus only on Lung Cancer.

Lung cancer is also called Bronchogenic Carcinoma, because the cancer which begins in internal organs is a carcinoma, and in this case, it affects the lung. It is one of the most common cancers in the world.

There are different types of lung cancer. Therefore, depending on the way they grow and spread, they are treated in different manners. As cancer has its origins in a tumour, on the one hand, we can find benign lung tumours, which usually mean there is no need to remove them, and they do not spread to other parts of the body, either. On the other hand, we can find malignant tumours, which may cause death, they may also grow again after being removed, and they can invade other organs, too. Cancer

cells break away from the tumour, they enter blood vessels and then they attach to other organs and form new tumours called metastasis.

We can classify lung cancer into two different groups: the ones which grow and spread more slowly, referred to as lung cancer with non small cells, and lung cancer with small cells, which grow more quickly and the may invade other tissues.

Lung cancer with non small cells is the most common one, about 80%, and depending on the original cells, we can classify it into three main groups:

- Squamous
- Adenocarcinoma
- Large cell carcinoma

Tobacco is the main cause of lung cancer, even though there are other risk factors. Diagnosis and treatment will be different in each case.

2.2. DISEASE HISTORY

2.2.1 FIRST FINDINGS AND RESEARCHES

We cannot confirm when the first case of cancer appeared, as is the case with the first patient, because in fact, cancer is the result of several cells having mutated, and it often has genetic influences.

Ebert Papyrus, the most ancient medicine document written in Ancient Egypt around 1550 B.C., provides our earliest possible documentation of ancient awareness of tumours. The problem is that ancient medical terminology is widely misunderstood. It describes eight cases of breast tumours or ulcers in Egypt that were treated with cauterization. However, the document also says there is no treatment for cancer. Obviously, it has been impossible to investigate the existence of tumours in the tissues of the dead people of Ancient Egypt, but some skeletons have similar bone strains as today's bone cancer.

Hippocrates was the first to use the words "carcinos /carcinoma" to describe tumours and he thought it was better to leave cancer untreated because people who had been under treatment did not survive longer than those who were not. About 300 B.C., they could differentiate some benign tumours. 168 B.C. Galen said that a healthy diet and good climate were directly connected to the possibility of not suffering from cancer. He also thought that tumours should be operated and cancer could be curable in early stages.

Microscope discovery was very important, and during the Renaissance, experimental science grew quickly. Rudbeck, in 1652, explained lymphatic vessels and the new theory saying cancer could be spread through them. In 1750, John Hunter supported that cancers could be removed if they had not yet spread to other tissues.

2.2.2 DISCOVERIES FROM THE 19TH TO 20TH CENTURY

John Hill was the first to recognize the dangers of tobacco. In 1779, the first cancer hospital was built in Reims, but far from the city, in case cancer was contagious. Different reports and discoveries had been taking place over the years, but it was at the end of the 19th century, when some scientists began to carefully study the tumours and the cells they came from. In 1829 Joseph Claude Anthelm Recamier discovered metastasis. In 1838 Johannes Muller linked cancer to abnormal cells. In 1851 Washe

made the first description of malignant cells in the sputum. In 1895 Wilhelm Conrad Rontgen discovered X-rays, an in 1899 they were used to treat cancer. Before 1902 Chevalier Jackson made the first bronchoscope. In 1902, the first ECG (electrocardiogram) appeared, reading using a string galvanometer that Willem Einthoven had designed himself. In 1910, Peyton Rous discovered that a virus could cause a tumour in hens. It was in 1912 that Dr. Davis performed the first surgery for lung cancer. The same year, Adler, published the first monograph about this disease, which was considered a very rare one in those days. In 1914 Theodor Boveri proposed abnormal chromosomes as the cause of cancer. In 1915 cancer was induced in animal lab. In 1933 Evarts Ambrose Graham and Jacob Jesse Singer performed the first surgical removal of all parts of the lung for carcinoma. German scientists in Nazi Germany began to research the links between smoking and lung cancer. In 1946 Louis Goodman discovered the possibility to use nitrogen as chemotherapy against lymph sarcoma and leukaemia. In 1951, as cancerous cells are immortal because they do not stop growing, some of them were taken out of a patient who had died, and scientists made them grow in a lab, in order to study them. It was the first time that human cancerous cells were living in a lab. In 1960 there were talks about DNA provirus hypothesis of cancer. By 1962, the USA confirmed that smoking caused lung cancer. In l970, Varmus and Bishop discovered the oncogenes. In 1971, antigens were discovered, as a way to avoid malignant cells to make new blood vessels, and consequently to avoid growing. In 1972, the computerized tomography (CT)[1] was created. In 1973, the MRI (magnetic resonance imaging) was invented, very useful to diagnose different cancers. It is based on different signals obtained from different tissues subjected to high magnetic fields. In 1974 Michael Phelps and Ed Hoffman invented the PET[2], which gives high resolution computerized images based on the detection of radiation that is released from chemicals introduced into the body, and it also gives information about biochemical activity of the cells such as those in tumours. In 1976 Harold E.Varmus and J.Michael Bishop discovered the first cellular oncogenes. In1986 Stephen H.Friend isolated the first tumour suppressor gen,RB(retinoblastoma).In 1991 the first antiangiogenic called “caplostatine” is found. In 1995 the first DNA micro array chip was invented and it was tested in plant genes, and maybe it will be able to detect cancer in humans and to help designing individual treatments. In the future, Folkman discovered the angiostatine, as the first angiogenic

[1] A CT Scan shows pictures of your body parts, a small amount of dye may be put into a vein in your arm. This dye leaves your body after a few days. The test takes 15-20 minutes for each area you are having checked.
[2] Positron emission tomography scanner.

made by the human cells themselves. In 1999 there was the first successful creation of tumour cells, some cells were transformed into tumour cells in a lab, to study them.

2.3 EPIDEMIOLOGY

2.3.1 GENERAL STATISTICS

Cancer is a disease that can take up to 200 different forms. It causes about 7 million of deaths every year and the WHO -World Health Organisation- expects that in 2020 there will be 16 million new cases every year. Focussing on lung cancer, the epidemiologic evidence and the complementary biological understanding of respiratory carcinogenesis have supported the conclusion that the most relevant cause is exposure to tobacco smoke through active or passive smoking. Lung cancer is at the top cancer deaths lists, mainly in the USA, and its principal cause is smoking. 85% of lung cancers are directly caused by smoking. Both, active and passive smokers are in danger. At the end of the 20th century, lung cancer had become one of the world's leading causes of preventable death, and we say preventable death because smoking is not necessary, we smoke because we want to, and if we did not smoke the percentage of lung cancer would be reduced to a minimum, because obviously there are other causes apart from tobacco, but the present pandemic of lung cancer has followed the introduction of manufactured cigarettes with addictive properties, which resulted in inhaled carcinogens.

In terms of age, people mainly affected are between 55 and 65 years old, but in general, they are between 35 and 75. Being a smoker over 45 is considered an important risk.

Its early diagnosis is very important for treatment, not only for accurate treatment but also early diagnosis can lead to a 20% success rate. However, it is very difficult if it has already spread to other tissues. Due to this difficulty, the patient's life expectancy is only about 8 months from the moment the lung cancer is detected.

2.3.2. SPAIN'S STATISTICS

In Spain, lung cancer investigation for 15 years has increased from 6% to 12% the surviving patients' time in 5 years later. Every year there are about 20,000 new people suffering from lung cancer, which is approximately 18% of all cancers and 3.2% are women. Its death rate is 20% of the total amount. *(Fig. 4,5,6,7)*

2.3.3. ASIAN CASES

An important rise in lung cancer is expected in China and India in a few years. All around the world, more men suffer from it than women. They are usually people about 60 or 65 years old who began smoking when they were young and they still do.

2.3.4. COMPARISON OF CASES IN DIFFERENT COUNTRIES

Around the world, there will be about 12,000,000 ill new people who will suffer from cancer during the year 2009, and 200,000 of them will be in Spain, and 18,500 will be lung cancer. Among these twelve million new patients, 16% of all cancers will be in men and 7.6% in women. Most of the cases are in Eastern and Southern Europe, also in North America, but most of the women are in the North of Europe. In 2002, lung cancer was the first cause of cancer mortality in men, and the second in women. In general, lung cancer is detected in people between 55 and 75 years old, although some of them are 35-40.

On the one hand, the Spanish mortality of lung cancer in men is very high. It is only higher in Eastern Europe. On the other hand, regarding women, the rate is very low. However, it is decreasing in men, every year whereas it is rising in women.

2.3.5 COMPARISON OF MEN / WOMEN RATES

The death of many people, both men and women is caused by this type of cancer. In men, 22% of all cancers are lung cancer, and in women, 8%, but nowadays it is increasing.

Nowadays, the rate of men diagnosed is lower than some years ago, due to the anti-tobacco campaigns, but, the rate of women diagnosed is increasing, with reasons being unknown, especially among black women. Both, men and women rates of lung cancer, all over the world do not vary a lot, the highest rates occur in the same regions. Mortality rates may be higher in urban areas because of pollution.
It may affect anyone, but it is more usual in people over 50.

For women the highest rates of lung cancer are found in North America and northern Europe. Women in the USA have the world's highest lung cancer incidence

rates followed by Canada. *(Fig.8,9)* The lowest lung cancer incidence rates in both men and women are found in African and Asian countries.

Between 1997 and 2006, the incidence rates of male lung cancer decreased by a fifth (21%). Over the same period, there was little change in the female rates. For males and females combined, the lung cancer incidence rate decreased by 11%. A sample is in these statistics about Great Britain. Male lung cancer rates for males have fallen by 46% from 113 per 100,000 in 1975 to 61 in 2006. Over the same time period female lung cancer incidence rates have risen by 64% from 23 to 37 per 100,000 populations.

In 2006, in Spain 61,184 men died due to cancer, but 16,859 of them were lung cancers (unfortunately in the first position). At the same period, also in Spain, 36,862 women died due to cancer and 2,624 of them were lung cancers; much less women than men.

2.3.6. SHOCKING NUMBERS

The problem is that only 30% of these new patients can be treated through surgery because the other 70% has no possibility of success. And after 5 years of treatment, only 12% may be cured, of which there has been a 1% improvement each decade in the past 30 years. This is because lung cancer is very difficult to prevent due to the fact that the tumour is already advanced when the symptoms appear. That is why it is said that not smoking is one of the best ways to prevent it, and if we lead a healthy, active and nutritious lifestyle, then, lung cancer could be reduced by 50%.

2.4 AETIOLOGY

We can ask ourselves why does cancer appear, and what is the cause? Genes or the environment?

There are different causes of cancer. Maybe our genes are a little weak, or maybe some toxic circumstances affect DNA. It is believed that both are true. An example of environmental causes is that Chinese people risks later became the same as American people. That meant that the Chinese environment has something special that protect those people, consequently, scientists have thought that food could have an important influence. A similar test done with twins gave the same results; environmental risks were higher than genetic risks. That is why when scientists are researching, and paying more attention to finding how to prevent cancer than finding a cure because there are hundreds of different cancers ant it would be easier to have exact causes and prevent the disease, or if not, the possibility to deal with it more individually.

After a lot of investigation, we can consider 4 kinds of lung cancer causes:

- Tobacco smoking: active and passive smokers, depending how much on smokes, and when one started smoking.
- Indoor air pollution: arsenic, asbestos, chromates, chlorormethyl ethers, nickel, polycyclic aromatic hydrocarbons, radon progeny… some countries consider that smoke from cooking stoves and fires may influence, too.
- Outdoor air pollution: some carcinogen particles generated by combustion.
- Genetic causes, oncogenes.

2.4.1. FOOD CAUSES

Nowadays, in fact since 1980s, many investigations are linking diet to lung cancer; and they might have found that some dietary micronutrients could change the risk of cancer mainly in smokers. Seoul University says that some inorganic phosphates, such as additives used in fast food, soft drinks, and industrial bakery, may cause lung cancer.

2.4.2. ENVIRONMENTAL CAUSES

The main cause of lung cancer is smoking cigarettes, but there are some jobs that may also influence your chances, for example, being exposed to asbestos or radon for a long time. These two substances are very dangerous for people who work in shipyards and mines. However, there are other causes as well. Nowadays, scientists can confirm that radon in indoor environments is now considered to be a significant cause of lung cancer whereas some years ago; people thought that radon was a cause of lung cancer in underground mines. Outdoor air pollution, which includes combustion-generated carcinogens, contributes to lung cancer in urban dwellings. In addition, it is also indoor air which contains some respiratory carcinogens, including radon, and cigarette smoke. What is more, in some developing countries, we can find fumes from cooking stoves and fires associated with the risk of lung cancer.

The causes of lung cancer are mainly environmental, but it also depends on the susceptibility to respiratory carcinogens of everyone. Moreover, lower socioeconomic status is associated with lung cancer risks because this population works in risky jobs. Usually these risky jobs are for example, working in mines, as miners belong to the lowest socioeconomic status, although everyday preventing risks at work is becoming more important, the risk remains.

2.4.3. CIGARRETTES OR TOBACCO

Cancer risks vary depending on the number of cigarettes smoked, how much time the smoker has been doing it, and the age, because those people who started smoking at younger ages have more possibilities of becoming a regular smoker.

The advertisements on cigarette packages are not exaggerating: smoking can kill. Smokers have between 4 to 10 more possibilities of dying from lung cancer.

The worst components of tobacco are carbon monoxide, tar, and nicotine. A huge part of the other components are still under investigation. At present, tar is a complex mixture of many different chemicals which are cancer initiators.

A cigarette may have 5000 carcinogenic substances, such as ammoniac (the same as very aggressive cleaning products), or benzopyrene and methane (rockets petrol have it), arsenic (rat poison), butane (a type of domestic gas), cyanide (used in the gas camera), formaldehyde (a preservative), cadmium (found in batteries), monoxide of carbon.

In fact, smoke components are not very dangerous, but the problem is that, in our body, due to a reaction of an enzymatic system called AHH (aryl hydrocarbon hydroxyls), these components have a huge capacity to enclose with proteins and DNA and RNA, and then they can easily make mutations which can cause cancer.

Some research confirms that it is impossible to say which kind of cigarettes are more or less dangerous, because smokers do not always smoke the same, neither product compositions are the same. Nevertheless, they concluded that filtered cigarettes and lower tar yields reduce the risk of lung cancer. Especially the report also concluded that changes in the design and manufacturing of cigarettes over the last 50 years have not benefited public health, although the cigarettes composition has considerably changed since the 1950s.

The same composition that the smoker inhales is not found in a first grade or when he leaves the smoke in the air in a second grade. Most of the worst compounds are in the second grade (carbon monoxide and carbon dioxide, ammoniac, benzene, benzopyrene, aniline, acroleine, and others). Smoke is when in the air there is carbon monoxide, nitrogen oxides, ammoniac, hydrocyanic acid and acroleine and it causes cancer.

Carbon monoxide (CO) as it is similar to the haemoglobin of the blood moves the essential oxygen in breathing and then the cell oxygenation decreases. This may affect the nervous system, the vascular and the heart; the human body can quickly eliminate a big quantity of carbon monoxide, so many people feel stronger and more energetic when they stop smoking. Other compounds affect bronchus; causing cough and decreasing lung capacity to clean the inhaled air. It is already known that tar, a mix of hundred chemical substances, has no difficulty in causing malignant tumours; it is as a vehicle for all the poisons from the cigarette to the blood. Nicotine is what immediately affects our body because it is a drug that causes dependence, nearly similar to the heroine[3] or cocaine. It has different reactions depending on the person, but in general it makes the heart work harder, it needs more oxygen, and it can cause cardiovascular problems. It also makes that platelets blood stick inside the vessels and they may get blocked. Nicotine is inside tobacco leaves, and it is quickly absorbed by the blood and in 10 seconds it is in our brain, then the brain makes the chemical substance named dopamine[4], our brain easily gets used to receiving nicotine and it wants more when it is absorbed.

[3] The heroine is one of the most addictive drugs. A regular heroine taking makes the consumers need a bigger quantity for the same results, and the ways in which it is adulterated may affect breathing system

[4] Dopamine is a hormone, it is a neurotransmitter, it is very important in our brain especially on our emotions. The connection between heroine, dopamine and nicotine is that heroine the same as cocaine, provoke dopamine's release.

2.4.4. GENETIC INFLUENCES AND ONCOGENES

Although smoking is the main cause of lung cancer, not all smokers develop it. There are some genetic and DNA influences, it depends on everyone's metabolism and its relationship to carcinogen substances. DNA influences mean oncogenes role.

Our cells are always under stress and toxic substances called mutagens that may affect DNA. It also can occur that when the cell is dividing, an error appears. All these situations can cause mutations or unexpected changes in DNA, and although our body can repair these errors on its own, some mutations which are dangerous for the cells still may resist. These cells can damage RNA and the protein codified by this gene, and consequently, the protein that this gene will make from now on, might be completely different, and if the mutation makes that this protein is in bigger quantities, the cell will not stop growing, and in this case, the mutated gene is called oncogenes.

Oncogenes are some normal genes that have transformed into abnormal genes by a gene mutation, and these abnormal genes will transform one normal cell into a cancerous one, oncogenes is the transformed gene. But, one oncogene is not enough to provoke a cancer; it will be caused by a mutation of a group of oncogenes. In other words, oncogenes are those genes which can make a normal cell become a tumoruous cell. A normal cell has got some genes that may experience a modification and become transformed genes, they are called proto-oncogene. These proto-oncogenes often appear in an amplified way in tumoruous human cells, so they are being researched, and they are not the only cause of cancer either, because cancer is a group of multi-factorial diseases. All this evidence has been used since 1970s to confirm that cancer may be a hereditary disease, because there are some DNA genes mutations which pass from one generation to the other. Examples of these proto-oncogenes are: RAS, WNT, MYC, ERK and TRK. Their amplification affects many DNA gens. Erb B family gens codify for transmembrane receptors with tyrosin-quinasa activity.

A big quantity of proto-oncogenes or its production in inappropriate cells is what can cause a tumour, or also during its transformations if there is a change in the nucleotide sequence. *(Fig.11)*

Ras family is for small proteins which join GTA, and myc proteins are transcription factors. Therefore, all these families codify proteins that may be involved in sending signs, then their amplification, and extra-expression make the cell acts in a growing lower level, and they grow in a way that normal cells would not.

There are different ways in which a proto-oncogene becomes an oncogene. A mutation can cause a change in the protein, and then, there is an increase of the

protein activity, otherwise there may be a loss of regulation. More quantity of protein in the cell can also be caused by gene duplication, which is a chromosome abnormality. And also a chromosomal translocation can cause a wrong cell type at wrong times.

The effects of the oncogenes can be blocked by the microRNAs, that is small RNAs 21-25 nucleotides.

2.4.4.1 PROTEINS IMPORTANCE

Fortunately, there are some proteins which look for errors and problems in DNA, and they have to avoid that a cell becomes carcinogen. These proteins are called tumoral suppressors. One of these main proteins, p53, tries to stop it, and then, another type of protein appears, which are the repairing proteins, and after a while everything is right. In case it is not, then ,the cell eliminates itself, and this process is called apoptosis. That would be a perfect situation, because damaged cells are repaired or eliminated, but sometimes there is a second mutation which cancels our natural defences.

DNA has very important genes which control its development; two of them are p53 and Rb[5]. The p53 gene controls the cellular cycle, and if some DNA cells are damaged, it blocks its division, and The Rb gene stops the cellular cycle. If the damaged cell cannot be repaired, it is eliminated by a process called apoptosis and it avoids genetic transmission.

When the protection of these genes no longer exists or breaks down, a tumour appears.

Some proto-oncogenes are a very important link to cancer (lung cancer, too):

- RAS may be activated by a mutation in its protein structure.
- MYC loses its normal control if it is not located in chromosome 8 as it should be.

There must be a balance between growing factors and the factors which are apoptosis. Cancer appears when this balance imbalances to the growing factors.

To conclude all this explanation, we can say that genetics is important in lung cancer. The main oncogenes related to lung cancer are RAS and MYC families, and the antioncogene p53. However, recent research is considering a new oncogenes known as the gene SOX4.

[5] Rb means Retinoblatome (the first supressor discovered).

Biomedical investigations have noticed that half of the cancer cases appear when the p53 gene affected makes this protein inactive, so cancer appears only in case some essential mutations damage the cell. But one or two mutations do not cause cancer, because a carcinogen cell must grow without stop, it must get over apoptosis, and it must be able to invade the lymph system to spread itself into other tissues. That means that many genes have to suffer mutations and break down, causing cancer. Therefore, we could say that suffering cancer is only bad luck; it is like lottery, which is true, because if p53 did not exist to stop mutations, we would suffer cancer at a very early age. p53 is, then, very important. It also means that cancer does not appear suddenly, it is a very slow process, and it may last 10 or 20 years until it can be diagnosed. *(Fig. 10)*

2.5 SYMPTOMS

The most common symptoms in lung cancer are not the same in all patients. But the most relevant ones are:

- Difficulty in breathing, called dyspnoea, it means a shortness of breath.
- Coughing up blood, called haemoptysis; that is chronic coughing, and it worsens with time.
- Weight loss and a loss of appetite.
- Chest pain or pain in abdomen.
- Wheezing difficulty in swallowing, called dysphagia.
- Face and neck inflammation.
- Hoarse voice, called dysphonia.
- Clubbing of the fingernails; but this one is not as common as the other ones.
- Constant tiredness.
- Bronchitis or pneumonia, both incurable.

Lung cancer symptoms depend on its type, its location and its evolution, but the most frequent symptom is chronic coughing.

Those people who suffer from chronic bronchitis, their cough usually gets worse, sputum with blood is also possible, and in the worst case patients may suffer from haemorrhaging.

Wheezing is possible due to airway obstruction where the cancer is developing. If a bronchus is being blocked, it can cause an illness called “ateletacsia” by which a part of the lung is collapsed.

Another cause can be cough, fever, thorax pain and difficulty in breathing. If the tumour is inside the lung, it can provoke chest pain.

After these first symptoms, loss of appetite, weight loss and weakness may appear. Lung cancer often accumulates liquid in the pleura and consequently heart failure.

If the tumour is at the top of the lung, it may affect arm sensibility and also hoarse voice.

An important problem is that tumour can cause some food to go into the lungs, due to the difficulty in swallowing.

Lung cancer may spread into the heart that can cause face and neck inflammation, and chest veins to become bigger and darker. When the patient lies down, he can not see well, he can fall asleep and suffer from headaches.

Lung cancer can also spread into other tissues as the liver or bones, yet during the first stage of disease, especially if it is a small-cellular lung cancer. This is very difficult to diagnose because of the different symptoms.

Other types of lung cancer may provoke weakness, or skin inflammation. It may occur as the first symptom that the cancer repeats after a treatment.

Some types of cancers make hormones or similar substances, and consequently the skin is redder, with a wheezing breath. Men can suffer bigger breasts and women the excess of thyroid hormone. And although it is not very common, the patient can suffer clubbing of the fingernails. *(Fig.12)*

2.6 EVOLUTION

2.6.1 STAGES OF EVOLUTION AND CLASSIFICATION

Lung cancer has different stages of evolution, and the treatment to choose is mainly based on them. Moreover, the higher the stage, the less chance for cure:

1. The tumour is in the lung but the cells around it are healthy. At this stage, tumours are small and they are located only in the tissue of one lung. Its size is like a golf ball. 80-90% of these cases, surgery may have a good result.
2. The tumour may affect other parts of the lung.
3. It has already spread a little but in some cases, surgery is possible; in others not.
4. It is the worst. It has spread to other body organs such as the liver, the kidneys, in some bones or it is the brain.

These stages are used to classify non-small cell lung cancers, and we use the letters **TNM** to do so:

T: it refers to the tumours size, it can be between T1 and T4, depending on its size or if it affects other tissues as main bronchios, arteries or the heart

N: it means if the nearest lymphatic ganglies are affected or not. N0 (N, zero) means they are not. In case they are affected, diagnosis is very important. It is an important clue, and its named between N1 and N3. It is essential to know if the ganglies in the middle of the thorax are affected. This body area is known as the “mediastino”. If it is true, then the tumour can rarely be extirpated.

M: it means metastasis. M0 is when there is no metastasis, and M1 means it has already spread into other tissues.

With the small cells lung cancer, the classification is easier. We talk about limited stage and extended stage. The limited stage is a reduced one and there is no difficulty in using radiotherapy in this case. The extended stage is the one in which the tumour has grown too much to consider it to be in the limited stage; in other words, it has already spread into another tissue, and in this case radiotherapy is not useful.

Some research has their objective in premalignant evolution of lung cancer, because they have found there are some premalignant injuries in the beginning, and in order to save more lives, premalignancy is regarded as the disease, and carcinoma as the end.

Fluorescence bronchoscopy makes it easier to identify these early injuries, and they have appeared much more frequently in smokers than in non-smokers, and if they suffer airway obstruction, the risk for lung cancer increases a lot. Another clear symptom is atypical cells in sputum, that is premalignant cells, not malignant cells yet, which may be present in the sputum for several months to years warning a development of invasive carcinoma.

2.7 DIAGNOSE

After going through all treatments, lung cancer patients must have some checks-up. They must stop smoking, too. These checks-up are very important because if a lung-cancer disease is developing again during the next 5 years after treatment or if other primary tumours appear linked to the smoking habit, as soon as possible for both, the patient and doctor's benefit. It is not easy to survive a lung cancer despite all the treatments possible, because some people they have more possibilities than others to have another tumour in the same area as the first or metastasis to the bones or the brain. In these cases, it is better to apply chemotherapy to stop the tumour's development and give the patients a better quality of life.

Difficulty in breathing and thorax pain are the worst side effects and which the patients suffer more often. Breathing is associated to life, so if we have difficulties in it, we immediately think to extreme difficulty, tiredness…

All these difficulties and the thorax pain cause negative emotions, so patients should go to the doctor's soon because there are some medicines that may reduce the suffering.

There are different ways for lung cancer diagnosis, and not only one is enough to act correctly.

There is not a specific symptom, it depends on each person, but an important risk is to be a smoker older than 45. Another possibility is a thorax X-ray. If there is a tumour, searching its typology and its developing stage is the most important thing to do. It is also necessary to study the patient's condition. All these together will help the doctor in determining the treatment. In fact, the most important way to diagnose lung cancer is fibrobronchoscopy because it can show us a wide view of all the parts of the lung.

Lung cancer needs some years to develop, but it has only a short time as a clinical stage. On the other hand, from the first X-ray to the clear symptoms and diagnosis, it lasts about a year. This is the reason why lung cancer has often metastasised, so when it is diagnosed, we need a local diagnosis of the disease and another about its extension to other tissues.

The first thing to do is a complete patient medical history to get as many symptoms as possible, the risk factors and possible genetic influence. For this reason, a PET is mainly used to see biochemical activity of the cells in tumour. Then the doctor decides what is best to do to attack this cancer and the treatment to follow.

2.7.1 METHODS TO DETECT TUMOURS

Apart from these treatments, there are some methods to detect if a tumour is cancerigenous or not. They are not very aggressive:

1. Pulmonary Radiology
2. CT-Scan(Computerised Tomography): A CT-scan or otherwise known as a CAT scan is carried out if there is some doubt with the X-Ray detecting the spread of lung cancer, or if something unclear appears in the X-Ray.
3. Fibrobronchoscopy (FB): it is a procedure carried out by the use of a flexible 5mm in diameter tube with adequate visualisation. It is used to suck out secretions, insert forceps to remove samples for a biopsy or samples for microbiological analysis. It is carried out through local anaesthetic however sometimes general anaesthetic is used to remove samples from the lung tissue.

Complementary procedures to Fibrobronchoscopy:

a) Bronchial Suction: Sterile Saline solution is inserted in the throat and windpipe and then suction takes place.
b) Brushing: A brush is inserted through the air passages and the endobronchial lesions are brushed in order to obtain some cells for study and analysis. It is extremely useful in cases of lung cancer.
c) Transbronchial Biopsy: this is done in order to obtain samples for a biopsy, however normally the samples are small and therefore making it difficult for diagnosis. It may cause serious side effects in patients with anomalies with blood clot and serious respiratory problems.
d) Transbronchial Needle Aspiration: is done using a needle and a fine Teflon cather.
e) Transbronchial Needle Biopsy: this is similar to the previous procedure using forceps, instead of a needle.
f) Bronchial Biopsy Rinse: Salt water (Saline) is inserted to the throat and windpipe and with the same syringe suction takes place.

4. Bronchography: This is the evaluation by contrast radiology which allows us to visualise through X-Ray, but is rarely used nowadays since the CT-scan and the fibrobronchoscopy are more useful and less aggressive.

5. Pleuroscopy: Local anaesthetic or general anaesthetics are used, and they are carried out to explore the pleural in detail. There are few complications and after the test and tube must be left for drainage for a period of 48 to 72 hours.

6. Mediastinoscopy: Is rarely used as it may provoke, among other complications, paralysis of the vocal chords. A CT-scan and a pulmonary gammagraphy with gallium-67 is better.

2.7.2 A BIOPSY

A lung or pulmonary biopsy is carried out in order to obtain samples from a specific area of the lung tissue through suction by needle. Normally, it is used as an alternative to fibrobronchoscopy when a clear diagnosis cannot be made and this way can be analysed. When they must prick a nodule or lung masses, it is necessary to do a fluoroscopy or amplify the images and even sometimes do a CT-Scan. An open pulmonary biopsy is done when other less aggressive procedures have failed. A tiny sample of lung tissue is taken and normally it is done when the tumour to be analysed is big enough that there is no need to be exact with the point of insertion because you do not want to make a big incision to avoid extended hospitalization. As usual, the contradictions are the dangers that lead to haemorrhaging and respiratory insufficiency.

2.8 TREATMENT

2.8.1 DIFFERENT POSSIBILITIES

Lung cancer has different treatments, as there are different types of lung cancer. Firstly, we consider two types: the one with small cells, and the one with non small cells. Secondly, we will consider some individual facts, for example its evolution. When we say “evolution”, in this case we mean the tumour size and if it has spread to other tissues or not. We cannot forget some patient’s characteristics either, such as age, his lung’s possible activity and his general health.

There are three main options for the lung cancer treatment: surgery, radiotherapy, and chemotherapy. These may be used separated or mixed, according to the type of tumour and keeping in mind the possible side effects. Radiotherapy and chemotherapy are often applied together. There are two ways of applying the treatment: local and general.

The local one is in order to control the tumour, trying to avoid it appearing again in the same place. The general way is applied all over the body. It is applied in order to avoid the tumour spreading to other tissues, and to eliminate the primary tumour.

2.8.2 SURGERY

Surgery is one of the possible treatments. Those patients with non small cells lung cancer are mainly the ones whom the surgery should be applied to and with surgery, it is very important to consider the patient’s health for cardiovascular and breathing risks.

It consists of taking out the tumour. It may not be possible if the patient has breathing problems, but if there are no more problems in the lung but the tumour, the patient will be able to have a normal life after surgery. Death rates of the post-operation phase are about 4.4%. Surgery needs a lot of care from the doctors and nurses.

2.8.2.1 SIDE EFFECTS

During the treatment, the following side effects may appear:

- liquid and air in the pleura (it often appears after surgery and makes breathing difficult)

- Pain in the thorax: some days after surgery, the patient may suffer this; it is hard pain which needs a special treatment. It also makes the patient difficulty to move, even though in bed, coughing and breathing hard, which are very important to eliminate the liquid and air from the pleura.
- Sometimes it is very difficult for the injury to heal.
- It rarely happens, but some lung infections exist.

2.8.3 RADIOTHERAPY

- Radiotherapy is a local treatment. It has been used for more than a century, and it is very dangerous because the radiation is very high. Sometimes it is used before the surgery and some rays are applied in order to reduce the tumour, or after the surgery, and the rays should eliminate carcinogen cells left. It is also a good option to give the patient a better quality of life even though the metastasis has already spread into bones. The patient must go to hospital for several days to receive this treatment and it lasts about 20 minutes, it is a daily treatment. After these twenty minutes, the patient can go back home. It does not cause any pain.

2.8.3.1 SIDE EFFECTS

Its side effects could be some skin problems, sickness, vomiting and tiredness; but they last a short period of time. The worst thing about radiotherapy is that it can make the chemotherapy effects worse. The radiations used in this therapy are very high and the patient often feels very tired mainly during the last weeks of treatment. Some several side effects are:

-Difficulty in swallowing because it hurts, but there are some specific medicines for it.

-Mouth inflammation: mucous inside the mouth may inflame and there are some specific medicines to clean the mouth and calm the inflammation.

-Changes in the skin: it can become redder and drier, then they must avoid the sun and wear very soft clothes, the skin must be very clean and we cannot apply any cream or lotion without the doctor’s permission.

-Changes in hair: it may become weaker and stop growing, it is only a temporary change and after the treatment it will continue growing without any problem.

2.8.4 CHEMOTHERAPY

- Chemotherapy is the worst treatment for the patient, the most difficult one to suffer. Chemotherapy has the advantage that it acts not only on the primary tumour, but also on other cancerous cells or secondary cells located out of the lung. It is usually applied on small cells lung cancer because this kind of cancer is very sensible to chemotherapy. It consists of a mixture of different medicines and it may have some side effects, because sometimes it can damage healthy cells apart from killing carcinogen cells. It depends on the mixture of the medicines applied and also on the individual patient's characteristics. And this happens because carcinogen cells are similar to healthy cells and the medicine applied may affect both.

2.8.4.1 SIDE EFFECTS

The medicine used is very strong, that is why the side effects are very strong too. Therefore, this treatment is usually applied in several sessions , with an interval between them. Some side effects can be:

- Losing taste for food
- Some changes of our sensations to food or smells
- Sickness and vomiting
- Lack of appetite
- Hair loss
- And infection in the mouth called tonsillitis
- The patient may also feel very tired, that is due to the decreasing of white and red corpuscles and sometimes platelets, too.

All these side effects usually disappear after some days of the treatment, even though during the intervals of time between one chemotherapy cycle and the other. Nevertheless, the doctor should give some advice to reduce these side effects; special diets, rest, avoid the sun, wear cotton clothes and so on. In lung cancer, it is usually combined with some other medicine treatments. There are also some medicines used in chemotherapy which are still under investigation to make sure their efficiency on lung

cancer. In some hospitals, they give their patients the possibility to participate in these investigations. Some patients who have participated in them are very satisfied.

2.8.4.2 RELATED MEDICINES

Chemotherapy has been used for about 50 years, and it has not advanced very much , medicines are still the same. For example:

- Ciclofosfamida: it is derived from mustard gas, a toxic used during the First World War.
- Cisplatí : it has been used since 1978.
- Unicristina: and doxorubicine: since 1963, some chemotherapy medicines are anthibiotics, others are too aggressive, and that is why scientists experimented with mixing them.

2.8.4.3 TYPES

There are four kinds of chemotherapy:

- Combined: it is the most commonly used, it is applied combined with radiotherapy or surgery.
- Adjuvant: it is used after surgery, when the tumour is extracted, to avoid reproduction
- Neoadjuvant: it is used prior to surgery to reduce the tumour and make surgery easier.
- Palliative: the aim is not to cure the patient, but to give him a better quality of life and to reduce the tumour.

2.8.5 NEW THERAPIES

Nowadays, other treatments are being investigated but they cannot be used yet. These treatments are especially for those people who have lung cancer in the advanced stages. With treatment, the five-year survival rate is 14%.

2.8.5.1 ANTIANGIOGENESIS

Antiangiogenesis: One of the new treatments is called antiangiogenesis, that is a fight against the tumour capacity to make new blood vessels. It is very important to know about malignant cells but also their environment, called microenvironment. The new vessels bring blood from the normal lymph system to uncontrolled cells, so if we can attack the new vessels we will stop tumours from growing. Warburg theory insists on killing malignant cells by starving. Cancerous cells need more energy, and they get it from glucose. The idea would consist of taking the glucose so that the tumour could not get it. This process would be similar to the antiangiogenesis (avoid new blood vessels) or addicted cells. This theory is called Warburg because Otto Warburg (1931) discovered this relationship between glucose and cells.

Antiangiogenesis is still under investigation. Some medicines linked with it are: angiostatina, talidomida, avastina, endostationa, exavar, sutent…

2.8.5.2 CAM

Cam: MCA in Spanish, and CAM in English, is a Complementary and Alternative Medicine. For example acupuncture has been useful to chemotherapy effects. Well, many other possibilities are under investigation, for example trying to attack the metastasis, using cannabis, chemoprevention to avoid risks. Alternative medicine can also be very useful, but it will never replace modern medicine but complement it, mainly to reduce side effects in chemotherapy for example.

2.8.5.3 HYPERTHEMIA

Hyperthermia: Another way to treat cancer, with good results in lung cancer is Hyperthermia therapy. It consists of applying hot temperatures such as 43,5ºC for an hour on an specific area of the body where the tumour is. Hot temperatures can destroy cancerous cells with minimum damage to healthy tissues, it reduces tumours by killing cancerous cells and damaging protein structures in tumorous cells. This treatment is to be combined with radiotherapy and they give good results with low toxicity and better survival rates. There are different types of hyperthermia: the regional one is applied for lung cancer. Part of the blood is taken over, it is heated, and then it is pumped to the lung, at the same time chemotherapy is applied.

2.8.5.4 NEW TARGETED THERAPIES AND MEDICINES

New targeted therapies: applied during the last years have made important changes in cancer treatment. One problem is that too many years of investigation and tests had to pass until Herceptina (the medicine correspondent to the new receiver gene HER-2) was available to the patient in 1998.

New targeted therapies have their problems too, because not all the proteins can be attacked with these therapies, they must have a special structure.

Receivers are a kind of mutated proteins which are not inside the cell, they are on its surface and what they do is to join themselves to the inhibitor or antibody to come into malignant cell to avoid its function.

Ras is a protein used by these receivers. Mutations in Ras proto-oncogene group (that is H-RAS, N-RAS, and K-RAS) appear in many cancers, so it is very interesting to discover new chemical substances to control RAS, for example "Sorafenib" from "Bayer". F x"Herceptina" was the first medicine approved of these new generation of medicines, and it acts against a family receivers called EGFR, the same as "Erbitux" from "Imcole labs".

In any case, molecular medicine and targeted therapies have not been as useful as scientists expected. None of the new medicines could cure cancer. Only the one called "Glivec" seems to have a curable effect in one subtype of cancer in blood cells. In 2004, Zeneca labs confirmed that its medicine "Iressa" was only useful for a small subgroup of lung cancers.

These new medicines have not worked in a wrong way, but scientists were researching something that had fewer side effects, and the problem is that as cancer appears after several mutations, when scientists had chosen a cell, it has received a treatment; afterwards it makes a secondary mutation, because cancerous cells never stop growing. So from now on, cells that resist the treatment appear. To make it more understandable, it is comparable to antibiotics and the bacteria which resist. To conclude, scientists say that the future medicines will be a combination of different substances that will attack cells from different points avoiding its resistance.

A new medicine, ABT-757, is ready to be approved, and it will avoid cancerous cells not to fool.

In other words, researches are based on reviving the tumourours suppressors as p53, that is what Hoffman- Laroche is investigating with some molecules called "nut lines".

Another possibility is the theory about those addicted cells. That means that the cell which is continuously growing, is used to having proteins in excess, so it is addicted to these proteins, and when it does not receive them, it is blocked. Then there is a need to find a targeted therapy to solve a problem of one oncogene.

One more possibility: cancer is usually developed from an immortal cell which cannot stop growing. This is similar to what happens with stem cells. One stem cell could already have some mutations, and then become cancerous; it would only need a few mutations. If this were true, it would be easier to find a good treatment against cancer, because stem cells are very different from adult cells. Therefore, medicine could be prepared to attack only stem cells. An example could be “Rituximab”. In this case, OncoMed las and GlaxoSmithkline would sooner try some new products with some patients.

For a long time, scientists have been studying the possibility of human body to consider a cancerous cell as a rare cell and eliminate it. That is in the immunologic system, but it does not work perfectly in cancer cases. Then, a vaccine would be good, but as not all cancers are equal, it is too difficult to find one. There is also the risk that the vaccines affect normal cells too and then it might be an autoimmune system on ourselves, and that would be worse. There are some substances called interleucines which increase our immune system power but they have got high toxicity.

Investigations and research do not stop. And there are much more possibilities as there are a lot of kinds of cancers, but if we concentrate in lung cancer, the most modern investigations have been in cannabis, because they have “D_9 tetrahidrocannabinol” which is against cells growth, and it may be useful (as all other medicines and chemical substances) only with some cancers and lung cancer could be one of them, one day it may be used as a chemotherapy, but it is needed to find an exact dose to be efficient without creating bigger problems such as addiction. Two new projects are studying lung cancer nowadays; they are Cancer Genome Atlas and Cancer Genome Project, both studying different tumours and their mutations.
In Cuba, some scientists made a great discovery last July 2008. They discovered a new vaccine for lung cancer patients. It does not cure but it allows them to have not only a longer life, but also a better life, at a minimum of 5 months. That may seem not to be too much time, but it is, if we keep in mind that many patients die after about a year. This medicine is called “Cimavax EGP” and its advantage is that it does not provoke side effects like chemotherapy. Since 1992 that Giselo Gonzalez and other scientists have been investigating it. Although Cuba none is the first, there are other 3 therapeutic vaccines in a generic character around the world, but this one is especially for lung cancer. This vaccine

called CimavaxEFG consists of the protein EGF (epidermic growing factor), and with another protein it gives an immune answer against this EGF. EGF protein, when it gets to a cell membrane in a tumour, it causes its increase. After using the vaccine, our organism makes antibodies which avoid the EGF protein to link to the new cell, so the tumour can not increase.

However, scientists confirm after 400 experiences that the tumour decreasing depends on each patient.

Something similar has been produced by Roche Farma laboratories. It is a medicine which acts better than chemotherapy because it is less toxic and it attacks the patient tumoruous development. It is very important because it allows a better individual treatment for lung cancer with a mutation of the EGFR gens. It is also more comfortable to take by the patient as it is a biological medicine. It is the first medicine authorized in Spain for lung cancer that acts differency from chemotherapy. Nowadays it is used for non small cells lung cancer after a chemotherapy treatment with no result. Its use has shown that it delays symptoms manifestation and it may increase the survival rate. Erlotinib inhibits the gen factor which causes the tumour development. We will have to wait for the results of all their investigations.

2.9 SALVADOR MACIP

He is a great scientist, who hopes that in a period between 10 -30 years, cancer could become not a curable disease but rather a chronic one. He says that talking about a cure for cancer is being too optimistic, but he sees a possibility of controlling it. Nevertheless, nowadays, the main methods against these diseases are the same as 50 years ago (surgery, chemotherapy and radiotherapy). A new generation of medicines can provoke an important advance.

He has been working in cancer research in New York (Mount Sinai) and now he is at Leicester University. He hopes that one day we can talk about stem cells therapies; however, he doubts antioxidant solutions, being well-informed about healthy diets. He has got his hopes set on those targeted therapies.

2.9.1 INTERVIEW TO DR. SALVADOR MACIP

If we look into your biography, we can read you are not only an excellent scientist, but also a musician and writer. How can you enjoy such different subjects?

Science is a very absorbing profession, one that requires a great investment of time and effort. When I am out of the lab, I find it refreshing to focus on something else. I have always liked music and literature. I have been writing all my life, as a hobby, but lately it has become my second job. The good thing is that I enjoy my two jobs, and I hope I can continue doing both of them for a long time.

Well. Let's take your scientific part. Why did you choose being a researcher instead of being a doctor in hospital?

My fascination for science and medicine started very early, and probably simultaneously. I have always been interested in how the human body works and how we can repair it when something goes wrong. That is why I chose to go to a medical school. But I also like experimenting and finding answers to the most basic questions. The option that best combined both things was biomedical research. Working on the root of the problems, trying to understand them and finding a cure, to me is more rewarding than actually applying this knowledge in hospitals.

How could you describe a scientist's job? How can you always get subjects to investigate about? And when you get to the end of your research, how do you choose the next one?

Science is trying to observe nature and come up with possible explanations for what we see, that we call hypothesis. Then we have to test whether that hypothesis is true or not. Imagination is one of the most powerful tools of the scientist. Without ideas, there is no science. Research never ends. One answer comes always attached to ten new questions. There are always holes in the knowledge that need to be filled and one thing usually leads to another

Do you believe in "alternative medicine"?

Alternative medicine is a name usually given to therapies that have not been scientifically proved to be useful. These techniques will not cure a disease. However, they can have positive placebo effects that should not be disregarded since, if used in conjunction with proper interventions, could help patients cope with side effects and pain.

Let's talk about lung cancer especifically:

Do you think there is still a lot to research left to do regarding lung cancer, if people stopped smoking, it would not be necessary? Then, what about people who suffer from it because of the polluted air at work?

There is a good fraction of lung tumours that is not smoke-related. Without cigarettes, lung cancer would be less important, but we would still see it in large numbers, therefore research would be needed. In any case, the most important intervention we can do for lung cancer is prevention, both in personal habits and in the workplace.

Now it is time for the antioxidants- I am aware of the fact that not all antioxidants can stop or delay cancer development, even in some cancers the same antioxidant can cause it instead of stopping it.

The involvement of oxidants in cancer is too complex to think that antioxidants can provide a solution. Oxidants cause damage to DNA and that can lead to cancer. On the other hand, oxidants are needed for senescence and apoptosis, which are two mechanisms that our organism has to prevent cancer. Therefore, inhibiting oxidants may not be always a good idea. More research need to be done to fully understand the role of oxidants in cancer, but so far, most clinical studies do not show any benefit of using antioxidants.

Well, you have been very helpful. Thanks a lot again

2.10 PREVENTION

A balanced diet is very important, people who eat many fresh vegetables, carotenoides and vitamin C, may have a minor risk in suffering from lung cancer. But, although it seems the opposite, unfortunately, some clinical trials have demonstrated that a diet rich in vitamin antioxidants for smokers has increased the risk of lung cancer, but only for some smokers, it is like a rules exception..

Lung cancer can be a preventable death because smoking manufactured cigarettes with addictive properties is a big risk. Not only smokers, but also passive smokers are at risk, too. Even though the causes of lung cancer are nowadays well-known, investigation and research are still very important for its prevention.

Part of the research about lung cancer is linked with diet. One hypothesis is that diets with a high quantity of antioxidant nutrients may protect against oxidative DNA damage, which means a possible protection against cancer. These specific micronutrients are:

- retinol
- carotenoids
- B- carotene
- Vitamin C

Eating fruit and vegetables may help in prevention. About exposure causes, obviously, to prevent the risk of lung cancer, we must be able to reduce or eliminate people's exposure to these agents.

2.11 THE ROLE OF THE CARER

2.11.1 GOOD NUTRITION

Treatments for cancer disease are very aggressive. They may modify our sensations of taste and smell, so the patient may lose his appetite. Otherwise, good nutrition is essential to get better, so it is very important the role of the carer now to help the patient when he is not very hungry.

About the patient:

- He should eat small quantities, but very often all day long.
- It would be better to eat biscuits with nuts or cereal…
- He should drink a lot of liquids, which are very nutritive,
- He can have cool food such as ice-creams, yogurts, cream…
- Prepare some food differently and in an unusual way. Let's say make a milk-shake.
- The patient should have some light food before going to bed.
- Food should look nice on the dish.
- When the patient is hungry, he should eat bigger quantities, for example, if it is possible, have a good breakfast.
- He should not drink a lot during the meals in order to avoid feeling full. It is better to drink half an hour before or after the meals.
- He should do some physical activity if it is possible.
- He may prefer chicken or fish, rather than red meat.
- Make food tastier with sauces, wine, fruit juices.., use aromatic herbs to cook.
- Do not eat in the kitchen and avoid food smells until mealtimes.

2.11.2 ENCOURAGEMENT

After any treatment, cancer patients should do some physical activity, such as having a walk for an hour every day, or going to the mountains, or cycling or swimming once a week. Now the carer should encourage the patient to do so, and also going with him. In spite of being under treatment, going out for short walks is also recommended. Something important is that patients should avoid the sun. It is very difficult for a smoker to stop smoking, he will surely need some help, but it is essential to maintain

minimum health in the lungs. Recovering from a cancer is not easy, so encouraging the patient is very important to help him continuously to try to lead a normal life, we cannot forget that the patient is ill, but we cannot allow the illness become the centre of his life. Sadness and tiring sensation will not disappear suddenly or quickly, but the patient should take advantage of his good moments and enjoy life, doing things that make him feel happy.

It is also good for the patient, to go back to work a soon as possible, and if he can, he should do it gradually. Responsibilities will give meaning to his life. In fact, we should let the patient be alone when he wants. The patient needs to feel accompanied but he should not feel himself weighed down by anybody.

2.11.3 PSYCHOLOGY USEFULNESS

Doctors must tell the patient what he has diagnosed, as the patient has his own right to know everything he knows about his illness. Sometimes, when a cancer is diagnosed, some people are not sure to talk about it to their relatives, maybe they are too old, too young… but that is not true. Everybody has a great capacity to face difficulties. Sharing the diagnosis will help the patient reduce his anxiety. What is more, it will be easier for the family to help him, too. It is not easy to talk about cancer and the patient will be the one who in one or another way will decide when to do it and the limit to what he wants to talk about or know.

When lung cancer is diagnosed, not everybody accepts it in the same way. Some people close to the patient, may feel guilty, they may think that the patient is ill because they have not been good carers. Others may think about their risks to suffer from it and then, the best is to visit the doctor. Patients feel bad, but they are still an important part of the family, and they must find a good support system within it.

What often occurs is that the patient and his partner wonder if the person they love will be able to accept this disease. Then, there is an unknown atmosphere, in which some changes will be essential and an adaptation process is needed. Now, it is necessary again to keep as fit as possible, it is good for example to go for a walk together. Psychological help may be useful; nevertheless some people refuse it at first.

When lung cancer is diagnosed, the patient's life and that of his family will completely change. That is when a psycho-oncologist's work begins. He will help them for the duration of the illness and its treatment. He will help them in emotional needs such as anxiety, guilt and fear of death.

The main problem for the lung cancer patient is feeling guilty, because usually he is a smoker, and although he knows it is a bad habit, it is too difficult to give up smoking, and now he is afraid of death. Then, the patient's personality changes and life becomes harder for him and his family.

The role of the carer is very important, with the psycho-oncologist's help or without it; he must become a bit of a psychologist . He should look for and show a positive view, usually difficult to find, and encourage the patient to fight against his illness.

Often, the patient is afraid of death, of pain. He also thinks he will be a big burden on his family, or he may not accept his illness. The carer ought to try to help the patient dispite these ideas.

The patient and the carer should share help, support and advice.

There is an idiom which I think is suitable here: "what goes around, comes around" and that is true. In a situation of lung cancer, solidarity with the patient is the best we can do.

2.12 A REAL CASE OF LUNG CANCER

2.12.1 GIVING AN ACCOUNT OF EVENTS

Here is the story of a real case of lung cancer. According to the law any name will not appear .

He is 65. He is smoking about less than a half packet of cigarettes a day. He suffers high blood pressure and bronchitis. He is already retired and he is living with his wife. It is January, the weather is very cold, and he has had the flu for some days .

At the end of the month, he goes to the doctor because he has been feeling sick for a week , he is not hungry, he has got difficulty in breathing after every little effort, he has got hard cough and he has no fever. He has to stay in hospital for 13 days and the treatment he receives is blood test, thoracic TAC, a bronchography and fibrobronchoscopy. The diagnosis is a serious pneumonia, but with medicine he soon recovers from it. The problem is that apart from it, the doctors have detected something in this left lung, and they suspect it is a possible tumour. They decide to do a fibrobronchoscopy ; the result is a carcinoma, other test results are negative. The final diagnose is T2N0M0, so surgery is the best solution.

Surgery is not possible in Vic; he will be accepted in a hospital in Barcelona next month, in March. Everything goes well. It has been possible to remove the entire tumour. After a few days, he is ready to go home. He will continue being monitored in Vic.

Three months later, he goes to hospital again. It is June. This time he has got a backache and a urine infection. That is bad news. During these three months his disease has worsened, now the diagnosis could be a possible spread to the liver and bones. The treatment will be chemotherapy every week, but he doesn't need to stay in the hospital, he will be able to stay at home. His disease stage now is T2N0M1.

It is only after a month that he needs to go to hospital again, it is July, he is worse, he is absent-minded and his right leg hurts, it is broken. He needs a special treatment and he cannot stay at home, so he will stay in another hospital, Hospital de la Santa Creu in Vic, where he will receive all the support treatment needed.

Now there is nothing else to do. HGV has no more possible solutions or treatments, neither in Barcelona, Hospital Clínic, where surgery seemed to have been successful in this case. From now on the patient will receive very strong medicine to avoid suffering.

Once more, lung cancer has won the battle, this time it has lasted 8 months.

2.12.2 COMMENT

Looking attentively at his case, it is a good example of lung cancer.

The patient is a man, aged 65, that is the average age of people affected by a lung cancer. Although he is not smoking a lot now, he has been smoking since he was young, and that means a lot of dangerous substances in his lungs from tobacco, and what's more, he has chronic bronchitis that makes the causes worse.

He feels sick, the first symptoms appear: difficulty in breathing, cough, loss of appetite, etc. So the first test and treatments in order to get a more detailed diagnosis : blood test, thoracic TAC, and fibrobronchoscopy.

The result is T2N0M0. T2 means the tumour is middle-sized, N0 means it has not spread to other tissues yet, and M0 means there is no metastasis. According to all these facts, the best possible treatment is surgery and removal of the entire tumour and possible cancerous cells.

The operation has gone well and everything seemed to be ok, but not for a long time.

As most of lung cancer cases, after a few months (3 in this case), he feels sick again. Something is going wrong. New tests and new diagnosis, T2N0M1, now the tumour has reappeared and it has already created a metastasis, so now the best treatment is chemotherapy. Doctors prepare him for this strong treatment, they tell him the possible side effects, they give him a lot of advice to make him feel better, he also receives diet advice, and so on. His wife and his children take good care of him, he's told to be prepared for radiotherapy later, but the cancer wins this time, he worsens rapidly, and he dies before having the opportunity of radiotherapy treatment.

His disease lasted only 8 months, as many lung cancers, less than a year.

Apart from studying this real case, I have visited the hospital in Vic, the oncology department, to see how it works. It is not a special department, when a patient is ill and needs hospital attention, he stays there the time needed, and after the treatment, he may go back home or he may be moved to another hospital depending on the reason why he cannot stay anymore in this hospital. In Vic hospital not all treatments are possible such as surgery or radiotherapy, but chemotherapy is. That is why the patient I have studied received surgery in Barcelona, then he was monitored and received chemotherapy in Vic and he spent his last days in another hospital in Vic, because the main one is reserved for treatments and when there is nothing else to do for the patient, except palliative care, he is moved to "Hospital de la Santa Creu."

3. ANTIOXIDANTS

3.1 DEFINITION OF ANTIOXIDANTS

Antioxidants are some substances which exist in some food and they protect cells from damage caused by unstable molecules known as free radicals or oxidants. Free radicals may lead to cancer.

Free radicals are some imbalanced molecules, with atoms which have an electron. These incomplete molecules are more chemically reactive than the normal ones, and they need another electron to get their electrochemist balance. Once they are balanced, they are ready to destroy our cells. Our body cannot neutralize these free radicals, so we must have some food with antioxidants.

Antioxidants interact and stabilize free radicals and may prevent some of the damage free radicals might otherwise cause.

Some antioxidants include beta-carotene, lycopene, vitamins C,E,and A, and other substances.

3.2 HOW ANTIOXIDANTS MIGHT PREVENT CANCER

Antioxidants neutralize free radicals, they neutralize the electrical charge and prevent the free radicals from taking electrons from other molecules.

Exposure to various environmental factors, including tobacco, smoke and radiation, can also lead to free radical formation.
In humans, the most common form of free radicals is oxygen and -OH .

When an oxygen molecule (O_2) becomes electrically charged or radicalized it tries to steal electrons from other molecules, causing damage to the DNA and other molecules. Over time, such damage may become irreversible and lead to cancer.

3.3 SOME FOOD RICH IN ANTIOXIDANTS

Antioxidants are abundant in fruits and vegetables, as well as in other foods including nuts, grains, and some meats, poultry, and fish.

- *Beta-carotene:* foods orange in colour (carrots, apricots, pumpkin and mango). Also some green leafy vegetables like spinaches, kale and collar greens. Some researching results prove it does not protect against lung cancer.

- *Lutein:* well-known for its association with healthy eyes, it is abundant in green leafy vegeatables like spinaches, kale and collard greens.

- *Lycopene:* it is a powerful antioxidant found in tomatoes, watermelon, apricots, pink grapefruit, etc.

- *Vitamin A:* liver, sweet potatoes, carrots, milk, egg yolks, mozzarella cheese. We can find it in three main forms: retinol (Vitamin A-1), 3,4-didohydroretinol (Vitamine A-2), and 3-hydroxy-retinol (Vitamin A-3).

- *Vitamin C:* in many fruits and vegetables, cereals, beef, poultry and fish. It is also called ascorbic acid. Maybe apples, onions, and other fruits, may have some substances which might protect against lung cancer, because they protect bronchial mucosity.

- *Vitamin E:* in almonds, in many oils including wheat germ, safflower, corn, and soybean oils. It is also found in mangos, nuts, and broccoli.

- *Selenium:* it is not an antioxidant nutrient. It is a mineral; however it is a component of antioxidant enzymes. It is mainly in rice and wheat depending on the soil they are grown. Animals that eat grains or plants grown on selenium – rich soil have higher levels of selenium in their muscle.

- *Catechism:* mainly found in tea, although it should be green or black tea steeped for about 5 minutes, and it releases over 80% of its catechism. Instant iced tea for example, contains negligible amounts of catechism.

- *Resveratrol:* in red wine. Red wine is a rich source of biologically active phytochemicals, chemicals found in plants. Particular compounds called polyphenols found in red wine –such as catechism and resveratrol- are thought to have antioxidant properties. These types of polyphenols are a plant's defence system against disease. Polyphenols are found in the skin and seeds of grapes. Red wine contains more polyphenols than white wine, because to make white wine, the skins are removed after being the grapes crushed.

3.4 RESEARCHES RESULTS

Laboratory and animal research have shown that antioxidants help prevent the free radical damage that is associated with cancer. However results from recent studies in people, clinical trials, are not consistent.

In 1993 , a Chinese Cancer Prevention Study concluded that a combination of a beta-carotene, vitamin E, and selenium significantly reduced incidence of cancer overall.

In 1994 was demonstrated that lung cancer rated of Finish male smokers increased significantly with beta-carotene and were not affected by vitamin E.

In the same year, another study demonstrated a possible increase in lung cancer associated with antioxidants.

In 1996 it was showed that there was no change in cancer rates associated in the beta-carotene and aspirin. They conclude that there was no benefit or harm from beta-carotene supplements. Investigations of the effect of vitamin E are going on.

In the laboratory, studies have shown that tea catechism act as powerful inhibitors of cancer growth in several ways. They scavenge oxidants before cell injures occur, reduce the incidence and size of chemically induced tumours and inhibit the growth of tumour cells. Despite these experiences, study results involving humans have been contradictory, concluding that dietary, environmental, and population differences may account for these inconsistencies.

About red wine studies, recent evidence from animal studies suggest this anti-inflammatory compound as an effective chemo preventive agent in the three stages of cancer progress.

Some researches have been recently done about the effect of the supplemental use of antioxidants vitamin C, vitamin E, and coenzyme Q10 for prevention and treatment of cancer, but results are not positive, there are still many contradicitions.

4. PRACTICE IN THE LABORATORY

Oxidant substances may act at any cell and then, it provokes several diseases, such as cancer. These oxidant substances are mainly free radicals as OH and H_2O_2, and it is a natural reaction, but in lung cancer, it can also be influenced by tobacco, pollution, and unhealthy diets.

Our body has already got other substances which stop free radicals actions, called antioxidants. The most important antioxidants are vitamins A, C, E, and flavonoides. We can find them in chocolate, red wine, green tea, fresh vegetables and fruits.

When there is no balance between free radicals and antioxidants, cancer appears, and oxidant substances mutate DNA. If these mutations are not repaired, the tumour grows quickly.

During this work at the school's laboratory, we look upon the effect of antioxidant substances on oxidant substances.

AIM:

From a series of substances I would like to differentiate the antioxidant effect and which are more or less effective linked with oxidant substances.

HYPOTHESIS:

Antioxidant substances will reduce the oxidant effect on eukaryotic cells from the yeast treated with H_2O_2. Therefore, the main objective will be to test whether the addition of extracts of antioxidant-rich vegetables might counteract the oxidative damage to yeast caused by H_2O_2, resulting in a higher growth rates compared to yeast only treated with H_2O_2.

MATERIAL:

Yeast
distilled water
oven
hook
100 ml test tube
clock glass

Mc Farland tube
scale
spatula
glucose
100 ml flask
Slide
coverslip

Petri dishes "S+C"
optical microscope
flame
methylene blue
tube of sterile serum
pipette, ependors.
H_2O_2

ANTIOXIDANTS:

Kiwi, grapes, red wine, orange, cacao, green tea, smashed carrot.

PROCEDURE:

1. A dilution of yeast at 1% with distilled water is prepared and glucose at 4% is added.
2. Yeast is stained as follows:
   2.1. A little sample of the solution is put on a slide and fixed with the flame.
   2.2. This sample is dyed, already fixed with methylene blue, for two minutes.
   2.3. It is washed with distilled water to take over the methylene blue rests.
   2.4. It is left to dry a little and then, a coverslip is put on it.

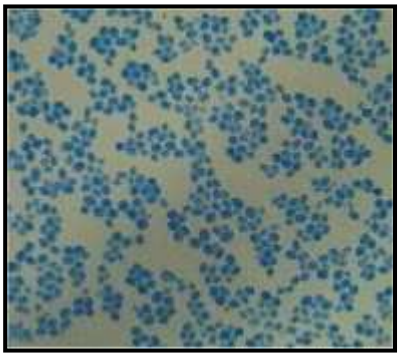


Fig.13. Yeast looks like this picture after having done this process.

   2.5. A little sample of the solution is put on a slide and fixed with the flame.
   2.6. This sample is dyed, already fixed with methylene blue, for two minutes.
   2.7. It is washed with distilled water to take over the methylene blue rests.
   2.8. It is left to dry a little and then, a coverslip is put on it.
   2.9. The sample is ready to be watched using the microscope.
3. Now, under an optical microscope, we will be able to see this cells reproduction, which is buddy.
4. Observation of oxidant and antioxidant effects:
   4.1. Three Petri dishes " S+C" are taken and each of them marked to differentiate them.
   4.2. In dish one, only yeast solution is put. In the second dish, yeast solution is put adding 1 ml of H_2O_2 at 15%. And finally, in the third and the last dish, the same as the second dish is put, but also adding 1 ml of an antioxidant substance. We must remember to work near the flame in order to keep sterile conditions.
   4.3. When the three dishes are ready, they are left for culture for 48 hours in the oven at about 30ºC.
   4.4. The number of the yeast cells is counted in every case:
      4.4.1. Using a hook, a sample of each dish is taken, the same quantity approximately; and dissolved in a tube of sterile serum.

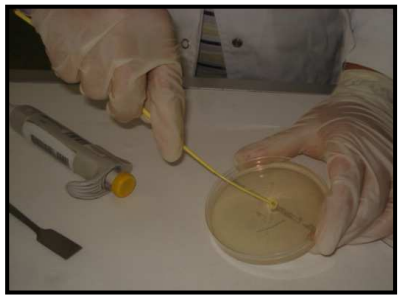


Fig.14 It is shown how we take a simple of each dish using a hook.

Each tube must be numbered. To obtain an equivalent concentration between all the samples, they are compared using a Mc Farland tube.

4.4.2. 50 μM of methylene blue is added.

4.4.3. This solution adding 200 μM into each tube is dissolved.

4.4.4. 50 μM of these last solutions is taken and then, put in a cell culture plate.

5. This procedure is done with every Petri dish.

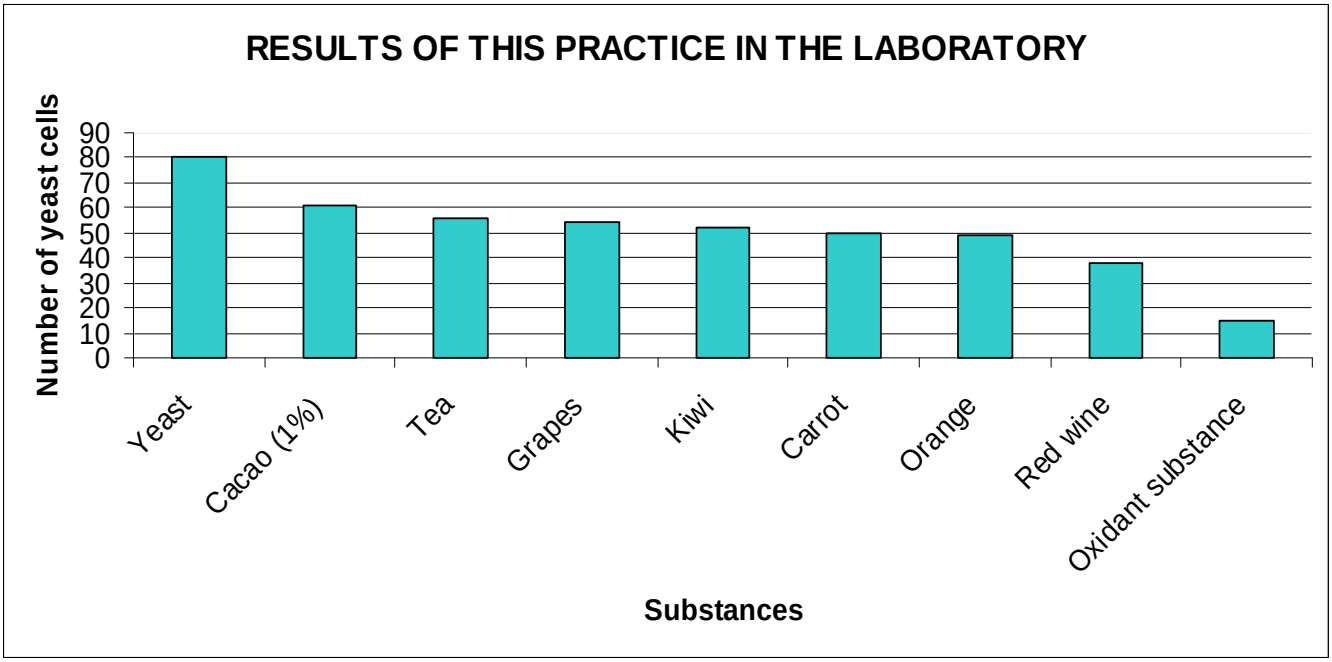
5.1.1. Using the microscope, the number of yeast in each cell is counted.

6. The effect of oxidants and the effect of antioxidants substances on them has been proved.
7. The same procedure is done for every antioxidant substance that we are interested in.

RESULTS:

Days	Substances	Number of yeast cells
1st day	Yeast (control)	76
	Oxidant (H_2O_2) + control	8
	Control + H_2O_2 + kiwi	52
	Control + H_2O_2 + grapes	54
	Control + H_2O_2 + red wine	38
2nd day	Yeast (control)	84
	Oxidant (H_2O_2) + control	22
	Control + H_2O_2 + orange	49
	Control + H_2O_2 + cacao(1%)	61
	Control + H_2O_2 + tea	56
	Control + H_2O_2 + carrot	50

We can verify that the control of this practice has been the Petri dish with only yeast due to the fact that a control is the sample which is in environmental conditions and it tells us that other influences do not change the experiment results.



Once I have finished this practise, I can assert that the dependent variable of it is the number of yeast cells, and the independent variable is the variety of antioxidant substances.

CONCLUSION:

The reason why I can state which one is the dependent variable and the independent variable is because the number of yeast cells depends on the antioxidant substances.

The research on cancer and diet suggests that antioxidants in certain food may protect against DNA damage that can cause malignant cells.

In general, antioxidant systems prevent reactive species from being formed, or remove them before they can damage vital components of the cell. However, since reactive oxygen species do have useful functions in cells, such as redox signaling, the function of antioxidant systems is not to remove oxidants entirely, but instead to keep them at an optimum level.

The beneficial nutrients found in broccoli, cauliflower, and brussel sprouts (isocyanates) may suppress tumour growth and hormone production. Flavonoids, found in apples, grapefruit, and red wine, and also lycopene, found in tomatoes, are good at protecting against cancer. The curious thing is that while these diets appear

protective, supplements containing the same chemicals have given disappointing results.
Some data indicates that diets with abundant fresh fruits and vegetables may protect against lung cancer both, in smokers and non-smokers.

I have chosen these antioxidants and not other ones because each nutrient belongs to a different group of antioxidants, and once I have finished this practice, I should conclude that the most antioxidant substances are the ones which belong to the *cathechism* group, and that there is not a huge difference between the *beta-carotene* and the *vitamin C* groups. Finally, the one that seems to be less antioxidant is the *resvernatrol* group; in this case, red wine represents it. I just can say that my hypothesis was right, by only watching the graphs, as it seems that addition of antioxidants enhances cell growth compared with control, and no differences are seen among antioxidants.

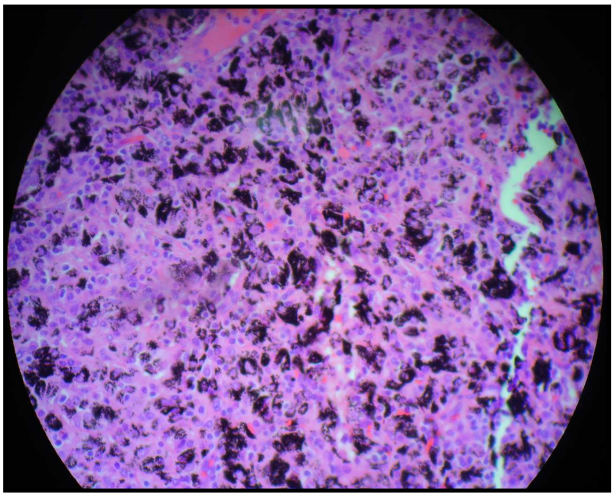
5. VISIT TO "HOSPITAL CLÍNIC" IN BARCELONA

After having finished this research project, I had the opportunity to go to Barcelona and see the difference between a healthy lung and a lung cancer tissue.
I met a pathologist who showed me where pathologists work and what they use to identify if a tumour is cancerigenous or not.

First of all, they have a piece of lung which seems to have some carcinogen cells, they verify if it is a malignant tumour or not. They cut the little piece - the white part- because it will probably be a tumour, and they make a block with it. Afterwards, once the block is done, they cut some very thin slices (its size is μ). Then, they take two pieces of these slice and they put them on a slide. These slids – which have some samples of lung cancer tumour- are brought to a machine that washes and dyes them to be prepared for those pathologists who have to observe it and assure if it is malignant or not. Finally, this machine takes a coverslide and fixes it on the slide. Then, pathologists will be able to see it as much as they need, under an optical microscope.

There, they also showed me how to identify if it consists of cancer or not. Once this procedure was finished, we watched this particular case under some optical microscopes and we could affirm that unfortunately it was lung cancer.

This is a picture of a lung from a lung cancer patient. The white part is the one that first of all seemed to be carcinogen.



This is a picture of what we could see under an optical microscope. The conclusion was that this patient had cancer.

6. CONCLUSION

"Cancer is a curious thing…Nobody knows what the cause is, though some pretend they do. It is like some hidden assassin, waiting to strike at you. Childless women get it and men when they retire. It is as though they needed an outlet for that foiled creative fire".

That is what Mr. W.H.AUDEN said, but now that I have finished my project, I can only partially agree with him, because scientists have already realised that lung cancer is not curable yet, although they know a lot about its prevention.

Cancer is a group of cells which grows in an uncontrolled way, and it becomes a malignant tumour. We can not forget that some tumours are benign, they do not invade other tissues and they can be removed with no problem.

The most important aim of my project was to know about the cancer disease, but as I was advancing in my work, I realised that cancer was a wide disease and I had to narrow it down to only one type of cancer, lung cancer, and complement it with antioxidants effect.

To conclude this research project, I think I should assert some statements:
There are many different types of cancer, so there are many causes, too. One of them is genes and their mutations, but if we change some of our habits, we can reduce risks. Regarding lung cancer, smoking is the main cause.
Some oncogenes may produce cancer, but our body has got suppressors which inhibit the malignant ones. It depends on our habits that oncogenes or suppressors act; with a good diet, antioxidants will help.
It is very important an early diagnose to avoid the tumour spreads.
Radiotherapy and chemotherapy are the two most widely-used therapies to control cancer disease, but we cannot forget that alternative medicines are investigating, too. They do not supply one to the other, but they supplement each other.
If we have a good diet, increasing fresh vegetables and fruits in it, we have fewer possibilities to suffer cancer, because antioxidant substances stop free radicals damage. Cancer will be a chronic disease, but controlled.

Something I have proved is the effect that antioxidants substances cause on oxidant substances. In this case, at the school science laboratory I have used yeast because it is a way to study cancer with eukaryotes cells, it is not only a simple way to work in the laboratory, but also it is easy to handle.

In addition, the part that I have found enthralling has been my work at the laboratory: I really enjoyed working there, trying to find a conclusion with oxidant substances and antioxidants; which has been that antioxidants substances have neutralized oxidant effects on eukaryotes cells.

I have been surprised by the conclusion that while men are more and more affected by lung cancer, the statistics show that these cases are decreasing but women cases are increasing. In fact, if I pay attention to society I can obviously prove it, because with non smoking advertisements, less men smoke but more women become smokers. And what still bothers me is the fact that it cannot be detected in at their early stages.

The reason why I have chosen lung cancer and antioxidants is that I strongly believe that cancer is a relevant disease, and I did not know much about it, so I thought this was a good opportunity to study it. I thought lung cancer would be an interesting subject to work on, because there are many people affected and I was curious about why most of them die before finishing their treatment.

Nowadays, new targeted therapies are very well accepted, and although they can not cure, they are less aggressive than chemotherapy and radiotherapy, and they let a longer and more comfortable life to the patient.

It has been a nice experience my visit to Hospital Clínic in Barcelona where I met Míriam Cuatrecases, a pathologist who showed me how they work and the methods they follow to analyse a tumour if it is malignant or not. I could see a sample of a lung cancer case and its cells with the nicotine effects. There, I learnt also how to differentiate a healthy lung and a carcinogen lung.

I hope research on stem cells will progress and they will find how to control the disease.

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MACIP, Salvador. *Immortals, sans i perfectes*. Barcelona: Edicions 62, 2008

PUJOL GEBELLÍ, Xavier. *Biografía del cáncer*. Barcelona: Ed 62, S.L.U., Edicions Península, 2004

FARRERAS – ROZMAN. *Medicina interna, volumen I.*Barcelona: Ed. Doyma, 2009.

7.2 ELECTRONIC RESOURCES

- *Antioxidants and Cancer Prevention: Fact Sheet*

<http://www.cancer.gov/cancertopics/factsheet/antioxidantsprevention>

- *National Cancer Institute*

http://www.cancer.gov/

- *Cancer care*

http://www.cancercare.org/espanol/#publicaciones

- *Sociedad Española de Oncología Médica*

http://www.seom.org/

- *Vital imaging, helping you stay healthy*

http://www.vitalimaging.co.uk/?OVRAW=Lung%20Cancer&OVKEY=lung%20cancer&OVMTC=standard&OVADID=1296439531&OVKWID=11206543031

- *International Agency for Research on Cancer*

http://www.iarc.fr/?info=EXLINK

- *Medline plus, trusted health information for you*

http://medlineplus.gov

http://www.nlm.nih.gov/medlineplus/antioxidants.html

- *Agency for Health care Research and Quality*

http://www.ahrq.gov

- *U.S. National Library of Medicine National Institutes of Health*

http://www.pubmed.gov

- *Cuerpo y mente*

http://www.cuerpomente.es/

- *Revista* Cubana Oncología

http://bvs.sld.cu/revistas/onc/vol15_2_99/onc09299.htm

- *Web MD, Better information, better health*

http://www.webmd.com/lung-cancer/lung-cancer-support-resources

- *Amercian Cancer Society*

http://portal.acs.org/portal/acs/corg/content

- *Nacional Comprehensive Cancer Network*

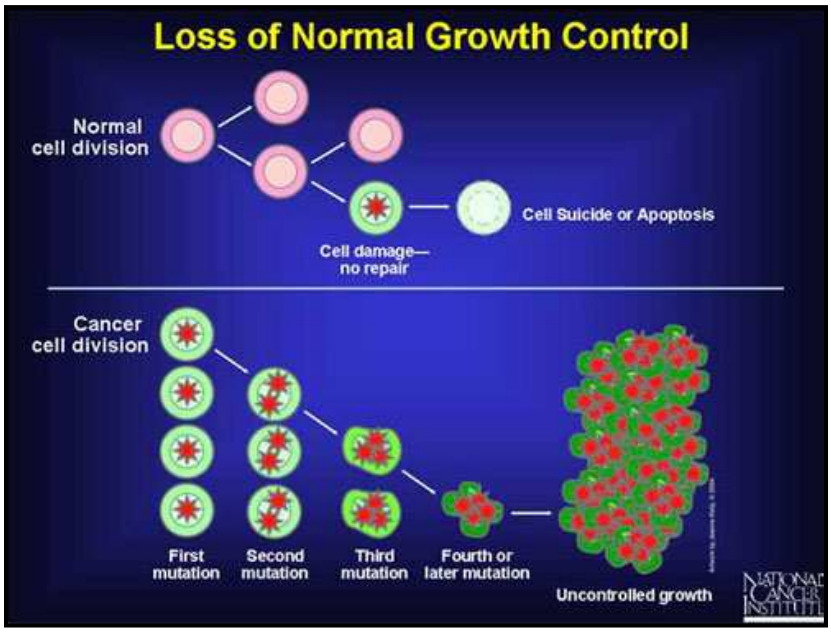
http://www.nccn.org/index.asp

8. ANNEX

Fig. 1

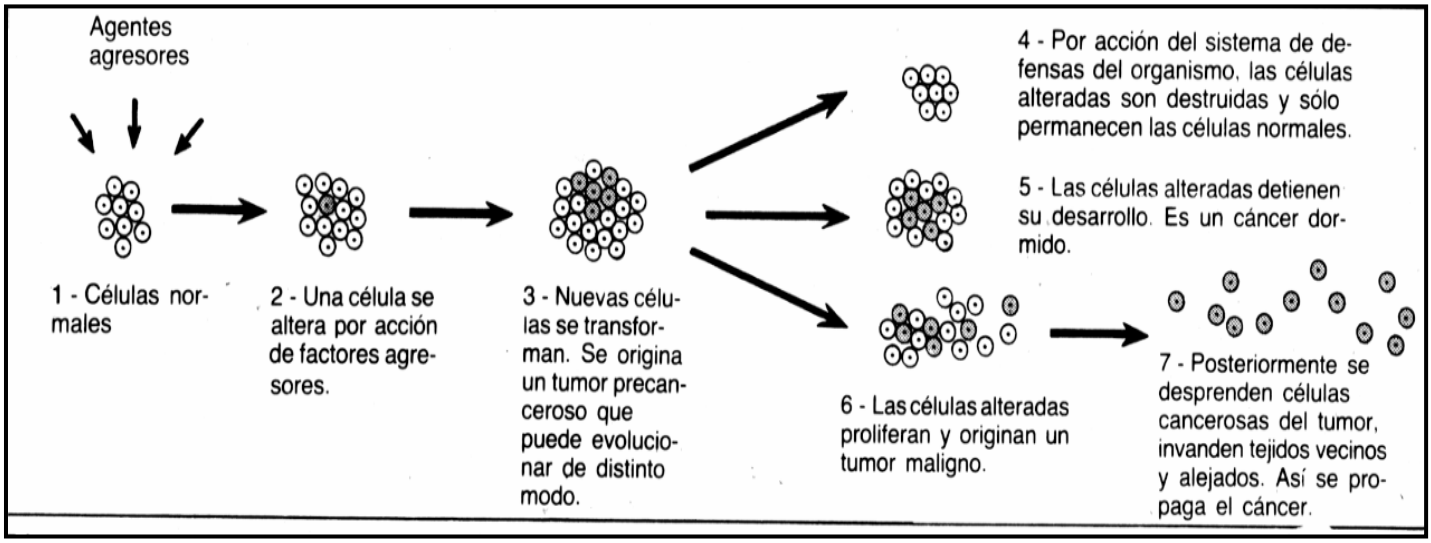
In this picture, it is shown the difference between a normal cell and a malignant cell, the second one is completely a mess.

Fig.2



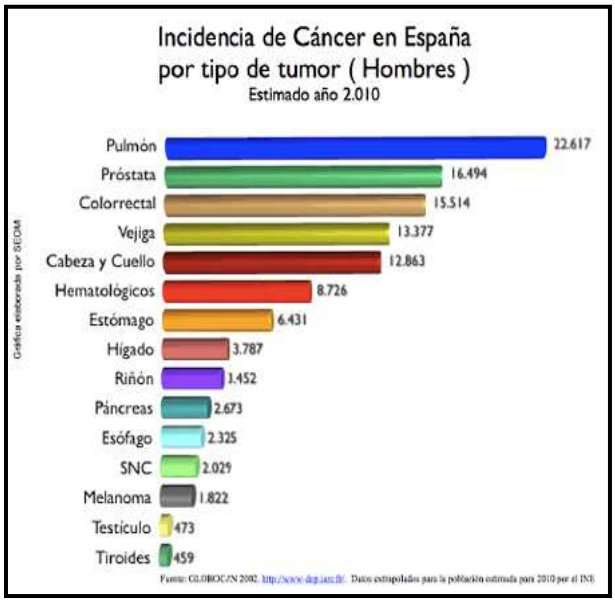
This one is a scheme of the anormal growth control. In the first part we can see that it is the normal growth of a cell, and the second part is when it becomes a tumour because of the uncontrolled growth.

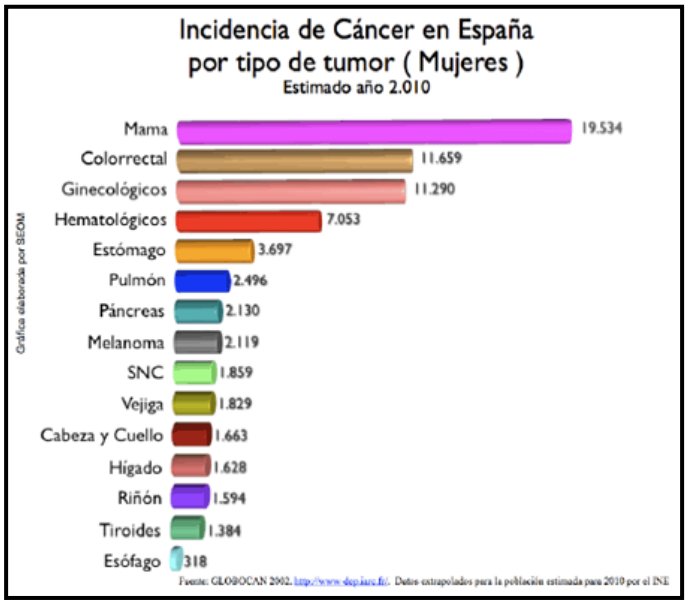
Fig. 3



Here, there is what happens when a normal cell becomes a tumour, and that means cancer. After some normal cells have been attacked by aggressors agents, the tumour appears. And there can be three possible endings: that anormal cells are destroyed, so, only the normal ones rest; or that anormal cells stop its development, it is a slept cancer; or the other possibility is that malignant cells continue growing and they invade other tissues, and that is when cancer appears.

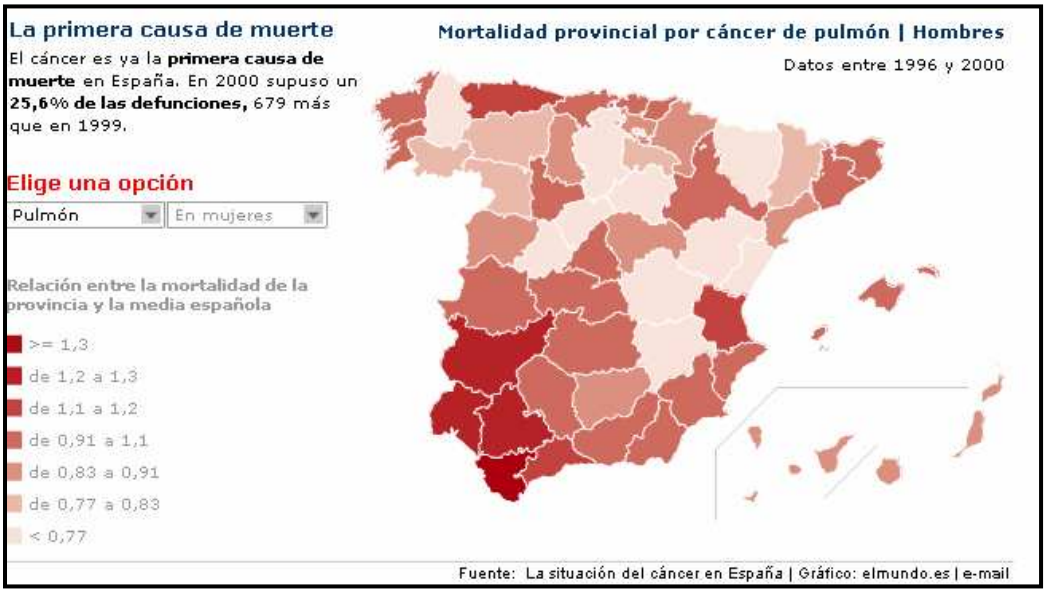
Fig. 4 and 5

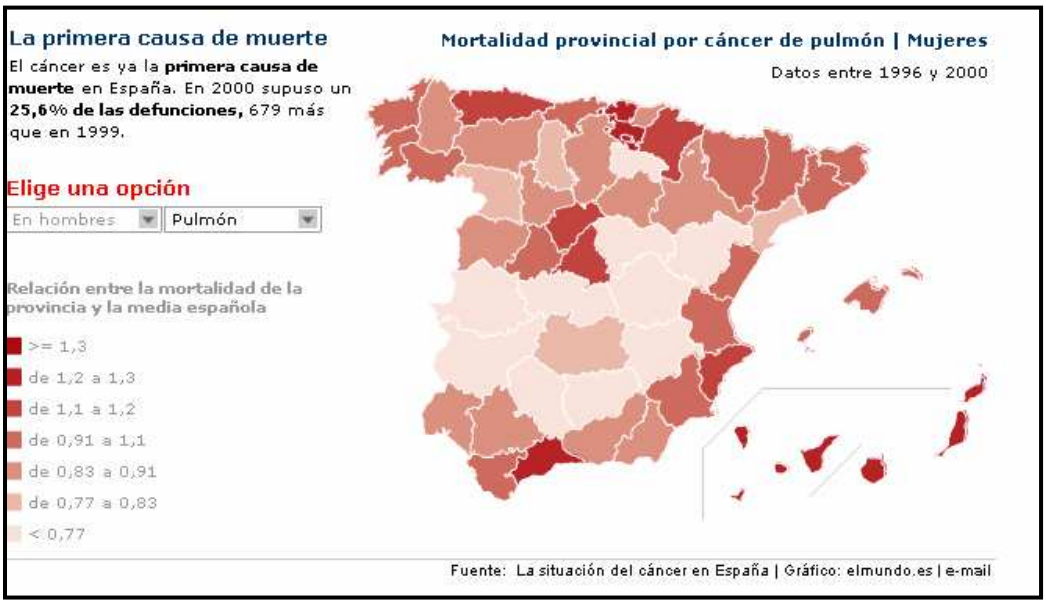




These statistics show that lung cancer in men is the first one, and in women, it is the fifth. So, lung cancer is one of the most common one in Spain.

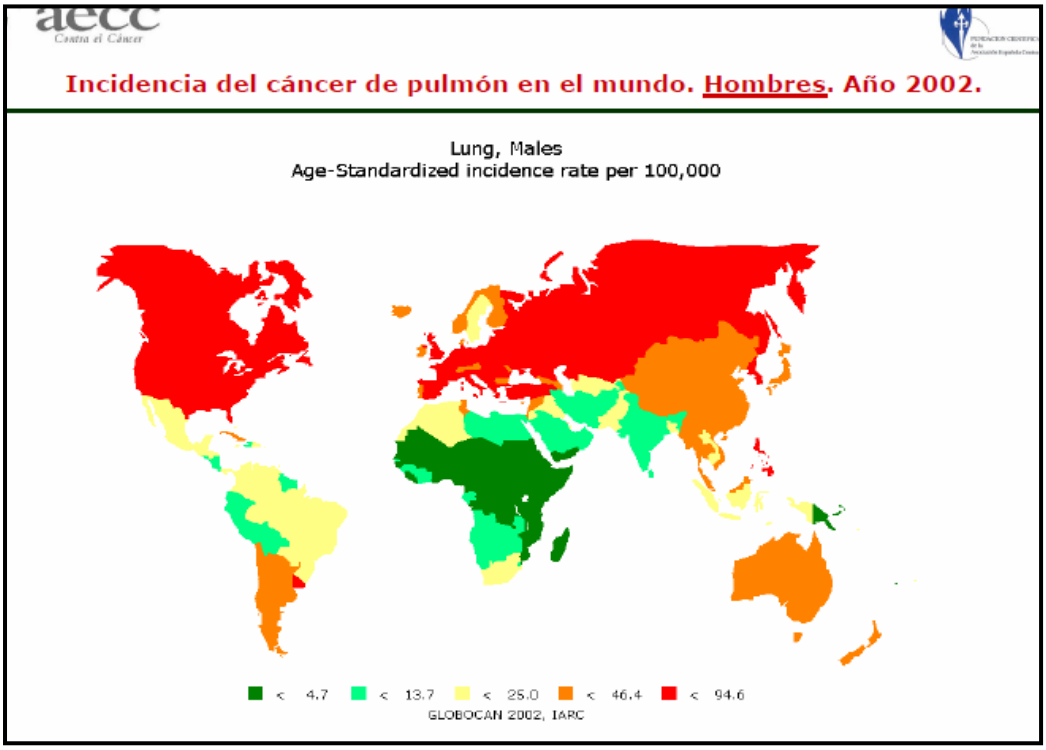
Fig. 6 and 7

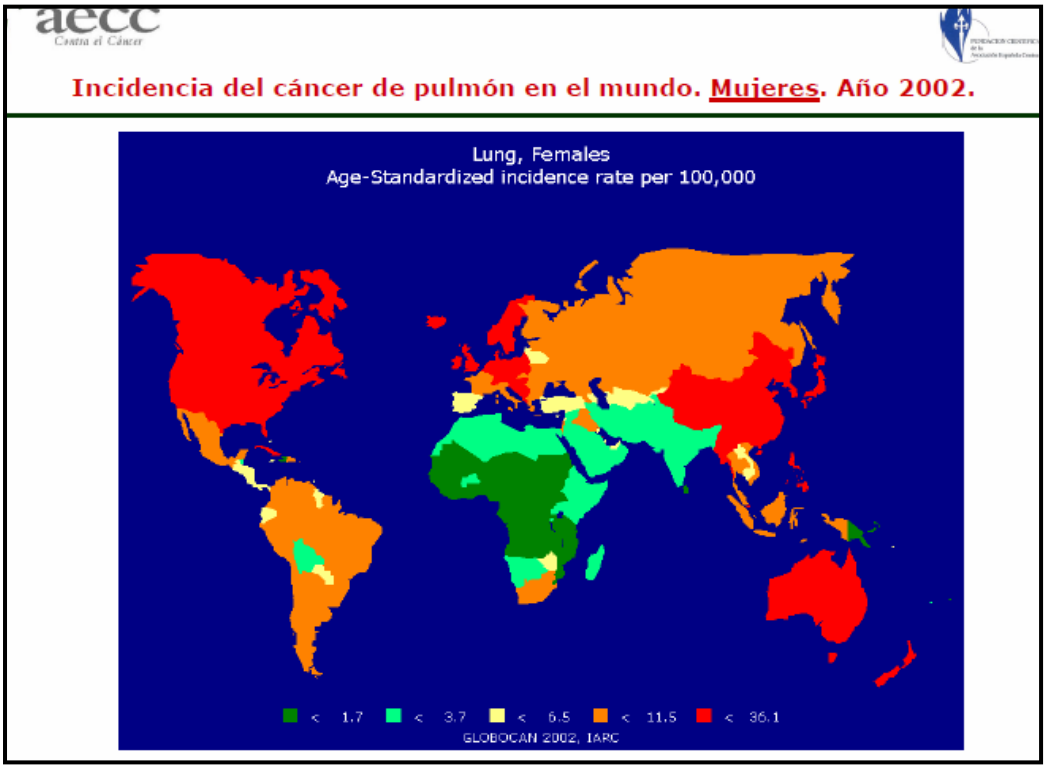




As we can see in these maps, the regions from Spain where most men die are the most rich in mines. But if we compare with Spanish women, they die where there is more stress, more development… Smoking is not the only cause of lung cancer.

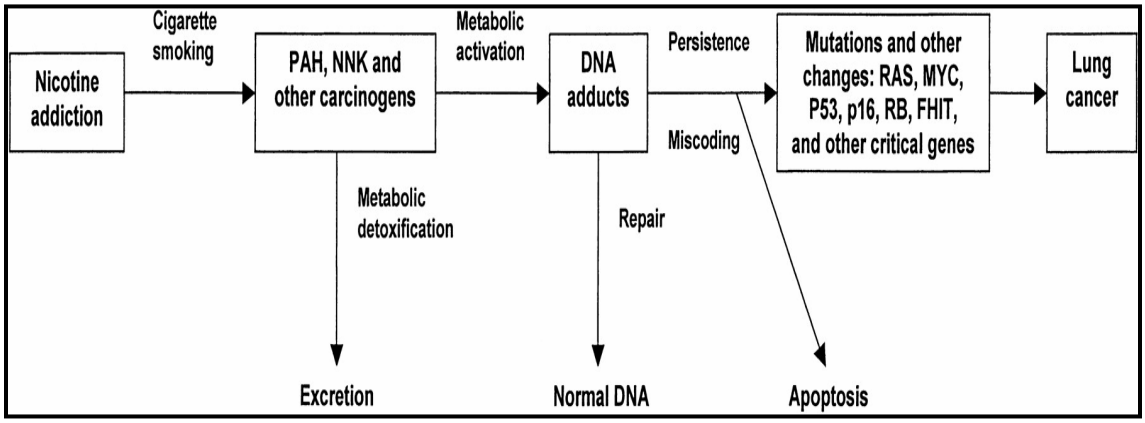
Fig. 8 and 9





As we can see, the statistics around the world are similar to the Spanish ones. There are more lung cancer patients in the most populated and developed countries, pollution influence too. Otherwise, the North Eastern of Europe has a much lower percentage.

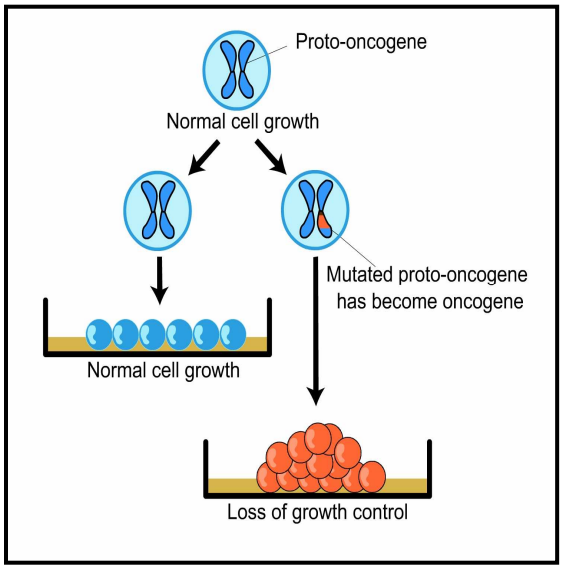
Fig. 10



This picture is a Scheme linking nicotine addiction and lung cancer via tobacco smoke carcinogens and their induction of multiple mutations in critical genes.

If we smoke, we keep nicotine and we become addicted, then, some carcinogens are excreted by some metabolic detoxification, and if DNA adducts is repaired, it becomes normal DNA. If there is apoptosis, cancer doesn't appear because malignant cells are destroyed by this process called apoptosis; but if not, if there are some mutations and changes in genes, lung cancer appears.

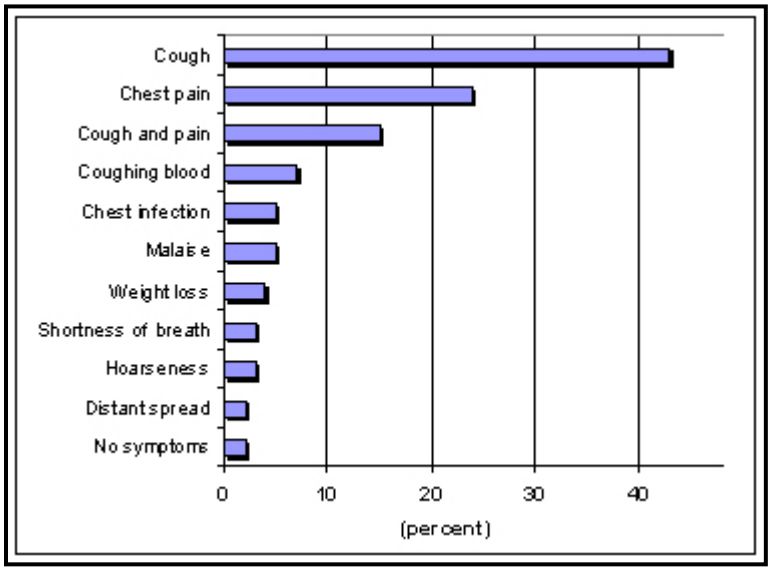
Fig. 11



This scheme shows us perfectly what a proto-oncogene is and what an oncogene is. A proto-oncogene is a gene that if it suffers a mutation, it becomes an oncogene, and if not, it is just a simple gene.

After several mutations, the tumour appears.

Fig. 12



Different symptoms cause lung cancer, which is why sometimes, it is difficult to diagnose.
The first and common symptom is coughing.

WORKING AT THE SCHOOL'S LABORATORY AND EXPERIMENTING THE ANTIOXIDANT SUBSTANCES EFFECT WITH YEAST

Fig. 15

Here, I was comparing the concentration of each tube because; I had to obtain an equivalent concentration between all the samples, using a Mc Farland tube.

Fig. 16

This picture is when I was working with methylene blue to dye the solution in order to see the cells better with the microscope.

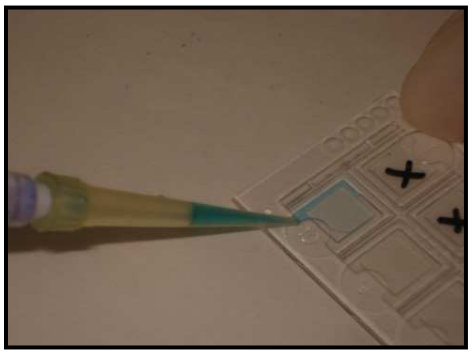


Fig.17

I was preparing everything to be watch with the microscope.

Fig. 18

There, I watched through the microscope if the results were what I expected. Fortunately, they were well done.

VISIT TO HOSPITAL CLINIC IN BARCELONA

Fig.19

It is a picture of a lung. The white part is a tumour. That is what pathologists are going to see, because it could be benignant or malignant.

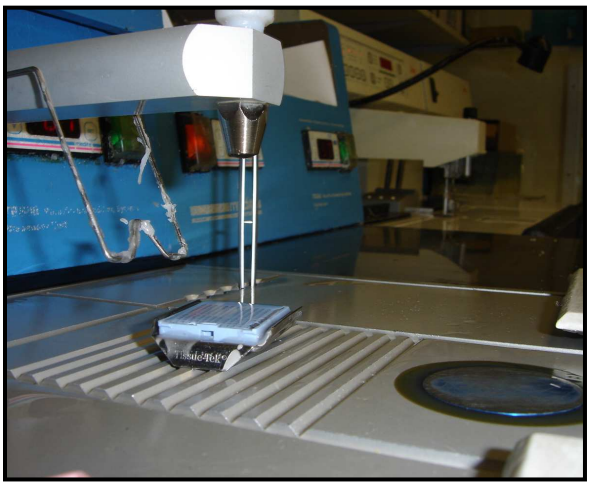


Fig.20
After, having chosen the tissue that they want to observe, they make a block with it.

Fig.21
Once they have the block cleaned, they slice the blocks with very thin slides. Then, these slides are washed and dye to be ready for its observation.

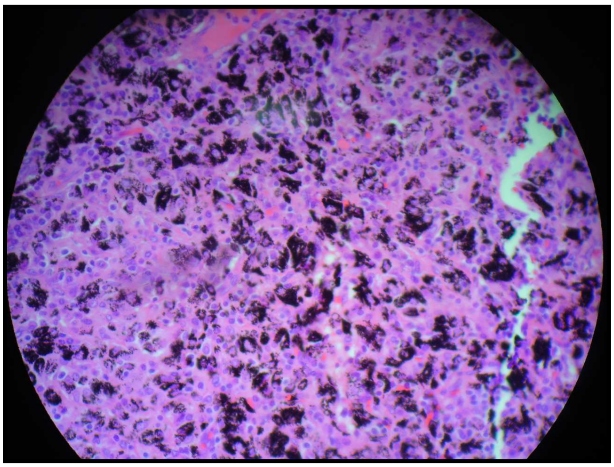


Fig.22
That is what we saw with the microscope.

G L O S S A R Y

A

Adenocarcinoma : A type of non-small cell lung cancer. Types of lung cancer are determined by the type of cells in the cancer.

Adjuvant therapy : Treatment given after the main treatment to help cure a disease.

Aantiangiogenesis therapy : Using drugs or other treatments to stop new blood vessels from forming in tumors to try to limit tumor growth.

Antibodies : Proteins in the body made by the immune system that fight infection and disease.

Antioxidants: Substances that may protect cells from damage cost caused by unstable molecules known as free radicals.

Apoptosis: it is the programme of cells' death. It occurs when a cell kills itself and it activates the apoptosis to avoid a worse situation to the organism it belongs

Asbestos : A natural material that is made of tiny threads or fibers. The fibers can enter the lungs as a person breathes. Asbestos can cause many diseases, including cancer. Asbestos was used to insulate houses from heat and cold. It has also been used in car brakes and for other purposes. Some old houses still have asbestos in their walls or ceilings.

Aspiration: Removal of a sample of fluid and cells through a needle. Aspiration also refers to the accidental sucking in of food particles or fluids into the lungs.

B

Benign: Not cancer. Not malignant . A benign tumor does not invade surrounding tissue or spread to other parts of the body. A benign tumor may grow but it stays put (in the same place).

Beta-carotene : A vitamin found in orange, bright yellow, and dark green fruits and vegetables.

Biopsy : To remove cells or tissues from the body for testing and examination under a microscope.

Bronchial carcinoma: Cancer that grows in the bronchi, which are the large airways connecting the windpipe to the lungs.

Bronchoscopy : A way to look at the inside of the windpipe, the bronchi, and/or the lungs using a lighted tube. The tube is inserted through the patient's nose or mouth. Bronchoscopy may be used to find cancer or as part of some treatments.

C

Cancer: An abnormal growth of cells which tend to proliferate in an uncontrolled way and, in some cases, to metastasize (spread). Cancer is not one disease. It is a group of more than 100 different and distinctive diseases. Cancer can involve any tissue of the body and have many different forms in each body area. Most cancers are named for the type of cell or organ in which they start. If a cancer spreads (metastasizes), the new tumor bears the same name as the original (primary) tumor.

Carbon dioxide: A gas which is the byproduct of cellular metabolism and which collects in the tissues, is cleared from the tissues by the blood within the veins, is carried by the hemoglobin in the red blood cells, and removed from the body via the lungs in the exhaled air. Abbreviated CO2

Carcinogenic: Causing cancer or contributing to the causation of cancer. Pertaining to a carcinogen.

Carcinoma: Cancer that begins in the skin or in tissues that line or cover body organs. For example, carcinoma can arise in the breast , colon, liver, lung, prostate, and stomach.

CAT scan : Pictures of structures within the body created by a computer that takes the data from multiple X-ray images and turns them in pictures on a screen. The CAT (computerized axial tomography) scan can reveal some soft-tissue and other structures that cannot even be seen in conventional X-rays. Using the same dosage of radiation as that of an ordinary X-ray machine, an entire slice of the body can be made visible with about 100 times more clarity with the CAT scan. .

Cervical mediastinoscopy A surgical procedure to examine the central area of the chest, called the mediastinum. (The heart, windpipe, bronchi, blood vessels, lymph nodes, and esophagus are found here.) The doctor makes a small incision (cut) in the neck to get to the mediastinum. Cervical mediastinoscopy can be used to help learn the stage of disease. It also helps doctors see if cancer has spread to the lymph nodes.

Chemoprevention : Using things such as drugs or vitamins to try to prevent or slow down cancer. Chemoprevention may be used to help keep someone from ever getting cancer. It is also used to help keep some cancers from coming back.

Chemotherapy : A chemical that binds to and specifically kills microbes or tumour cells. In oncology, drug therapy for cancer. Chemotherapy is usually systemic treatment, meaning that the drugs flow through the bloodstream to nearly every part of the body. Anticancer drugs are given through the catheter..

Chest X-ray: An X-ray of the inside of the chest. X-rays are high-energy radiation used to take pictures of the inside of the body. These pictures can be used to find cancer and other diseases.

Clinical trial: A kind of research study where patients volunteer to test new ways of screening for, preventing, finding, or treating a disease. Also called a clinical study.

D

Dysphagia : Trouble swallowing.

Dyspnea : Shortness of breath.

E

EGFR inhibitors: Stands for epidermal growth factor receptor inhibitors. Epidermal growth factor is a protein in the body that stimulates some cells, including some cancer cells, to grow and multiply. EGFR inhibitors are a class of anti-cancer drugs. They work by blocking epidermal growth factor from stimulating cells to grow.

F

Fine needle aspiration: The use of a thin needle to withdraw material from the body. For example, this method is commonly used to determine whether a nodule in the thyroid gland is benign or malignant. A fine gauge needle is placed into the nodule and a drop of blood is withdrawn. The cells are studied under the microscope by an pathologist.

Free radicals: Oxygen atoms that can seriously damage our cells and in pair our body's ability to fight against illness.

G

Gene: The basic biological unit of heredity. A segment of deoxyribonucleic acid (DNA) which contains the necessary information to make a protein.

Gene therapy: Treatment that changes a gene. Gene therapy is used to help the body fight cancer. It also can be used to make cancer cells more sensitive to treatment.

L

Lobe: Part of an organ that appears to be separate in some way from the rest. A lobe may be demarcated from the rest of the organ by a fissure (crack), sulcus (groove), connective tissue or simply by its shape. For example, there are the frontal, parietal, temporal, and occipital lobes of the brain.

Lobectomy: An operation done to remove a lobe of an organ such as the lobe of a lung or a lobe of the thyroid gland.

M

Magnetic resonance imaging: A special radiology technique designed to image internal structures of the body using magnetism, radio waves, and a computer to produce the images of body structures. In magnetic resonance imaging (MRI), the scanner is a tube surrounded by a giant circular magnet. The patient is placed on a moveable bed that is inserted into the magnet. The magnet creates a strong magnetic field that aligns the protons of hydrogen atoms, which are then exposed to a beam of radio waves. This spins the various protons of the body, and they produce a faint signal that is detected by the receiver portion of the MRI scanner. A computer processes the receiver information, and an image is produced. The image and resolution is quite detailed and can detect tiny changes of structures within the body, particularly in the soft tissue, brain and spinal cord, abdomen and joints.

Malignant: In regard to a tumor, having the properties of a malignancy that can invade and destroy nearby tissue and that may spread (metastasize) to other parts of the body.

Mediastinoscopy: A procedure in which the doctor inserts a tube into the chest to view the organs in the mediastinum. The tube is inserted through an incision above the breastbone.

Mediastinum : The part of the body between the lungs. The heart, windpipe, esophagus, bronchi, and lymph nodes are found in this area.

Metastasis: 1. the process by which cancer spreads from the place at which it first arose as a primary tumour to distant locations in the body.

Metastasize: The spread from one part of the body to another. When cancer cells metastasize and cause secondary tumours, the cells in the metastatic tumour are like those in the original cancer.

Molecular treatment: this therapy consists on blocking genes in malignant cells

N

Nicotine: An alkaloid (a nitrogen-containing chemical) made by the tobacco plant or produced synthetically. It is very addictive. When someone becomes habituated to nicotine and then stops using it, they experience the symptoms of withdrawal, including anxiety, irritability, restlessness, shortened attention span and an intense, sometimes irresistible, craving for nicotine.

Non-small cell lung cancer: Cancer of the lung which is not of the small cell carcinoma (oat cell carcinoma) type. The term "non-small cell lung cancer" applies to the various types of bronchogenic carcinomas (those arising from the lining of the bronchi) which include adenocarcinoma , squamous cell carcinoma , and large cell undifferentiated carcinoma.

O

Oncogene: A gene already transformed into carcinogen cell.

Oncologist: A doctor who specializes in studying and treating cancer.

P

Pathologist: A doctor who identifies diseases by studying cells and tissues under a microscope.

PET scan: Stands for positron emission tomography scan. A PET scan is a way to find cancer in the body. In a PET scan, the patient is given radioactive glucose (sugar) through a vein. A scanner then tracks the glucose in the body. The scanner's pictures can be used to find cancer, since cancer cells tend to use more sugar than other cells.

Protoncogene: A normal cellular gene which may become into oncogen.

R

Radiotherapy / radiation therapy: The use of high-energy rays to damage cancer cells, stopping them from growing and dividing. Like surgery, radiation therapy is a local treatment that affects cancer cells only in the treated area. It is a ionizing radiation.

Radon: An odorless, colorless gas known to increase risk of cancer. Radon comes from rocks and dirt and can get trapped in houses and buildings.

S

Side effects: Problems that occur when treatment goes beyond the desired effect. Or problems that occur in addition to the desired therapeutic effect.

Small cell lung cancer: A type of lung cancer made up of small, round cells. Small cell lung cancer is less common than non-small cell lung cancer and often grows more quickly. The name is often shortened to SCLC. Another name for SCLC is oat cell cancer.

Sputum: Mucus and other things brought up from the lungs in coughing.

Squamous cell carcinoma : A type of non-small cell lung cancer that begins in the squamous cells of the lungs. Squamous cells are found in the skin, the lining of the hollow organs (such as the stomach), and in the breathing and digestive tracts.

Stem cells: no differentiated cells which can divide themselves indefinitely and create different types of cells

Stage: How much cancer is in the body and how far it has spread.

Supressors: a type of genes will avoid the cell became malignant

T

Targeted therapies: new medicines to fight against cancer which should attack directly to the protein that it is not working correctly in the damaged cell

Tissue: A tissue in medicine is not like a piece of tissue paper. It is a broad term that is applied to any group of cells that perform specific functions

V

Vaccine : A substance meant to help the immune system respond to and resist disease.

Vitamin C : A vitamin that is important to the immune system and many other body functions. Vitamin C is found in citrus fruits such as oranges, limes, and grapefruit. It is also found in vegetables such as tomatoes, green pepper, and potatoes.

Vitamin E : A vitamin that helps protect cells in the body against damage.

W

Wheezing: A whistling noise in the chest during breathing when the airways are narrowed or compressed.