

3734 Schurch^U, Winterstein A: Experimenteller Beitrag zur Frage Tabak und Krebs. Z Krebsforsch 46: 414-419. 1937. [SOA 246 TOP 2048; Key P246, Cited P264 P291] #246

(From the Surgical University Clinic of Zurich.
Chairman: Prof. Dr. P. Clairmont).

Experimental Contribution Concerning the Question of
Tobacco and Cancer

by O. Schurch and A. Winterstein, Basel.

with three illustrations.

(Received August 4, 1937).

(1) Two years ago we reported on our experiments concerning the relationship between tobacco and cancer (*Z. Cancer Research* 42, 76, 1935). (2) In our experiments, we chemically examined extensively the precipitates resulting from tobacco smoke (tobacco tar) and found that these deposits did not contain any polycyclic, aromatic hydrocarbons. (3) Carcinogenic hydrocarbons like the ones found in coal tar are not present in tobacco tar.

(4) Furthermore, we extensively examined this so-called tobacco tar in experiments on mice and rabbits. (5) We could not induce carcinomas by applying tobacco tar by itself or in conjunction with thermal and mechanical damage. (6) We were further unable to induce carcinomas when distilling the tobacco tar into various high-boiling fractions and applying only these individual fractions.

(7) Whereas tobacco tar had a different effect on rabbits, which showed some "general damage" caused by cholesterol-rich food and temporary application of coal tar. (8) We succeeded in causing tar warts in some of the damaged animals and, in one single case, we could observe the development of a carcinoma.

(9) Lu Fu-hua reported about similar experiments. (10) He simultaneously brushed coal tar on one ear and tobacco tar on the other rabbits' ear. (11) While he observed an acceleration in the development of coal tar carcinomas, he also noted the occurrence of carcinomas on the ear brushed with tobacco tar in three rabbits. (12) He further observed that, after a sudden injection of larger quantities of cholesterol, a carcinoma developed on the animal treated with tobacco tar.

(13) The experiments of Lu Fu-hua, Schurch and Winterstein as well as earlier findings of Roffo and Chikamatsu indicate that the carcinogenic effect of tobacco is rather small and, in fact, that tobacco can only be considered an occasional cause of cancer in an existing predisposition to cancer. (14) This view derived from experiments corresponds, on the whole, to clinical experience; however, much still remains unclear concerning the relationship of tobacco and cancer.

(15) The so-called tobacco carcinomas which we observe in hospitals are always tumors which developed after decades of exposure to tobacco. (illegible sentence dealing with the fact that the time factor has not been adequately taken into account in the experiments). (16) Regarding the time factor, one has generally

2018019486

2018019486

referred to findings from experiments with coal tar. (17) While Roffo reports that he noticed a carcinoma after three years of treatment with tobacco tar, the other scientists mention shorter periods of time. (18) Our experiments, as well, do not exceed 2 1/2 years.

(19) In order to further examine the time factor for the development of cancer, we continued to apply tobacco tar to the surviving rabbits and to administer cholesterol-rich food, following the conclusion of our experiments in 1934. (20) We report on our observations of three animals, which we treated with tobacco tar for 4-5 years as follows:

(21) No. 1. The experiment started in September 1931 by feeding cholesterol-rich food to the animal and by applying coal tar to one ear twice a week. (22) The application of coal tar is continued until May 1932, when two small tar warts develop on the right ear. (23) We then interrupt the treatment and brush tobacco tar to the previously untreated left ear three times a week. (24) In December 1933, the ear treated with tobacco tar reveals two very small papillomatous growths in close proximity to one another, whereas the warts caused by coal tar receded. (25) In July 1936, the skin treated with tobacco tar reveals a pronounced pachydermia and a spread of multiple, tiny warts, which give the skin the appearance of a grater. (26) These deformations remain until December 1936, when the animal dies.

(27) Summary: The application of coal tar to a rabbit's ear until two tar warts develop. (28) The application of tobacco tar on the other ear and the feeding of cholesterol-rich food for 4 1/2 years. (29) After the application of tobacco tar for 4 1/2 years, pachydermia and small tar warts could be induced in the animal.

(30) No. 2. Start of the experiment in the fall of 1931; the application of coal tar and the feeding of cholesterol-rich food. (31) The application of tobacco tar beginning in August 1932. (32) In September 1932, the ear treated with coal tar, which reveals extensive wart formations, is amputated. (33) Continuation of the treatment with tobacco tar three times a week until June 1937. (34) As early as 1933, the skin brushed with tobacco tar reveals pronounced pachydermia. (35) In 1934, a verrucous tar wart the size of a pea, which recedes until 1935. (36) After that, no other changes can be observed until 1937, when the experiment is concluded.

(37) Summary: Tobacco tar is brushed on a rabbit's skin, which has been prepared with cholesterol and coal tar, for five years. (38) Pronounced verrucous formations which, however, receded in each case, can be induced.

(39) No. 3. Start of the experiment in September 1931. (40) The application of coal tar twice a week, the feeding of cholesterol-rich food. (41) The application of coal tar is continued until the first little tar wart develops (in the spring of 1932). (42) Start of the application of tobacco tar in May 1932,

2018019487

continuation until September 1936. (43) As early as August 1932, the little tar wart resulting from the application of coal tar has disappeared and the skin is completely smooth so it is not necessary to amputate the ear. (44) In January 1933, the ear treated with tobacco tar reveals some pachydermia. (45) January 1934: the pachydermia has remained unchanged, occasional minute tar warts. (46) October 1935: in addition to pachydermia, a raspberry-like, flat, broad-seated tar wart develops. (46a) June 1936: the tar wart observed one year before has substantially changed, it has become broader and flatter and starts to exulcerate at the top. (47) In August 1936, the tumor has ulcerated, it measures about 4:3:2 cm., proliferates the whole depth of the ear and also manifests itself as a pronounced tumor on the other side. (48) No glandular metastases. (49) The animal starts to lose weight rapidly and is killed in September 1936, since it is no longer eating. (50) The left ear which had been treated with tobacco tar shows the tumor described above, which has already disintegrated to a large degree proliferating the whole ear. (51) Moreover, the skin of the whole ear shows some pachydermia and many isolated warts not exceeding the size of pinheads. (52) The autopsy revealed the following additional changes: a papillomatous, more recent wart the size of a pinhead on the nick skin of the left eye. (53) The following changes can be noticed in the rectum: the mucous membrane of the upper part of the rectum is swollen in four areas in a peculiar manner, it feels like a pillow and has not ulcerated, but is extremely hyperemic. (54) Below, an ulcerated nut-sized tumor with a rather smooth surface penetrates into the intestinal lumen. (55) The section shows a rough tumorous tissue of grayish-white color. (56) Glands or other metastases cannot be proven anywhere. (57) The histological examination, which was verified by Priv. Doz. Dr. E. Uehlinger, Pathological Institute of the University of Zurich, reveals the following:

1. Tumor of the left ear. (58) One notes a multi-layered, very callous, keratous epithelium, which turns into papillomatous proliferations or into narrow or wide solid cell streaks. (59) These cell streaks infiltrate into the sub-epidermal tissue, destroy and perforate the cartilage buckles. (60) The streaks reveal substantial differentiations, extending to the formation of numerous callous pearls; many mitoses. (61) The callous pearls reveal partial decay and infiltration by pieces of nuclei. (62) Lymphocytous infiltrations of the interstitial tissue.

(63) Diagnosis: callous plate cell carcinoma of the ear. (Illustration 1).

Illustration 1. Callous keratous cell carcinoma after the application of tobacco tar to the rabbit's ear.

2. Wart on the nick skin of the left eye: (64) The papillomatous tissue reveals a pronounced swelling of the multi-layered superficial keratous epithelium and the development of several not very branched papillae. (65) The basis is constituted by

2018019488

2018019488

connective tissue rich in capillaries, the epithelium reveals regular layers, marked delimitation from the base, no mitoses.

(66) Diagnosis: Papilloma of the nick skin of the left eye. (Illustration 2).

Illustration 2. Papilloma of the nick skin of a rabbit after the application of tobacco tar to the skin.

3. (illegible line). (67) In the areas of the pillows one notices large, rounded hollow spaces separated from one another by narrow septa infiltrating both the tunica propria and the submucosa. (68) The hollow spaces are filled with erythrocytes and lined with a single-layered flat endothelium. (69) The septa consist of tight fibroid connective tissue with xanthomatous cell nests.

(70) Diagnosis: Multiple cavernous haemangiomas of the rectum. (Illustration 3, p. 418).

Illustration 3. Multiple cavernous angiomas and spindle cell carcinomas after the application of tobacco tar to the rabbit's skin.

4. Isolated tumor of the rectum: (71) The isolated nut-sized tumor of the rectum consists of tissue very rich in spindle cells. (72) The spindle cells form clusters and streaks which intertwine in all directions. (73) Oval-shaped nuclei of relatively equal size, with fine-grain chromatin structure; occasional mitoses. (74) Delicate collagenous fibrillae are sparsely discharged between the spindle cells. (75) The tumorous tissue is streaked with numerous thick-walled vessels and capillaries. (76) The walls of the arteries are generally intact; the walls of the veins are occasionally split up by spindle cells.

(77) Diagnosis: Spindle cell sarcoma (Illustration 3).

(78) Summary: Preparation of an animal with cholesterol-rich food and the application of tar to the ear until a fine tar wart develops. (79) Then the other ear is being brushed with tobacco tar for 4 years. (80) After four years, development of a callous, keratous epithelium carcinoma on the area of the nick skin of the left eye, of a sarcoma of the rectum and of multiple cavernous haemangiomas of the colon.

(81) These observations indicate that the time factor plays a more important role than has been generally assumed in the development of carcinomas through tobacco tar. (82) While the carcinogenic effect of tobacco is relatively small, we succeeded, after an extremely long application of tobacco tar, in inducing more carcinomas or precanceroses than was to be expected from the experiments conducted so far.

(83) Case No.3 is especially remarkable, since it reveals the development of various tumors in different areas on the same animal.

2018019489

2018019489

(84) It is clear that the carcinoma of the ear is a direct result of the exposure to tobacco tar. (85) It is also known from experiments with coal tar that precancerous warts or papillomas develop in area distant from the area of the application. (86) The papilloma of the nick skin described above can be explained in this sense. (87) Primary spontaneous sarcomas in rabbits are rare.

(88) Kato describes a spindle cell carcinoma in the subcutaneous tissue of the back, Wallner a sarcoma of polymorphous nucleus sarcoma containing giant cell formations and multiple metastases of unknown origin. (89) Katase also describes round cell carcinomas of the jaw in the oral cavity.

(90) We cannot decide whether the spindle cell carcinoma developed in our case can be considered as a spontaneous coincidence or as a consequence of the exposure to tobacco tar. (91) It may be possible that the rabbit licked the tobacco tar and that it subsequently could have affected the intestinal membrane. (92) However, our extended experiments concerning the application of tobacco tar to the mucous membrane of the mouth, which did not cause alterations of the membrane in any area and in any of the animals, even after several years of application, speak against such a hypothesis. (illegible sentence). (93) We do not think, however, that these multiple angiomata can be linked to exposure to tobacco tar.

Summary

(94) Supplementing earlier experiments, we report about the effect of tobacco tar on the rabbit's skin for 4-5 years. (95) The description of a case which, after four years of application, we could observe a keratous epithelium carcinoma of the ear and a papilloma of the nick of the skin of the eye. (96) Moreover, the same animal developed multiple intestinal spindle cell sarcoma.

Bibliography.

This Translation
is certified

on 1/9/56 by
The Language Exchange

Louise B. Smith, Director

2018019490

2018019490