Environmental Health
PERSPECTIVES
Journal of the National Institute of Environmental Health Sciences

http://ehis.niehs.nih.gov

Reprinted from:

May 2001
VOLUME 109 | NUMBER 5

The National Institute of Environmental Health Sciences
National Institutes of Health

A Rat Mammary Tumor Model Induced by the Organophosphorous Pesticides Parathion and Malathion, Possibly through Acetylcholinesterase Inhibition

Gertrudis Cabello,[1] Mario Valenzuela,[1] Arnaldo Vilaxa,[1] Viviana Durán,[2] Isolde Rudolph,[3] Nicolas Hrepic,[4] and Gloria Calaf[1,5]

[1]Biology and Health Department, Faculty of Science, University of Tarapacá, Arica, Chile; [2]Juan Noé Hospital, Arica, Chile; [3]Pharmacology Department, University of Concepción, Concepción, Chile; [4]Chemistry Department, Faculty of Science, University of Tarapacá, Arica, Chile; [5]Center for Radiological Research, Department of Radiation Oncology, College of Physicians and Surgeons, Columbia University, New York, New York, USA

Environmental chemicals may be involved in the etiology of breast cancers. Many studies have addressed the association between cancer in humans and agricultural pesticide exposure. Organophosphorous pesticides have been used extensively to control mosquito plagues. Parathion and malathion are organophosphorous pesticides extensively used to control a wide range of sucking and chewing pests of field crops, fruits, and vegetables. They have many structural similarities with naturally occurring compounds, and their primary target of action in insects is the nervous system; they inhibit the release of the enzyme acetylcholinesterase at the synaptic junction. Eserine, parathion, and malathion are cholinesterase inhibitors responsible for the hydrolysis of body choline esters, including acetylcholine at cholinergic synapses. Atropine, a parasympatholytic alkaloid, is used as an antidote to acetylcholinesterase inhibitors. The aim of this study was to examine whether pesticides were able to induce malignant transformation of the rat mammary gland and to determine whether alterations induced by these substances increase the cholinergic activation influencing such transformation. These results showed that eserine, parathion, and malathion increased cell proliferation of terminal end buds of the 44-day-old mammary gland of rats, followed by formation of 8.6, 14.3, and 24.3% of mammary carcinomas, respectively, after about 28 months. At the same time, acetylcholinesterase activity decreased in the serum of these animals from 9.78 ± 0.78 U/mL in the control animals to 3.05 ± 0.06 U/mL; 2.57 ± 0.15 U/mL; and 3.88 ± 0.44 U/mL in the eserine-, parathion-, and malathion-treated groups, respectively. However, atropine alone induced a significant ($p < 0.05$) decrease in the acetylcholinesterase activity from the control value of 9.78 ± 0.78 to 4.38 ± 0.10 for atropine alone, to 1.32 ± 0.06 for atropine in combination with eserine, and 2.39 ± 0.29 for atropine with malathion, and there was no mammary tumor formation. These results indicate that organophosphorous pesticides induce changes in the epithelium of mammary gland influencing the process of carcinogenesis, and such alterations occur at the level of nervous system by increasing the cholinergic stimulation. *Key words*: acetylcholinesterase, atropine, malathion, parathion, rat mammary cancer. *Environ Health Perspect* 109:471–479 (2001). [Online 3 May 2001]
http://ehpnet1.niehs.nih.gov/docs/2001/109p471-479cabello/abstract.html

Environmental chemicals may be involved in the etiology of breast cancers. Many human tumors have been causally attributed to exposure to environmental carcinogens, pollutants, pesticides, drugs, ultraviolet light, radiation, and tobacco (*1*). The incidence of breast tumors in women is increasing, and environmental chemicals have been partially implicated in this increase (*2*). *In vivo* and *in vitro* data have shown that environmental substances (e.g., DDT, polychlorinated biphenyls, 4-nonylphenol, 4-octylphenol) can promote mammary cancer (*3,4*).

The toxic effect of organophosphorous insecticides, which represent a major class of agricultural chemicals, is to conjugate with the natural complement of cholinesterase enzymes in the body, thereby inactivating them. Parathion [0,0-diethyl 0-(4-nitrophenyl)-phosphorothyoate] and malathion [0,0-dimethyl *S*-(1,2-dicarbethoxy-ethyl)-phosphorodithioate] are organophosphorous pesticides that are extensively used to control a wide range of sucking and chewing pests of field crops, fruits, and vegetables. They have structural similarities with naturally occurring compounds, and their primary target of action in insects is the nervous system. Malathion is also present in lotions and shampoos marketed for the treatment of head lice and mites in humans. Exposure of the skin to these two pesticides has been shown to result in a small amount of systemic absorption (*5,6*).

Eserine [(3α,*S-cis*)-1,2,3,3α,8,8α-Hexahydro-1,3α,8-trimethylpyrrolo (2,3-*b*) indol-5-ol methylcarbamate] is an ester obtained from calabar beans, the seeds of the vine *Physostigma venenosum*. It is used as a miotic drug and for atony of gastrointestinal tract, but it is very toxic if inhaled or swallowed (*5*). Eserine, as well as parathion and malathion, is incorporated through the epithelium of the skin, mouth, and respiratory tract (*5,6*). In the liver, parathion and malathion are activated by enzymatic processes producing paraoxon and malaoxon, respectively (*5,6*). Eserine, parathion, and malathion are acetylcholinesterase (AchE) inhibitors and are responsible for the hydrolysis of body choline esters, including acetylcholine (Ach) at cholinergic synapses (*5–7*). The inhibition of these enzymes increases the availability of Ach, which in turn can stimulate cholinergic receptors producing both nicotinic and muscarinic effects in the organism such as muscle contractions and secretions in many glands (*5*). Atropine is a parasympatholytic alkaloid used as an antidote to AchE inhibitors (*5,6*); it acts through competitive occupation of nicotinic and muscarinic cholinergic receptors (*8*).

The high level of cell proliferation and differentiation that occurs during mammary gland development makes this organ an attractive experimental animal model for examining its susceptibility to different carcinogenic actions. Cell proliferation in the mammary gland is not a random event, but is intimately related to both topography of the mammary parenchyma and specific stages of the gland development that are modulated by age, hormonal variations, and parity history. Different compartments, such as ducts, ductules, and intralobular terminal ducts, have been observed in rats. The intralobular terminal duct is equivalent to the terminal ductal lobular unit in the human breast, considered the site of origin of human breast carcinomas (*9–14*).

The mammary gland is a complex organ that undergoes continuous changes under the influence of body growth as well as cyclic hormonal stimulation from birth to senescence. Under these influences, the

Address correspondance to G. Cabello, Departamento de Biología y Salud, Facultad de Ciencias, Universidad de Tarapacá, Velásquez 1775, Arica, Chile. Telephone: 56 58 205420. Fax: 56 58 205419. E-mail: gcabello@uta.cl

We thank S. Rauth for helpful discussions.

This work was supported by an Institutional Grant from University of Tarapacá, Arica, Chile, and Avon grant CU51470301.

Received 23 May 2000; accepted 14 November 2000.

histology of the gland becomes extremely heterogeneous. The rat mammary glands are distributed in pairs along the milk line, with one pair located in the cervical, two pairs in the thoracic, one in the abdominal, and two in the inguinal region. The basic development of all the glands follows a uniform pattern, and previous studies (*9*) have established criteria for evaluating mammary growth, development and differentiation. With such criteria, the mammary parenchyma is divided into thirds along the longitudinal axis. The third closest to the nipple, called zone A, is composed of the main lactiferous ducts. The intermediate area, called zone B, contains more abundant lateral buds, and it is in this area where most of the secondary ducts arise. The distal third of the gland, or zone C, contains the terminal structures ending in bulbous clubs or terminal end buds (TEBs) (*9*). The mammary gland is composed of a single primary or main lactiferous duct that branches into three to five secondary ducts at birth and during the first week of postnatal life. The ducts are narrow and straight and end in small, club-shaped terminals, the TEBs. During the second week, further sprouting of ducts occurs up to the sixth cell generation. This sprouting of ducts causes a marked increase in the density of TEBs, which reaches its maximum magnitude when the animal is 21 days old (*9*). Histologically, TEBs are composed of three to six layers of medium-sized epithelial cells. After the rat reaches 21 days of age, further sprouting of lateral buds occurs, and numerous TEBs begin to cleave into three to five smaller buds, the alveolar buds (ABs). The differentiation of the mammary gland induces a progressive decrease in the number of TEBs and a concomitant increase in the number of ABs (*9–13*).

The crucial role that topography plays in susceptibility of the breast to carcinogenesis in young nulliparous rats involves the presence of TEBs. The TEBs are the most highly proliferating structures in the breast and therefore are the most susceptible to neoplastic transformation (*9–13*). The study of the pathogenesis of mammary cancer in experimental models has shown that the susceptibility of the mammary gland to chemical carcinogenesis is directly related to the rate of cell proliferation of the glandular epithelium at the time of the exposure to the carcinogen (*11*).

The most widely used experimental systems for the study of mammary tumorigenesis are the models in which tumors are induced in the Sprague-Dawley rat by dimethylbenz[α]anthracene (DMBA) (*15–17*) or in the Sprague-Dawley or Fischer 344 rat by *N*-nitrosomethylurea (NMU) rats of different ages induced tumors with an incidence that was directly proportional to the density of highly proliferative TEBs (*12*). Tumor incidence of 94–100% was obtained when DMBA was administered to rats 30–55 days of age; but the highest number of tumors per animal was observed when the carcinogen was given to animals when they were 40–46 days of age—a period when TEBs were most actively differentiating into ABs (*9–13*).

Many studies have addressed the association between cancer in humans and agricultural pesticide exposure, both occupational (e.g., farmers, pesticides mixers, and appliers) and nonoccupational. Nonoccupational exposures occur in farmers exposed to pesticides stored in homes, contaminated clothing, household dust containing pesticides, contaminated ground and surface water, contaminated soil, and drift from aerial

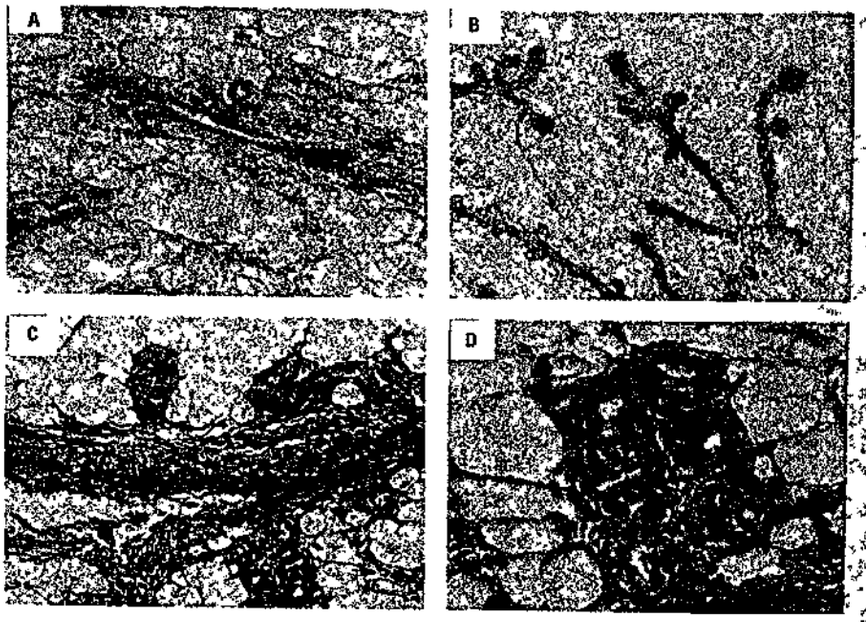


Figure 1. Structures of a normal rat mammary gland composed of a main lactiferous duct (*A*; 350×), which begin to cleave into smaller TEBs and ABs forming lobules (*C*). (*B*) Whole-mount preparation of representative TEBs. (*D*) Higher magnification of a lobule formed by ABs found in cross-section of (*C*). Hematoxylin-eosin, 400×.

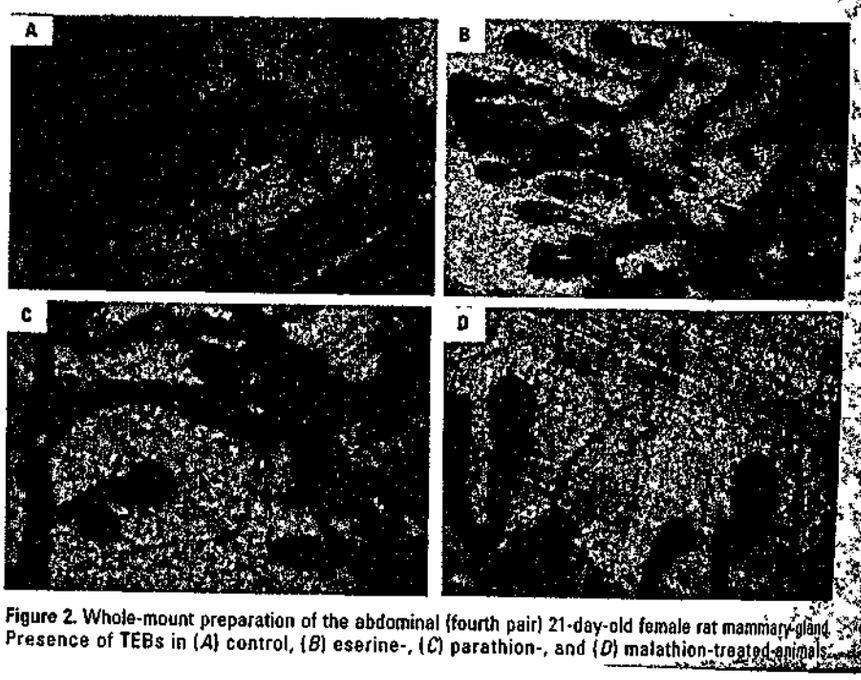


Figure 2. Whole-mount preparation of the abdominal (fourth pair) 21-day-old female rat mammary gland. Presence of TEBs in (*A*) control, (*B*) eserine-, (*C*) parathion-, and (*D*) malathion-treated animals.

spraying of pesticides. Mortality and incidence studies have reported slightly increased rates for the following cancers: breast, non-Hodgkin lymphoma, Hodgkin disease, multiple myeloma, leukemia, prostate, and ovary (19–21).

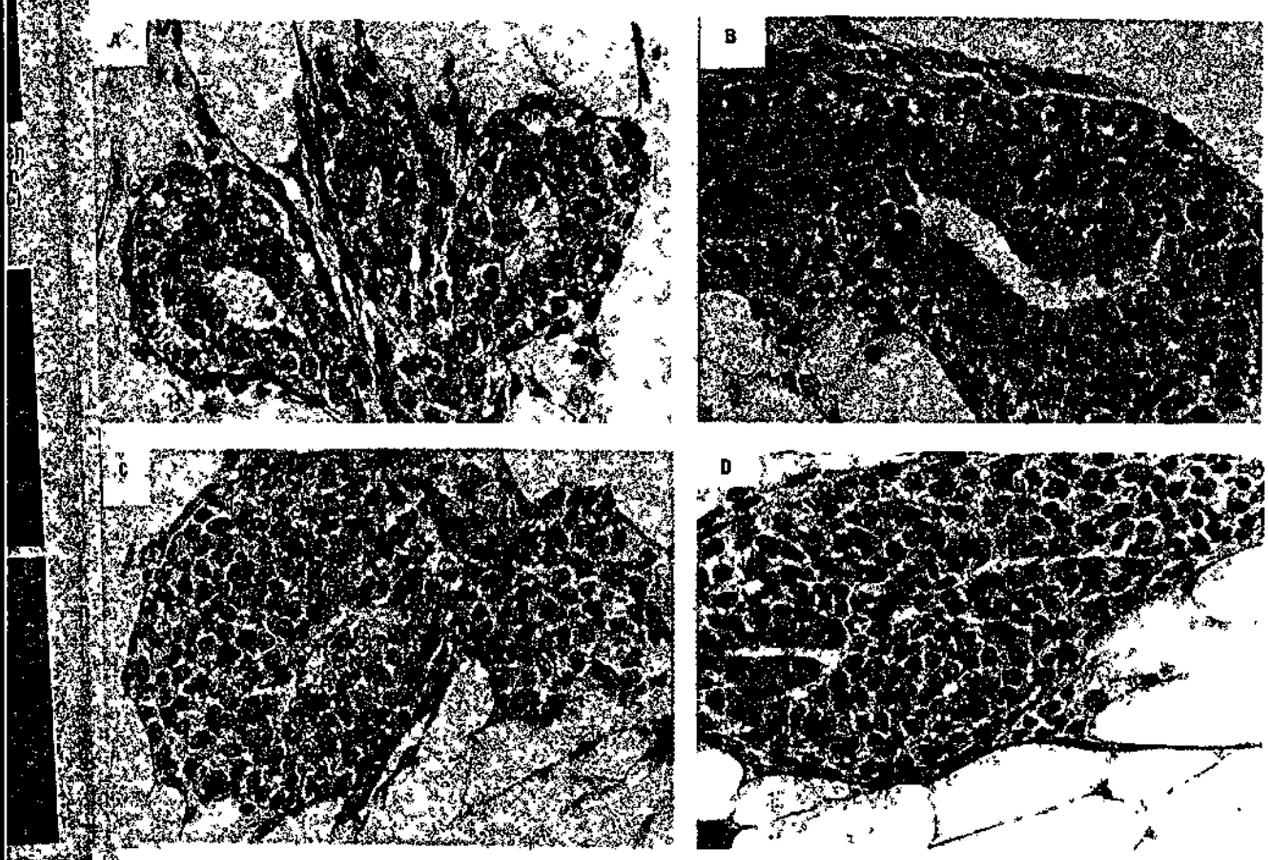
Our purpose was to test the susceptibility of the mammary gland to organophosphorous pesticides. Therefore, we analyzed whether eserine, parathion, and malathion can induce mammary tumors in rats, whether the alterations induced by these substances alter the cholinergic activation influencing malignant transformation of the mammary gland, and whether such action can be inhibited by a parasympatholytic alkaloid, such as atropine.

Materials and Methods

Female Sprague-Dawley rats were obtained from the Catholic University of Chile (Santiago, Chile). These animals were raised and bred in a barrier animal facility located in accordance with the standards outlined in *Guide for the Care and Use of Laboratory Animals* (*22*). All animals were allowed continuous access to a standard laboratory chow diet (Champion, Santiago, Chile). The first experiment was performed with 35 virgin female Sprague-Dawley rats 16 days old. Seven groups of five animals received injections twice a day for 5 days subcutaneously (sc) or intraperitoneally (ip) in the inguinal region of the body. Animals were injected with one of the following substances: saline solution (sc); eserine (sc; Sigma, St. Louis, MO, USA), 33 µg/100 g body weight (bw); parathion (sc; Bayer, Santiago, Chile), 250 µg/100 g bw; malathion (sc; Fyfanon TM, Cheminova, Denmark), 17 mg/100 g bw; atropine (ip; Sigma), 250 µg/100 g bw; combination of eserine and atropine; and combination of malathion and atropine at the dosages previously indicated. The LD_{50} values of the substances for eserine, parathion, and malathion were 0.64, 3.6, and 1,000 mg/kg, respectively. However, the doses used in these experiments were one-half the LD_{50} for eserine and parathion and one-sixth the LD_{50} for malathion, which allowed a 100% survival of animals after 5-day treatment.

The second experiment was performed under identical conditions but the experiment started when the animals were 39 days old. Sixteen hours after the last injections, the animals from these two experimental designs were anesthetized by ip injections of sodium pentobarbital (8 mg/100 g bw) and opened by a midline incision from the pubis to the submaxillary area to remove the mammary glands. The skin was dissected to expose the six pairs of mammary glands, the thoracic, abdominal, and inguinal mammary glands. The left side of control and treated rats was prepared for whole-mount preparation and the right side for histologic studies.

Mammary glands for the whole-mount studies were fixed in alcohol, formaldehyde, and acetic acid (1:1:1) for 24 hr at room temperature, stained with hematoxylin-eosin, and mounted between two slides to visualize under a Zeiss Video Plan (Chicago, IL, USA) (*10*). The mammary gland of rats is sufficiently flat to allow the determination of the area and the quantification of structures in areas of 1 mm^2. We counted 50 areas located mainly distal to the nipple in each gland, and we counted the density of TEBs and ABs in these whole-mount preparations. The density of these structures was expressed in number of structures per square millimeter. To determine the histology, we fixed the glands in Bouin's fixative and embedded them in



Histologic section of TEBs of the mammary gland from the control and 21-day-old treated female rats. Presence of ... treated animals. Hematoxylin-eosin, 400×.

ABs in the control (Figure 2A), eserine- (Figure 2B), parathion- (Figure 2C), and malathion- (Figure 2D) treated 21-day-old animals. Figure 3 shows a cross-section of mammary glands of the same animals, which corroborated the presence of TEBs in the control (Figure 3A), eserine- (Figure 3B), parathion- (Figure 3C), and malathion- (Figure 3D) treated animals. These results indicated that there was no significant difference in the density of TEBs per square millimeter of mammary gland between either the control or the eserine-, parathion-, and malathion-treated 21-day-old rats, and that ABs were absent in the control as well as in the treated animals (Table 1).

Whole-mount preparations in 44-day-old rats showed a significant ($p < 0.05$) difference in the density of TEBs and ABs between control (Figure 4A) and treated animals (Figure 4B–D). Table 2 shows that treatment with eserine and the pesticides parathion and malathion induced a significant increase ($p < 0.05$) in the density of TEBs in the 44-day-old animals. The TEB density increased from 3.30 ± 0.27 TEBs/mm^2 to a maximum of 12.04 ± 1.77 TEBs/mm^2 in parathion-treated animals (Table 2). The AB density decreased in treated animals from 20.80 ± 1.68 AB/mm^2 in controls to a minimum of 0.75 ± 0.44 AB/mm^2 in eserine-treated animals (Table 2). Parathion- and malathion-treated animals also showed a significant ($p < 0.05$) decrease in the density of ABs. A representative whole-mount preparation of a 44-day-old rat mammary gland of control animals and a schematic representation of ABs are presented in Figure 5A and B, respectively. Representative whole-mount preparation from a pesticide-treated rat mammary gland and a schematic representation of such structures, which gives an overview of TEBs, are shown in Figures 5C and D, respectively.

Histologic examination of mammary tissue of 44-day-old control and treated rats supported the results seen with the whole-mount preparation. The control rats had normal lobule formation and presence of ABs, whereas no ABs were observed in any group of treated animals (Figure 6A–D). The eserine-, parathion-, and malathion-treated animals showed a significant ($p < 0.05$) increase in the size of TEBs of the mammary gland, as well as in the number of the epithelial layers (Figure 6B–D). Furthermore, such structures increased in size until tumors started to appear. However, after 840 days the control animals did not develop any kind of tumors. After pesticide injections, treated animals developed tumors at a rate of 8.6–24.3%. Table 3 shows the number, size, and latency of these tumors after 28 months of treatment. Among the 560 animals used in this experiment, 6 out of 70 eserine-treated animals, 10 out of 70 parathion-treated animals, and 17 out of 70 malathion-treated animals developed mammary tumors. Tumor size ranged from 9.26 ± 3.43 to 22.1 ± 7.2 cm^3. The malathion-treated group had smaller tumors, but they appeared earlier than with the other treatments. The tumor latency range fluctuated between 54 and 840 days. Treated animals exhibited only mammary tumors that appeared exclusively in the mammary fat pad of the axillary and abdominal-inguinal regions of the animal (Figure 7A,B). Histologic diagnosis of the mammary tumors revealed that they were adenocarcinomas, grossly nodular and encapsulated, with areas of cribiform or papillary patterns (Figure 7C, D). Most of the tumors developed in the abdominal region, with only one tumor in the cervical region. Analysis of lungs, heart, intestinal tract, ovaries, and uterus did not show any tumors. Neurologic symptoms that might have suggested tumors of the nervous system were not observed.

Tables 1 and 2 also show the effect of atropine either alone or in combination with eserine or malathion on the density of structures present in the rat mammary glands. Neither atropine nor the combination of atropine with eserine or malathion induced changes in the density of TEBs per square millimeter in the mammary gland of 21-day-old animals in comparison to control animals (Table 1). There was no significant difference among these groups in comparison to control animals. Table 2 shows the density of TEBs and ABs in the mammary gland of 44-day-old animals treated with atropine alone or in combination with the eserine or malathion. Treatment of animals at this age with atropine alone or in conjunction with eserine or malathion did not induce any change in the density of TEBs in comparison to the control animals (Figure 8A). However, atropine caused a significant ($p < 0.05$) inhibition of formation of ABs in these animals compared to controls. Atropine treatment in combination with either eserine or malathion caused a significant ($p < 0.05$)

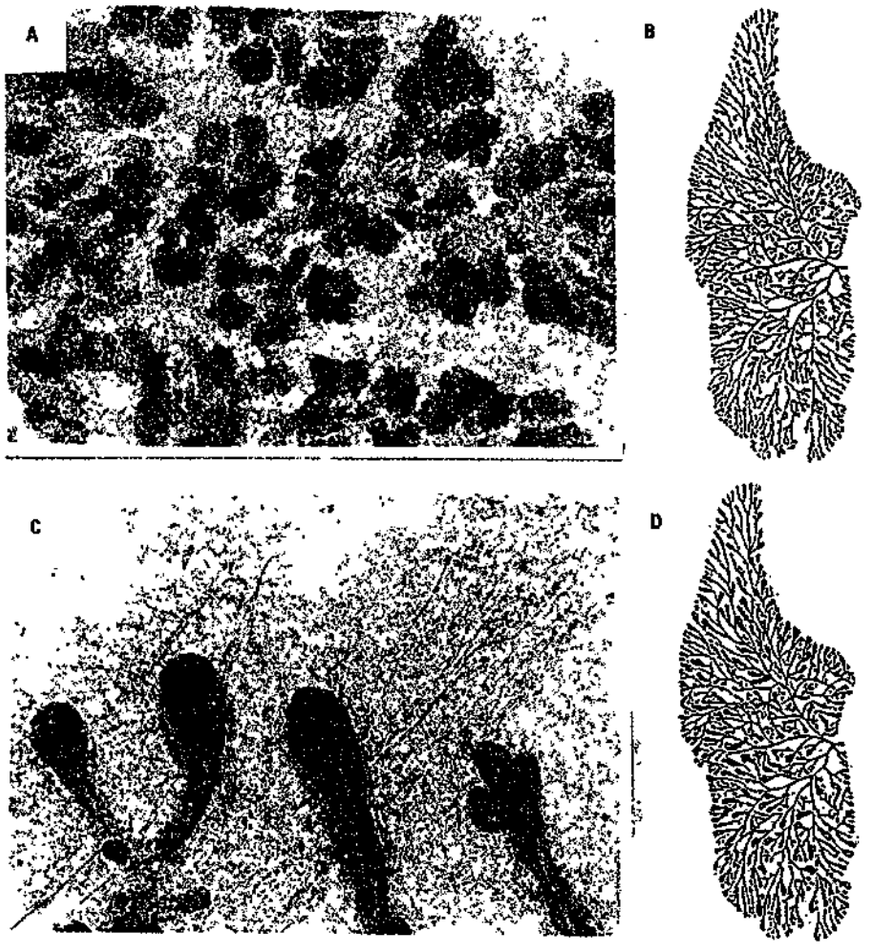


Figure 5. Whole-mount preparation of the mammary gland. (*A*) ABs; (*B*) a schematic representation of these structures; (*C*) TEBS in pesticide-treated animals; and (*D*) an overview of (*C*). 400×.

inhibition of density of TEBs in comparison with the eserine, parathion, and malathion alone. However, there was an increase in the density of ABs similar to that of controls (Figure 8B) and a significant ($p < 0.05$) increase in the density of ABs in comparison to animals treated with eserine, parathion, and malathion. In addition, there was no rat mammary tumor formation after the injection of atropine alone or with the combination of atropine and eserine or malathion. Figure 9 shows the correlation between the density of TEBs and AchE activity in the serum of the 44-day-old control and treated animals. These results showed a significant ($p < 0.05$) decrease in the AchE activity in serum of eserine, parathion, malathion, atropine, and combination of atropine either with eserine- or malathion-treated animals in comparison to controls. The atropine induced an even greater decrease ($p < 0.05$) in such activity from 4.38 ± 0.2 U/mL in the atropine-treated group to 1.32 ± 0.02 and 2.39 ± 0.2 when combined with the eserine and malathion, respectively.

Discussion

Our study demonstrates that parathion and malathion induced tumor formation in a specific target organ, the mammary gland. This is the first report that organophosphorous pesticides induce changes in mammary gland associated with carcinogenesis. Our results showed that initiation occurs primarily in the epithelium of TEBs while they are developing into ABs because these structures were affected by pesticides. This is an important finding because such structures are considered equivalent to the terminal ductal lobular unit described in the human breast (*9–13*). Treatment with these substances induced significant changes at a cellular level. Forty-four-day-old animals showed a significant increase in the density of TEBs, inhibiting the normal process of differentiation from TEBs to ABs that was seen in the control animals. These results indicated that the proliferative changes observed in the TEBs may have induced the formation of mammary adenocarcinomas.

Breast tissue seems to be very sensitive to ionizing radiation when exposure occurs between the ages of 15 and 19 years (*9*), which suggests that events that occur during the early years of a woman's life have a significant effect on lifetime risk of breast cancer. An understanding of the mechanisms that make the mammary glands of young women more susceptible to carcinogenesis can be achieved by using an adequate animal model system. Previously, researchers (*10,15*) have demonstrated that mammary carcinoma formation in rats can be induced by a chemical carcinogen, mainly DMBA, which seems to provide such a model. Mammary tumors thus induced were adenocarcinomas arising from TEBs of incompletely differentiated glands (*10,12*). The administration of DMBA to virgin rats of different ages induced tumors with an incidence that was directly proportionally to the density of highly proliferating TEBs (*10*). A tumor incidence of 94–100% was obtained when DMBA was administered to rats 30–55 days of age, but the highest number of tumors per animal was observed when the carcinogen was given to animals when they were 40–46 days of age, a period when TEBs were most actively differentiating into ABs. The high susceptibility of the TEBs to neoplastic transformation is attributed to the cell kinetic properties of its lining epithelium, whose rate of cell proliferation is shown by DNA synthesis. The TEBs were also characterized by having a high growth fraction, proliferative fraction of the cell cycle, which diminished in the more differentiated ABs and lobules (*9–13*).

To determine whether cell kinetic parameters varied among the different compartments of the breast in the human female and whether they were affected by age and gland topography (*24*), samples of normal human breast tissue were studied in organ culture systems. The results indicated differences among the mammary glands of young and old women. The correlation of different parameters related to cell cycle determination indicated that values for growth fraction and DNA synthesis or DNA-labeling index were higher in the intralobular terminal ducts and lower in alveoli and ducts. Studies done on the influence of age and gland topography on cell kinetics of normal human breast indicated that both young and

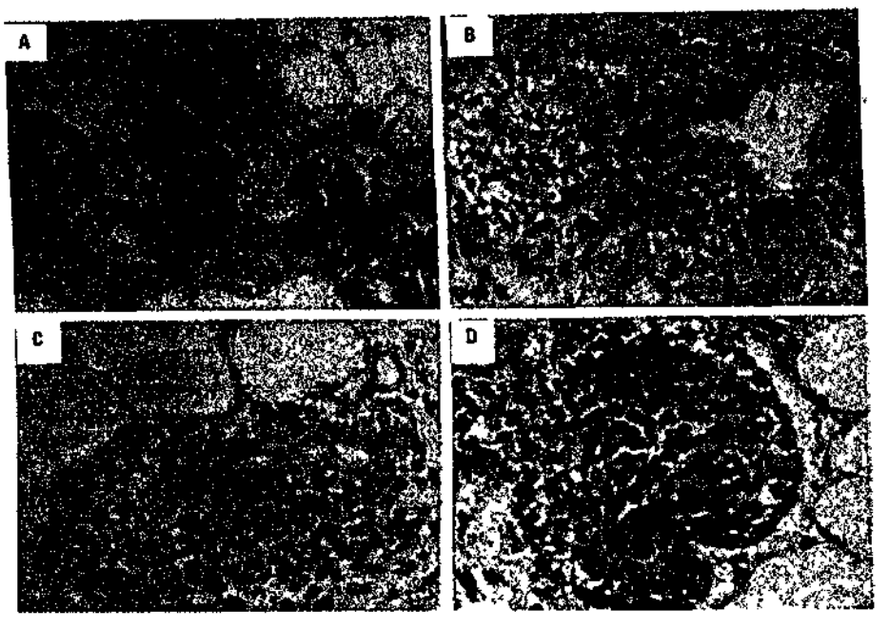


Figure 6. Histologic section of 44-day-old female rat mammary gland. (*A*) Histologic section of ABs of the mammary gland from the control animal. The proliferative characteristics of TEBs in (*B*) eserine-, (*C*) parathion-, and (*D*) malathion-treated animals are appreciated here. Hematoxylin-eosin, 400×.

Table 3. Analysis of mammary gland tumor formation by the effect of eserine, parathion, malathion, atropine, and combinations of eserine + atropine, parathion + atropine, and malathion + atropine in female Sprague-Dawley rats treated from 39 to 44 days of age.

Treatment	No. animals with tumors/total animals	Mean tumor size ± SE (cm^3)[a]	Mean latency ± SE (days)[b]
Control (saline)	0/70	—	—
Eserine (33 µg/100 g bw)	6/70	22.10 ± 7.20 (5.4–49.56)	488 ± 60 (402–840)
Parathion (250 µg/100 g bw)	10/70	16.50 ± 5.60 (2.5–45.00)	569 ± 16 (490–619)
Malathion (17 mg/100 g bw)	17/70	9.26 ± 3.43 (0.08–42.30)	(509 ± 45) (54–653)
Atropine (250 µg/100 g bw)	0/70	—	—
Atropine + eserine	0/70	—	—
Atropine + parathion	0/70	—	—
Atropine + malathion	0/70	—	—

[a]Range in tumor size. [b]Range of number of days before tumors appeared.

older women had the highest growth fraction and DNA-LI in the intralobular terminal ducts. The length of the cell cycle in these structures increased from 200.3 to 847.0 hr in the older women (*24*). The high rate of cell proliferation was associated with the shortened length of the cell cycle. Other reports (*9–13*) have shown that DNA-LI among young virgin rats was much higher than among old virgin rats. The DNA-LI studies in young women paralleled those results. The TEBs of young virgin rats had a cell cycle of an average length of 11 hr, lengthening to 21 and 28 hr in the terminal ducts and ABs, respectively.

According to previous observations, the susceptibility of the mammary gland to neoplastic transformation is related to its degree of development and proliferative activity (*25*). *In vitro* oncogenesis models of different types of cells have yielded important knowledge about the pathogenesis of neoplasia. Attempts to obtain transformation of human breast epithelial cells in culture have been also successful (*25–27*). Miyamoto et al. (*27*) observed neoplastic transformation of mouse mammary epithelial cells by *in vitro* exposure to NMU. McCormick et al. (*28*) reported neoplastic transformation of epithelial cells by the effect of NMU in mammary gland *in vivo*. The formation of tumors observed in eserine-, parathion-, and malathion-treated animals correlates with the greater density of TEBs in the mammary gland present in the 44-day-old treated animals. The concomitant increase in the area of ABs in the control animals and lack of tumors in control animals allows corroboration of our results with what other groups have found (*12*).

Models for studying mammary carcinogenesis have been developed in Sprague-Dawley rats, with the chemical carcinogen DMBA (*15–17*), which induced mammary carcinomas in 100% of the animals with a latency period of 86 days (*15*). Another widely used experimental system to study mammary tumorigenesis is the model in which tumors are induced in the Fischer 344 rats by a single dose of NMU; such tumors had latency similar to that observed by the group mentioned above (*18*). In contrast to these potent carcinogens, which induce mammary carcinomas in 100% of intact females (*14*), organophosphorous pesticides seem to have a slow and less infiltrating and potent effect. We observed that parathion and malathion induced 14.3% and 24.3% of mammary carcinomas, respectively. The type of tumors observed had papillary adenomatous patterns and ductal carcinomas with cribiform pattern.

Mammary tumors formed in various strains of rats induced by chemical carcinogens or radiation have been classified by several authors (*9,14,29*). There is agreement that tumors appearing histologically malignant in the rat have features in common with most frequently observed tumors in humans. Intraductal and infiltrating ductal carcinomas in the rat, unlike in the human, constitute a minority of the tumors developed under the commonly used regimens for tumor induction. Most tumors induced in young virgin rats can be classified within three major groups: intraductal

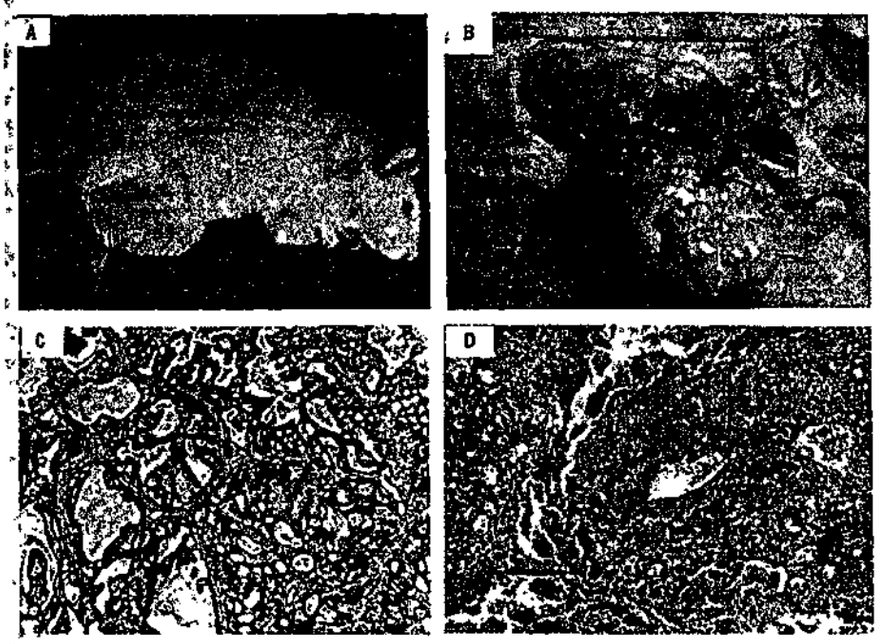


Figure 7. Mammary gland tumors developed in the mammary gland region by the effect of (*A*) parathion and (*B*) malathion in the female Sprague-Dawley rats. (*C*) Cross-sections of a papillary adenocarcinoma, grossly nodular, encapsulated, with areas of cribiform or papillary patterns. It was removed after 84 days of 5-day malathion treatment. (*D*) The histologic sections of another mammary tumor removed after 96 days of 5-day malathion treatment that revealed a ductal carcinoma. Hematoxylin-eosin, 400×.

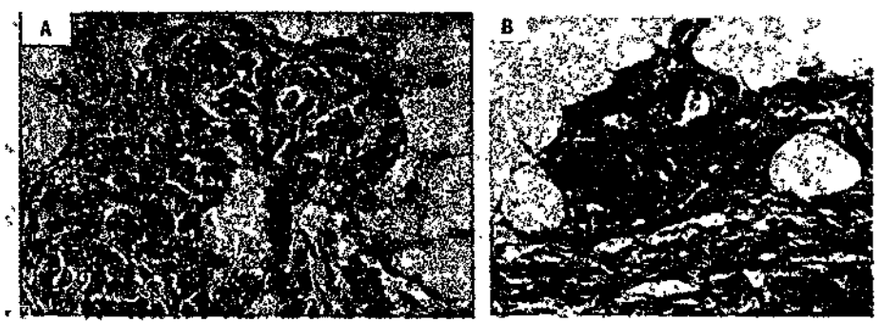


Figure 8. (*A*) Cross-section of structures present in the mammary gland of a rat injected with atropine (400×). (*B*) Cross-section of ABs of a rat treated with the combination of atropine and pesticide. Hematoxylin-eosin, 400×.

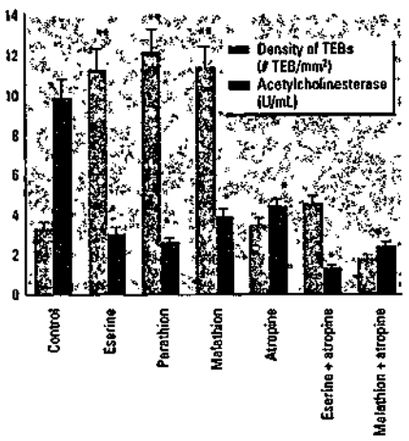


Figure 9. Correlation between the density of TEBs of the mammary gland and the AchE activity (U/mL) present in the serum of 44-day-old control and treated animals. The bars represent the mean ± SE of five animals per group.
*$p < 0.05$ versus control; **$p < 0.05$ versus control.

papillomas, composed of a hyperplastic epithelium; papillary carcinomas, which may be composed of epithelial cells with varying degrees of cytologic atypia, growing in solid, papillary adenomatous patterns; and ductal carcinomas with cribiform pattern. All three kinds of tumors were observed in the eserine-and pesticide-treated animals.

The density of TEBs was almost 4 times greater, and the density of ABs was 10 times lower in the pesticide-treated 44-day-old animals than in the control ones. Even though the pesticides seem to act on undifferentiated structures (i.e., TEBs), they also seem to have a different mechanism of action, probably through the inhibition of AchE that increases Ach availability. For that reason, the incidence of such tumors seems to be slower through the inhibition of AchE than with the direct-acting carcinogen DMBA. Our results confirmed this interaction because 8.6% of the animals treated with eserine also had mammary gland tumors.

Atropine alone did not induce changes in the cell proliferation of mammary gland of 44-day-old rats compared to the control, whereas atropine induced inhibition in formation of ABs compared to the controls. However, the atropine treatment in conjunction with either eserine or malathion produced a decrease in the density of TEBs and an increase in the formation of ABs similar to control animals. On the other hand, we also observed that atropine treatment either alone or in combination with eserine or malathion decreased three to five times the AchE activity in the serum of animals, compared to controls. The ABs reached the normal development of the mammary gland similar to the control animals, and there was no tumor formation. The interesting finding of these studies was that mammary tumors were found only in the eserine-, parathion-, and malathion-treated animals. Our experiments indicated that the pesticides induced AchE inhibition which remained for at least 3 months, suggesting that there was constant cholinergic stimulation. It has been previously reported that animals treated with AchE inhibitors presented a higher tolerance to cholinergic agonists (*5,6*). Under normal physiologic conditions, the cholinergic receptors are usually operative through Ach action, and atropine is known to occupy the cholinergic receptors and interfere with the action of Ach (*5,6*). Therefore, atropine may inhibit the stimulatory effect of pesticides on the Ach receptor.

Previous work (*30*) has shown that a single injection of isoproterenol increases incorporation of thymidine into DNA of salivary gland of rats and mice. This substance is a β-parasympathomimetic amine

changes in the cell membrane implicated in the control of cell proliferation. Hypertrophy and hyperplasia of parotid salivary gland has been indicated by DNA synthesis. Other reports (*31*) have indicated that reserpine, a drug that alters the autonomic nervous system by depleting the noradrenergic endings, also induces remarkable changes in the salivary gland. We have previously shown that eserine, which acts on the autonomic nervous system, can induce changes in DNA synthesis of rat submandibular gland after a 5-day *in vivo* treatment (*32*), which confirmed the proliferative effect of this substance.

Parathion is highly toxic to mammals, and the LD_{50} values in rats have been reported to be 3.6 mg/kg, and the acute oral LD_{50} values were 13 mg/kg (*33,34*). The dosage of parathion in these studies was low (250 µg/100 g bw); therefore, prolonged exposure to low doses of pesticides may eventually cause serious health effects in the population. Among other factors that may be involved with pesticide-induced mammary carcinogenesis is the metabolism of the organophosphorous insecticides, because they can undergo a variety of metabolic transformations *in vivo* and *in vitro* (*35*). Thus, although the original insecticides are poor inhibitors of AchE, the oxygen analogs are several orders of magnitude more potent in their inhibition of the target enzyme, AchE. Benke and Murphy (*36*) have reported pathways of metabolism that may contribute to age differences in toxicity of pesticides. A gradual decrease in the susceptibility to toxicity by parathion with increasing age was observed in rats. Because of changes in the rates of reactions in the detoxification pathways for methyl paraoxon and paraoxon rather than in the metabolism of the original insecticides, the animals became less sensitive to the acute effects of these two substances with increasing age. Brodeur and Dubois (*37*) found that weaning rats 23 days old were more susceptible than adult animals to organophosphorous pesticides, implying that age is another factor in pesticide exposure.

We can conclude that the mechanism of action of parathion and malathion occurs probably through the inhibition of AchE, the enzyme responsible for the hydrolysis of Ach at cholinergic synapses (*5,6*) as it occurs with eserine treatment. Thus, alterations at the nervous system level seem to increase the cholinergic stimulation and probably alter the molecular pathways that initiate the proliferation leading to mammary carcinogenesis. Because parathion and malathion have been used extensively in Latin American countries as well as in many other countries, these stud-

References and Notes

1. Perera FP. Environment and cancer: who are susceptible? Science 278:1068–1073 (1997).
2. Estrogens in the Environment, III: Global Health Implications. Environ Health Perspect 103(suppl 7) (1995).
3. Falck F, Ricci AJ, Wolf MS, Godbold J, Deckers P. Pesticides and polychlorinated biphenyl residues in human breast lipids and their relation to breast cancer. Arch Environ Health 47:143–146 (1992).
4. Wolf MS, Toniolo PG, Lee EW, Rivera M, Dubin N. Blood levels of organochlorine residues and risk of breast cancer. J Natl Cancer Inst 85:648–652 (1993).
5. Taylor P. Anticholinesterase agents. In: The Pharmacological Basis of Therapeutics (Goodman Gilman A, Rall TW, Nies AS, Taylor P, eds). New York:Pergamon Press Inc., 1990;131–147.
6. Klaasen C. Nonmetallic environmental toxicants: air pollutants, solvents and vapors, and pesticides. In: The Pharmacological Basis of Therapeutics (Goodman Gilman A, Rall TW, Nies AS, Taylor P, eds). New York:Pergamon Press Inc., 1990;1615–1635.
7. Silman I, Futerman A. Modes of attachment of acetylcholinesterase to the surface membrane. Eur J Biochem 170:11–20 (1987).
8. Yamamura HI, Snyder SH. Muscarinic cholinergic receptor binding in the longitudinal muscle of the guinea pig ileum with ^{3}H quinuclidinyl benzilate. Mol Pharmacol 10:861–867 (1974).
9. Russo J, Russo IH. Mammary tumorigenesis. In: Modification of Tumor Development in Rodents (Ito N, Sugano H, eds). Prog Exp Tumor Res 33:175–191 (1991).
10. Russo J, Russo IH. DNA-labeling index and structure of the rat mammary gland as determinants of its susceptibility to carcinogenesis. J Natl Cancer Inst 61:1451–1460 (1978).
11. Russo J, Russo IH. Influence of differentiation and cell kinetics on the susceptibility of the rat mammary gland to carcinogenesis. Cancer Res 40:2677–2687 (1980).
12. Russo J, Tay LK, Russo IH. Differentiation of the mammary gland and susceptibility to carcinogenesis. Breast Cancer Res Treat 2:5–73 (1982).
13. Russo J, Russo IH. The etiopathogenesis of breast cancer prevention. Cancer Lett 90:81–89 (1990).
14. Wellings SR, Jensen HM, Marcum RG. An atlas of subgross pathology of the human breast with special reference to possible precancerous lesions. J Natl Cancer Inst 55:231–273 (1975).
15. Huggins C, Grand LC, Brillantes FP. Critical significance of breast structure in the induction of mammary cancer in the rat. Proc Natl Acad Sci USA 45:1294–1300 (1959).
16. Huggins C, Yang NC. Induction and extinction of mammary cancer. Science 137:257–262 (1962).
17. Welsch CW. Host factors affecting the growth of carcinogen-induced rat mammary carcinomas: a review and tribute to Charles Brenton Huggins. Cancer Res 45:3415–3443 (1985).
18. Gullino PM, Pettigrew HM, Grantham FH. N-nitrosomethylurea as mammary gland carcinogen in rats. J Natl Cancer Inst 54:401–404 (1975).
19. Zham SH, Ward MH, Blair A. Pesticides and cancer. In: Occupational Medicine: State of the Art Reviews, Vol 12, No. 2 (Keifer MC, ed). Philadelphia, PA:Hanley and Belfus Inc., 1997;269–289.
20. Blair A, Dosemeci M, Heineman EF. Cancer and other causes of death among male and female farmers from twenty-three states. Am J Ind Med 23:729–742 (1993).
21. McDuffie HH. Women at work: agriculture and pesticides. J Occup Med 36:1240–1246 (1994).
22. Institute of Animal Laboratory Resources. Guide for the Care and Use of Laboratory Animals. Washington, DC:National Academy Press, 1996.
23. Perelmont A, Abeijon C, Hirschbers C, Inestrosa N, Brandan E. Differential association and distribution of acetyl and butyrylcholinesterases within rat liver subcellular organelle. J Biol Chem 265:214–220 (1990).
24. Russo J, Calaf G, Roi L, Russo I. Influence of age and gland topography on cell kinetics of normal human breast tissue. J Natl Cancer Inst 78:413–418 (1987).
25. Russo J, Calaf G, Russo I. A critical approach to the malignant transformation of human breast epithelial cells. Crit Rev Oncog 4:403–417 (1993).

27. Miyamoto S, Guzman RC, Osborn RC, Nandi S. Neoplastic transformation of mouse mammary epithelial cells by *in vitro* exposure to N-methyl-N-nitrosourea. Proc Natl Acad Sci USA 85:477–481 (1988).
28. McCormick DL, Adamowski CB, Fiks A, Moon FC. Lifetime dose-response relationships for mammary tumor induction by a single administration of N-methyl-N-nitrosourea. Cancer Res 41:1690–1694 (1981).
29. Young S, Hallowes RC. Tumours of the mammary gland. IARC Sci Publ 11(5):31–73 (1973).
30. Novi AM, Baserga R. Association of hypertrophy and DNA synthesis in mouse salivary glands after administration of isoproterenol. Am J Pathol 62:295–308 (1971).
31. Martinez JR, Adelstein E, Quissel D, Barbero GJ. The chronically reserpinized rat as a possible model for cystic fibrosis. I. Submaxillary gland morphology and ultrastructure. Pediatr Res 9:463–469 (1975).
32. Calaf G, Garrido F, Cabello G. Effect of eserine treatment on DNA synthesis of rat submandibular gland. IRCS Med Sci 14:343–344 (1986).
33. Gaines T. Acute toxicity of pesticides. Toxicol Appl Pharmacol 14:515–534 (1969).
34. DuBois KP, Kinoshita FK. Influence of induction of hepatic microsomal enzymes by phenobarbital on toxicity of organic phosphate insecticides. Proc Soc Exp Biol Med 129:699–702 (1968).
35. Dauterman WC. Biological and non-biological modifications of organophosphorus compounds. Bull WHO 44:135–150 (1971).
36. Benke GM, Murphy SD. The influence of age on the toxicity and metabolism of methyl parathion in male and female rats. Toxicol Appl Pharmacol 31:254–269 (1975).
37. Brodeur J, Dubois KP. Comparison of acute toxicity of anticholinesterase insecticides to weaning and adult male rats. Proc Soc Exp Biol Med 114:509–511 (1963).

ARICA

LINEAS DE INVESTIGACION

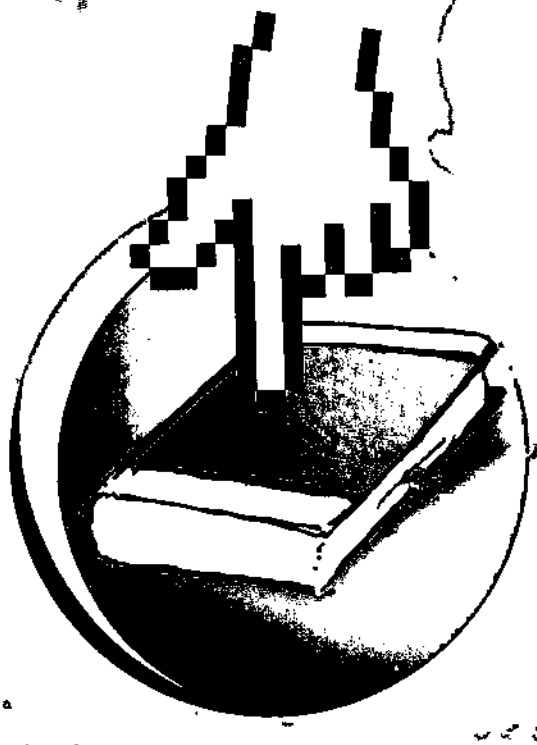
AREA	DISCIPLINA	INVESTIGADOR	CORREO
Facultad de Cs. Sociales Administración y economía.			
Depto. Filosofía y Psicología	Filosofía	J. Alfonso V.	jalfonso@uta.cl
	Psicología,	N. Alvarez R.	nalvarez@uta.cl
	salud física	G. Cayo R.	gcayo@uta.cl
	Sicología de la educación y	S. Chaigneau	schaigne@uta.cl
	cognitiva	J. Gómez M.	jgomez@uta.cl
Depto. Arqueología y Museología	Arqueología	J. Hidalgo L.	jhidalgo@uta.cl
	Antropología y cultura social	C. Santoro V.	csantoro@uta.cl
	Arqueología	H. Gonzalez	hgonzale@uta.cl
	Etnología	V. Standen G.	vstanden@uta.cl
	Estructuras y relaciones sociales	B. Arriaza T.	
		F. Rothhammer	
		L. Briones	lbriones@uta.cl
Depto. Finanzas y Economía	Administración de empresas	E. Rodriguez P.	
	Administración de negocios		
	Administración públlca		
Facultad de Ciencias			
Depto. de Biología y Salud	Biología Celular	G. Cabello F.	gcabello@uta.cl
	Toxicología	O. Espinoza N.	oespino@uta.cl
	Ecología y Ciencias Ambientales	A. Vilaxa	avilaxa@uta.cl
		M. Valenzuela	mvelenzu@uta.cl
Depto. Física	Física de sólidos	E. Lazo N.	elazo@uta.cl
	Mecánica Cuántica	M. Pedreros A.	mpedrero@uta.cl
	Astronomía	M. Rivas A.	mrivas@uta.cl
	Meteorología, climatología	JC. Flores A.	cflorres@uta.cl
	Sistemas no lineales	E. Martín G.	emarti@uta.cl
	Sistemas dinámicos	H. Calisto P.	hcalisto@uta.cl
	Atmósfera		
Depto. Matemática	Análisis	H. Bravo A.	hbravo@uta.cl
	Otras especialidades de las	L. Hernández V.	lhernand@uta.cl
	matemáticas	H. Román F.	hroman@uta.cl
		A. Flores F.	aflores@uta.cl
		S. Lorca P.	slorca@uta.cl
Depto. Química	Química analítica	L. Fgueroa T	lfiguero@uta.cl
	Físico - química	L. Cornejo P.	lcornejo@uta.cl
	Ciencias del suelo	N. Roberstson C.	nroberts@uta.cl
	Química ambiental		

Facultad Educación y Humanidades			
Depto. Educación	Pedagogóa y educación Sicología de la educación y cognitiva	L. Godoy V.	lgodoy@uta.cl
Depto. Educación Física	Ed. formación y perfecionamiento y reciclaje Educación física Evaluación	A. Aranda R.	aaranda@uta.cl
Depto. Antropología, Geo. e Historia	Geografía y geografía física Otras especialidades de ciencias de la tierra	P. Zavala O.	pzavala@uta.cl
Depto. Español	Literatura Lingüística	P. Ubeda U. V. Espinosa S. J. Lagos C.	pubeda@uta.cl vespinos@uta.cl jlagos@uta.cl
Facultad de Ingeniería			
Depto. Electrónica	Ingeniería en telecomunicaciones Ingeniería eléctrica Sistema de telecomunicaciones Equipos de telecomunicaciones Ing. biomédica y bioingeniería Física de plasma	H. Mendizábal J. H. Torres S. M. Zamorano L.	hmendiz@uta.cl htorres@uta.cl mzamorano@uta.
Depto. Industrias	Finanzas Otras especialidades de la economía	L. Pedraja R. M. Ramirez H.	lpedraja@uta.cl mramirez@uta.cl
Depto. Mecánica	Ingeniería de materiales Energía y energía Mecanizado Automatización y control electrónico	E. Galvez S. J. Godoy R. E. Ponce	egalvez@uta.cl jgodov@uta.cl eponce@uta.cl
Depto. Computación e Informática	Técnicas de manufacturas Pedagogía y educación Educación formación y perfeccionamiento y recciclaje Informática	Y. Ossandón N. H. Bustos A. A. Heredia H.	yossando@uta.cl hbustos@uta.cl aheredia@uta.cl
Facultad de Agronomía	Agricultura y horticultura Genética vegetal Fitopotología Fruticultura y viticultura Agronomía y otras especialidades Entomología	P. Gallo D. M. Jiménez R. H. Escobar A. L. Tapia I. H. Vargas C. F. de la Riva M. E. Sotomayor L.	pgallo@uta.cl mjimenez@uta.cl hescobar@uta.cl ltapia@uta.cl hvargas@uta.cl fdelariv@uta.cl csotomay@uta.cl
Diexu - Cento de Arte	Música Etología Escultura Cultura Social	M. mamani M. J. Díaz F E. Medel A.	mmamani@uta.cl jdiaz@uta.cl emedel@uta.cl

LINEAS DE INVESTIGACION

AREA	DISCIPLINA	INVESTIGADOR	CORREO
Facultad de Cs. Sociales Administración y economía.			
Depto. Filosofía y Psicología	Filosofía	J. Alfonso V.	jalfonso@uta.cl
	Psicología,	N. Alvarez R.	nalvarez@uta.cl
	salud física	G. Cayo R.	gcayo@uta.cl
	Sicología de la educación y	S. Chaigneau	schaigne@uta.cl
	cognitiva	J. Gómez M.	jgomez@uta.cl
Depto. Arqueología y Museología	Arqueología	J. Hidalgo L.	jhidalgo@uta.cl
	Antropología y cultura social	C. Santoro V.	csantoro@uta.cl
	Arqueología	H. Gonzalez	hgonzale@uta.cl
	Etnología	V. Standen G.	vstanden@uta.cl
	Estructuras y relaciones sociales	B. Arriaza T.	
		F. Rothhammer	
		L. Briones	lbriones@uta.cl
Depto. Finanzas y Economía	Administración de empresas	E. Rodriguez P.	
	Administración de negocios		
	Administrasión pública		
Facultad de Ciencias			
Depto. de Biología y Salud	Biología Celular	G. Cabello F.	gcabello@uta.cl
	Toxicología	O. Espinoza N.	oespino@uta.cl
	Ecología y Ciencias Ambientales	A. Vilaxa	avilaxa@uta.cl
		M. Valenzuela	mvelenzu@uta.cl
Depto. Física	Física de sólidos	E. Lazo N.	elazo@uta.cl
	Mecánica Cuántica	M. Pedreros A.	mpedrero@uta.cl
	Astronomía	M. Rivas A.	mrivas@uta.cl
	Meteorología, climatología	JC. Flores A.	cflorres@uta.cl
	Sistemas no lineales	E. Martín G.	emarti@uta.cl
	Sistemas dinámicos	H. Calisto P.	hcalisto@uta.cl
	Atmósfera		
Depto. Matemática	Análisis	H. Bravo A.	hbravo@uta.cl
	Otras especialidades de las	L. Hernández V.	lhernand@uta.cl
	matemáticas	H. Román F.	hroman@uta.cl
		A. Flores F.	aflores@uta.cl
		S. Lorca P.	slorca@uta.cl
Depto. Química	Química analítica	L. Fgueroa T	lfiguero@uta.cl
	Físico - química	L. Cornejo P.	lcornejo@uta.cl
	Ciencias del suelo	N. Roberstson C.	nroberts@uta.cl
	Química ambiental		

Facultad Educación y Humanidades			
Depto. Educación	Pedagogóa y educación Sicología de la educación y cognitiva	L. Godoy V.	lgodoy@uta.cl
Depto. Educación Física	Ed. formación y perfecionamiento y reciclaje Educación física Evaluación	A. Aranda R.	aaranda@uta.cl
Depto. Antropología, Geo. e Historia	Geografía y geografía física Otras especialidades de ciencias de la tierra	P. Zavala O.	pzavala@uta.cl
Depto. Español	Literatura Lingüística	P. Ubeda U. V. Espinosa S. J. Lagos C.	pubeda@uta.cl vespinos@uta.cl jlagos@uta.cl
Facultad de Ingeniería			
Depto. Electrónica	Ingeniería en telecomunicaciones Ingeniería eléctrica Sistema de telecomunicaciones Equipos de telecomunicaciones Ing. biomédica y bioingeniería Física de plasma	H. Mendizábal J. H. Torres S. M. Zamorano L.	hmendiz@uta.cl htorres@uta.cl mzamorano@uta.
Depto. Industrias	Finanzas Otras especialidades de la economía	L. Pedraja R. M. Ramirez H.	lpedraja@uta.cl mramirez@uta.cl
Depto. Mecánica	Ingeniería de materiales Energía y energía Mecanizado Automatización y control electrónico	E. Galvez S. J. Godoy R. E. Ponce	egalvez@uta.cl jgodov@uta.cl eponce@uta.cl
Depto. Computación e Informática	Técnicas de manufacturas Pedagogía y educación Educación formación y perfeccionamiento y recciclaje Informática	Y. Ossandón N. H. Bustos A. A. Heredia H.	yossando@uta.cl hbustos@uta.cl aheredia@uta.cl
Facultad de Agronomía	Agricultura y horticultura Genética vegetal Fitopotología Fruticultura y viticultura Agronomía y otras especialidades Entomología	P. Gallo D. M. Jiménez R. H. Escobar A. L. Tapia I. H. Vargas C. F. de la Riva M. E. Sotomayor L.	pgallo@uta.cl mjimenez@uta.cl hescobar@uta.cl ltapia@uta.cl hvargas@uta.cl fdelariv@uta.cl esotomay@uta.cl
Diexu - Cento de Arte	Música Etología Escultura Cultura Social	M. mamani M. J. Díaz F E. Medel A.	mmamani@uta.cl jdiaz@uta.cl emedel@uta.cl



Integração das Universidades do Centro Oeste Sul-Americano

Argentina ○ Bolívia ○ Brasil
Paraguai ○ Peru ○ Chile

Serafim Carvalho Melo

Os sem-terra de Arequipa

No início deste mês, aproveitando a folga de um domingo, fui visitar um projeto integrado de assentamento de microprodutores rurais, distante 100 km de Arequipa, Peru, a convite de um peruano e ex-colega da Escola de Minas de Ouro Preto, atualmente residindo em Arequipa. Como se sabe, esta é uma cidade histórica, patrimônio da humanidade, com 462 anos de idade, a segunda maior do Peru, com 1.000.000 de habitantes, situada no sul do país, a 2.600 m de altitude, a meio caminho entre o mar e as maiores altitudes dos Andes, no deserto mais seco do mundo, que é o deserto de Atacama.

A área de 25.000 ha da Etapa I do projeto, em pleno deserto, a uma altitude média de 1.400 m e temperatura média anual de 19° centígrados, é cortada pelo asfalto que demanda a Lima, distante 1.000 km. Trata-se de um Projeto Integrado de Desenvolvimento Regional do governo peruano com apoio técnico e financeiro da União Européia, concebido no início dos anos 70, com o objetivo de assentar microprodutores rurais, reduzir os níveis de pobreza e dinamizar a economia da região sul do país.

Nos primeiros 11 anos de existência do Projeto denominado de Projeto Majes-Siguas, construíram mais de 100 km de túneis e canais para captarem água do degelo, a 3.000 m de altitude que abastece uma represa de 285 milhões de m3 de água, que gera 1,6 MW de energia elétrica e atende o sistema de irrigação por gravidade por gotejamento e aspersão, utilizando tecnologia de Israel.

Cada módulo de 100 ha de terra do projeto é vendido ao assentado para pagamento em produtos. Através de seis cooperativas de produtores de leite, produzem atualmente 350.000 litros/dia de leite, constituindo-se na maior bacia leiteira do Peru e no principal produto do projeto, com 50.000 cabeças de gado de alta linhagem, ordenhas mecânicas, câmaras frias e os centros de produção de queijo, manteiga e iogurte.

No setor agrícola, as cinco associações de produtores de alho, cebola, pimenta páprica, batata e kiwicha, assistidas por equipes de engenheiros agrônomos e outros técnicos, incorporaram 15.000 ha de terra do deserto à produção com alta tecnologia. A assistência técnica e financeira são permanentes, com máquinas agrícolas, realização de dias de campo, cursos e controle de qualidade. A produção atende à demanda interna regional e exporta o excedente para o exterior. Em 2.001, estas exportações do projeto ultrapassaram US$2.000.000,00. No momento, desenvolvem a Etapa II do projeto numa área contígua de 50.000 ha.

Sem dúvida, é um modelo a ser seguido, pelo menos no que diz respeito à perseverança. Por outro lado, estão provando também que tecnologia não é só para os grandes. Estes microprodutores são intelectuais no trato da terra. Bastou lhes dar condições para que sua força de trabalho e perseverança se transformassem em alimentos. Passados trinta anos de sua concepção, partem para uma segunda etapa com o dobro da área, com mais uma represa de um bilhão de m3 de água para gerar 756 MW de energia elétrica.

Os produtos agrícolas da Irrigação de Majes-Siguas e o próprio projeto através de palestras e vídeos serão apresentados no Pavilhão Internacional da 38ª Expoagro, que se realizará em Cuiabá no período de 11 a 21 de julho.

Serafim Carvalho Melo é assessor de Projetos Especiais da SICM e coordenador do Conselho de Integração Internacional da Firmt.

LEITE
Novo padrão de qualidade
PÁGINA 3

GERENCIAMENTO
Campo informatizado
PÁGINA 12

ESTADO DE MINAS
AGROPECUÁRIO

DESAFIO À natureza

DIVULGAÇÃO/AUTODEMA

Uma surpreendente produção de 350 mil litros de leite ao dia, 2 mil toneladas de alho e 10 mil de cebola, além de uva, batata e condimentos nasce em pleno deserto peruano, em 15 mil hectares de terra cultivada pela Autoridade Autônoma de Majes (Autodema), no Sul do Peru, a 1 mil quilômetros da capital Lima. Tudo isso graças a um complexo sistema hidráulico de 200 quilômetros de túneis e canais que capta a água da Cordilheira dos Andes e a transporta, através das monatnhas, para o maior projeto de reforma agrária do país. Foram 11 anos de construção, finalizada em 1982. Duas décadas depois, os camponeses continuam desafiando a natureza e, depois de conquistar consumidores nos Estados Unidos, Espanha, Colômbia e Venezuela, preparam-se para aterrissar no maior mercado da América do Sul: o Brasil.

PÁGINAS 6, 7 E 8

ESPECIAL

UM COMPLEXO SISTEMA HIDRÁULICO, QUE CAPTA ÁGUA DA CORDILHEIRA DOS ANDES, PERMITE QUE 2,5 MIL PEQUENOS AGRICULTORES PERUANOS TIREM DA TERRA ÁRIDA UMA PRODUÇÃO AGROPECUÁRIA SURPREENDENTE, NO MAIOR E MAIS PRODUTIVO PROJETO DE REFORMA AGRÁRIA DO PAÍS

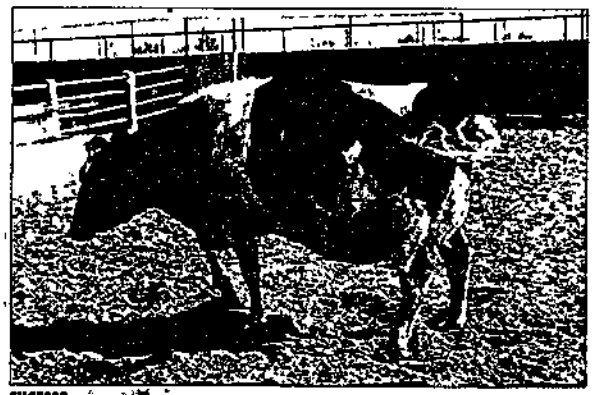
DESERTO PRODUTIVO

TACYANA ARCE
De Majes - Peru

Mais de 350 mil litros de leite ao dia, 2 mil toneladas de alho e 10 mil toneladas de cebola ao ano, além de uva, batata, páprica e outros condimentos. Essa é a produção obtida em 15 mil hectares de terra cultivada pela Autoridade Autônoma de Majes (Autodema), no Sul do Peru, a 1 mil quilômetros da capital Lima. A produção não seria surpreendente não fosse por um detalhe: tudo nasce no meio do deserto, em um planalto a 1,4 mil metros acima do nível do mar, onde o clima árido registra uma temperatura média de 19° C e a umidade relativa do ar está sempre abaixo dos 30%. Em Majes não chove nunca.

O que torna possível a vida no meio do deserto é um complexo sistema hidráulico de 200 quilômetros de túneis e canais que capta a água na Cordilheira dos Andes e a transporta para a região através das montanhas. Foram 11 anos de construção, finalizada em 1982, quando as primeiras famílias foram assentadas na região, no maior projeto de reforma agrária do país. Duas décadas depois, os camponeses continuam desafiando a natureza e, depois de conquistar consumidores nos Estados Unidos, Espanha, Colômbia e Venezuela, preparam-se para aterrissar no maior mercado da América do Sul: o Brasil.

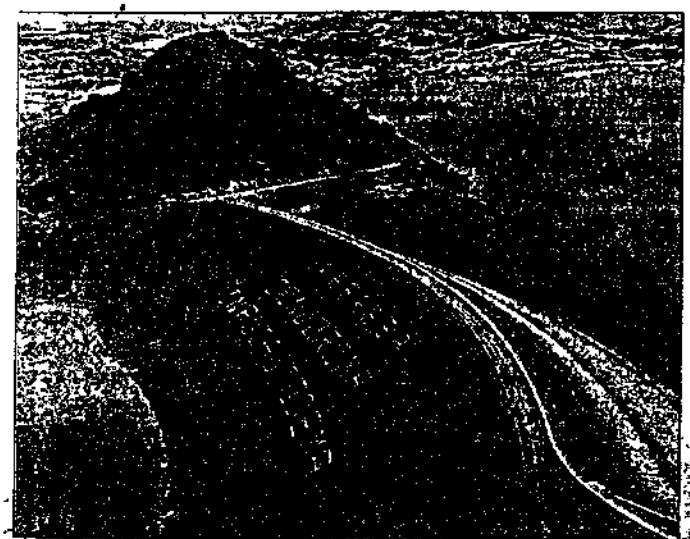
A esperança de vender a produção para os "hermanos brasileños" está depositada na recém-inaugurada rodovia Transoceânica, que liga a costa peruana a Corumbá, no Mato Grosso do Sul, passando pela Bolívia. Por ela, seria possível entregar os produtos peruanos em Cuiabá (MT), por exemplo, em três dias de viagem. Segundo o engenheiro Angel Rafael Chilque, técnico da Diretoria de Desenvolvimento de Negócios Internacionais e Qualidade Total de Autodema, a intenção é promover um intercâmbio entre os produtos dos dois países. "O Brasil está fortemente motivado em concluir a transoceânica. Os estados do Oeste brasileiro desejam exportar seus produtos, como soja e carne, via Pacífico, para a costa americana e a Ásia. A idéia é aproveitar as carretas que chegarem ao Peru trazendo produtos brasileiros para voltar ao Brasil com nossos produtos, em vez de voltarem vazias", explica.



SUCESSO
Majes é a primeira região leiteira do país, com 37% da produção nacional

"A IDÉIA É APROVEITAR AS CARRETAS QUE CHEGAREM AO PERU TRAZENDO PRODUTOS BRASILEIROS PARA VOLTAR AO BRASIL COM NOSSOS PRODUTOS, EM VEZ DE VOLTAREM VAZIAS"

■ Angel Rafael Chilque, técnico da Diretoria de Desenvolvimento de Negócios Internacionais e Qualidade Total de Autodema



FOTOS DIVULGAÇÃO/AUTODEMA

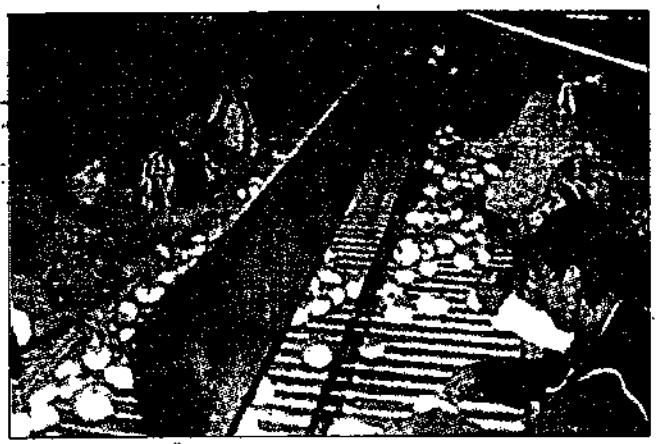
MILAGRE
Agricultores de Condoroma comemoram colheita no projeto de assentamento da Autodema

METADE DO PREÇO

Os primeiros contatos para exportação já foram feitos com comerciantes mato-grossenses, principalmente para a comercialização de alho e cebola. Produzidos em larga escala no sul peruano, os produtos podem chegar ao Brasil pela metade do preço pago aos produtos chineses e argentinos, que dominam o mercado brasileiro. Para atender à demanda, o governo peruano prepara-se para colocar em funcionamento a segunda etapa do projeto, que prevê a irrigação de outros 35 mil hectares de deserto, que também serão ocupados via reassentamento de famílias inscritas nos programas de colonização.

PARA SABER MAIS

- Autoridade Autônoma de Majes (Autodema) - (005154) 232103 - pamajes-camp@vmade.gob.pe ou anar-ca@hotmail.com
- Central de Centros de Produção de Leite da Irrigação de Majes - (005154) 586210
- Associação dos Produtores de Batata - (005154) 652691
- Associação dos Produtores de Cultivos de Exportação (Cebola amarela e roxa) - (005154) 692989
- Associação dos Produtores de Páprica - (005154) 601940
- Associação dos Produtores de Alho - (005154) 972010
- Associação de Produtores de Kiwicha - (005154) 610753



TIPO EXPORTAÇÃO
Por ano, nascem em pleno deserto 2 mil toneladas de alho

Emprego para 14 mil pessoas

Os 15 mil hectares de oásis no meio do deserto também são significativos para a economia peruana. O produto interno bruto da região é de US 37,7 milhões. Como 82% da área irrigada é utilizada para pastagem das 25 mil cabeças de gado, Majes se tornou a primeira região leiteira do país, respondendo por 37% da produção nacional. Em 2000, a irrigação gerou 14 mil empregos diretos, numa região que tem 40 mil habitantes.

Toda a produção é gerada por 2,5 mil pequenos produtores que têm cinco hectares de terra, onde criam, em média, 15 vacas leiteiras, além de pequenas plantações de cebola, alho e outros cultivos. Ultimamente, a produção que mais cresce é a de kiwicha, um cereal de alto valor protéico, utilizado em compostos alimentares, que se tornou moda nos Estados Unidos desde que a Nasa o inseriu na dieta obrigatória dos seus astronautas. A kiwicha,, conhecida desde a época do império incaico, nasce apenas no Peru.

Chegar a esse ponto, entretanto, não foi fácil. O engenheiro Victor Gusmán, chefe do serviço de assistência técnica aos colonos, lembra-se que há 30 anos, quando a Autoridade Autônoma de Majes (Autodema), um órgão do governo, foi instituída para viabilizar a irrigação do deserto e gerir o assentamento das famílias beneficiadas pela reforma agrária, houve muita resistência.

"Não apenas porque nunca tínhamos plantado no deserto e não conhecíamos a tecnologia, mas principalmente porque foi uma reforma social muito significativa. Os colonos que vieram para cá eram escravos de grandes senhores de terra, que viviam da exploração de mão-de-obra praticamente gratuita. Quebrar essa estrutura desgostou muita gente. Os agricultores eram os menos assustados com a situação. Para escapar da vida que levavam, aceitavam até semear no deserto", explica.

> "OS AGRICULTORES ERAM OS MENOS ASSUSTADOS COM O PROJETO. PARA ESCAPAR DA VIDA QUE LEVAVAM, ACEITAVAM ATÉ SEMEAR NO DESERTO"
>
> ■ Victor Gusmán, chefe do serviço de assistência técnica aos colonos

Atualmente, os colonos já estão organizados em associações de produtores, o que facilita a comercialização dos produtos. A equipe da Autodema, formada por engenheiros agrônomos, zootecnistas, veterinários, biólogos e adminstradores presta assistência técnica aos agricultores. É também a Autodema quem mantém um centro de aprimoramento de gado, onde os produtores de leite podem adquirir exemplares melhor adaptados para a vida no deserto. O maior desafio é auxiliar os produtores a incrementar as exportações.

Projeto atrai universidades

Além dos camponeses, a irrigação de Majes acabou atraindo institutos de pesquisa e universidades. O primeiro deles foi a Universidade Católica de Santa Maria, de Arequipa, cidade que fica a 100 quilômetros da sede da Autodema. O terreno onde a universidade está assentada foi doado pelo governo peruano há dez anos, para o desenvolvimento de pesquisas na área de ciências agrárias. Mas a presença da universidade acabou surtindo um efeito ainda maior. "Os filhos dos camponeses passaram a acreditar que poderiam chegar ao ensino superior para aprender como melhorar a produção de suas terras", explica o diretor de gestão empresarial da universidade, Victor Salinas Valencia.

Até o ano passado, o Centro de Produção de Bens e Serviços da Universidade de Santa Maria recebia apenas os alunos do último ano dos cursos de agronomia, zootecnia e veterinária, que trocavam as salas de aula e os laboratórios, em Arequipa, pela batalha diária no internato rural em Majes. Mas desde o início do ano, os formandos começaram a conviver com calouros. A universidade decidiu abrir uma turma de cada curso em Majes, pare receber os filhos dos camponeses que não podem deixar a região para se dedicar aos estudos na capital.

Para isso foram construídas salas de aulas e o restante da estrutura necessária para os cursos. "Os alunos de Majes fazem o caminho inverso aos dos alunos de Arequipa. Todas as sextas-feiras eles tomam um ônibus da universidade e vão ter aulas na sede da universidade, onde estão os laboratórios mais complexos. A qualidade dos cursos é a mesma. Eles vão sair com a mesma formação que os demais", explicá o diretor. A conquista dos alunos é um dos maiores orgulhos da universidade. "O papel de um instituto superior não é apenas formar mão de obra qualificada, mas também contribuir para o desenvolvimento do país. E dar a oportunidade destes jovens chegar ao ensino superior, e ensina-los a lidar melhor com a terra é permitir o desenvolvimento do potencial da região", completa.

Não são apenas os filhos dos agricultores que transitam na universidade. O Centro de Produção de Bens e Serviços ainda oferece capacitação técnica para os camponeses e mantém um viveiro para melhoramento das espécies plantadas na região. As mudas são vendidas aos agricultores, que também são estimulados a semear outros cultivos que podem ser bem adaptados para a região. "Nossa função é produzir conhecimento. Tentamos descobrir que outras culturas poderiam ser adaptadas às condições inóspitas da região, aumentando a produção e a lucratividade. Nem sempre é fácil, porque os agricultores são resistentes à mudança temendo ter prejuízos. Mas a presença dos seus filhos na universidade pode melhorar essa relação", acredita o engenheiro agrônomo Carlos Olazábal, responsável pelo centro.

SEMENTE
Nos viveiros, as mudas que vão gerar a eficiente produção

ESPECIAL

FOI PRECISO TRANSFORMAR A AREIA DO DESERTO EM TERRA PRODUTIVA, PARA CONSEGUIR CHEGAR À PRODUÇÃO DE 33 VARIEDADES DA FRUTA

Uvas são o maior orgulho

TACYANA ARCE
De Majes - Peru

Com 30 anos de dedicação ao projeto de irrigação do deserto, um dos maiores orgulhos do engenheiro Victor Gusmán é o centro vitivinícola, onde florecem 33 variedades de uvas e onde são produzidos diferentes tipos de vinhos, além do pisco, a tradicional aguardente peruana, a base de uvas. A plantação das uvas se iniciou em 1993, com ajuda da Comunidade Européia, que investiu o equivalente a 11 milhões de euros (US$ 11 milhões), com uma contrapartida de 25% do governo peruano.

Mas para chegar à variedade de plantações foi necessário pesquisar muito. Transformar a areia do deserto em terra boa para o cultivo não é tarefa fácil. Aí está a explicação para que mais de 80% dos terrenos sejam ocupados por pastagens. "A alfafa fixa o nitrogênio no chão. É o que chamamos de 'formar solo'. Depois de alguns anos com plantação de alfafa, a terra já é apropriada para outros cultivos. Mas como os colonos têm a compra do leite garantida, mesmo que o retorno financeiro não seja tão alto quanto a comercialização de outros produtos, eles preferem manter 80% do território ocupado com gado. É a garantia de que eles não terão prejuízo. Com a possibilidade de exportação, estamos tentando estimulá-los a investir mais na agricultura, mas não é fácil convencê-los", explica o assessor.

Mesmo com as dificuldades, a região de Majes é a que mais cresce no país. Há projeções de que em 2010 a região tenha 220 mil habitantes, impulsionados pela oferta de emprego em um país mergulhado na miséria. Tudo depende, entretanto, da conclusão da segunda etapa do projeto, que depende do término da construção da represa de Angostura, no distrito de Tisco, na Cordilheira dos Andes. Os investimentos já foram assegurados pelo presidente, Alejandro Toledo, que busca parceiros na iniciativa privada interessados em assumir a gerência das centrais hidrelétricas de Angostura, Lluta e Llucllа, que também entrariam em funcionamento gerando 756 Mw de energia.

DIVULGAÇÃO/AUTODEMA

BOA SAFRA
Das uvas de Majes são produzidos vinhos, além do tradicional pisco

TACYANA ARCE

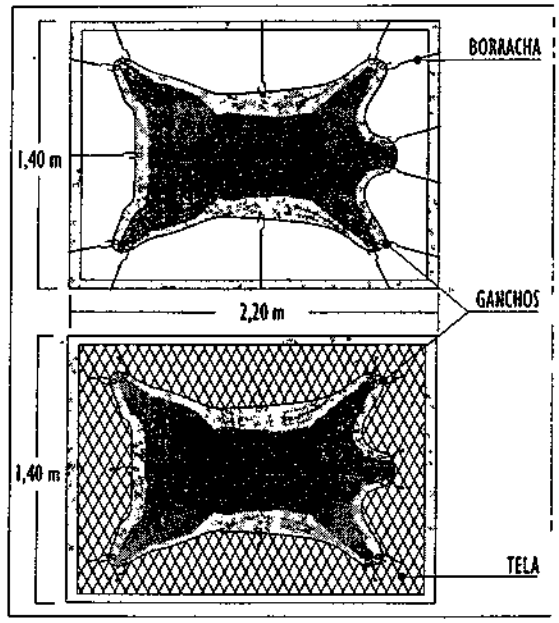
BATALHA
Victor Gusmán luta para ampliar a área destinada à agricultura

COMO FAZER

ESTAQUEADOR

TECNOLOGIA DE SECAGEM DE PELES DE OVINOS E CAPRINOS

Normalmente em pequenas propriedades que criam ovinos e caprinos, a secagem de peles não é processada de forma adequada. Assim, o produtor deixa de obter lucro maior na hora da venda. Além disso, os abates são espaçados e existe a necessidade de conservação das peles para formar um volume comercialmente apropriado.



O estaqueador é um quadro de madeira com peças de 3 cm de espessura e 20 cm de largura, medindo 2,20 metros de altura por 1,40 metro de largura, onde se prende a pele com ganchos de arame e tiras de borracha elástica, evitando-se, assim, os estragos causados pelas pontas de estacas usadas no método tradicional. Pode ser utilizado com fundo de tela de arame galvanizado de malha 5 para fixação dos ganchos ou serem os mesmos fixados no próprio quadro.

RECOMENDAÇÕES

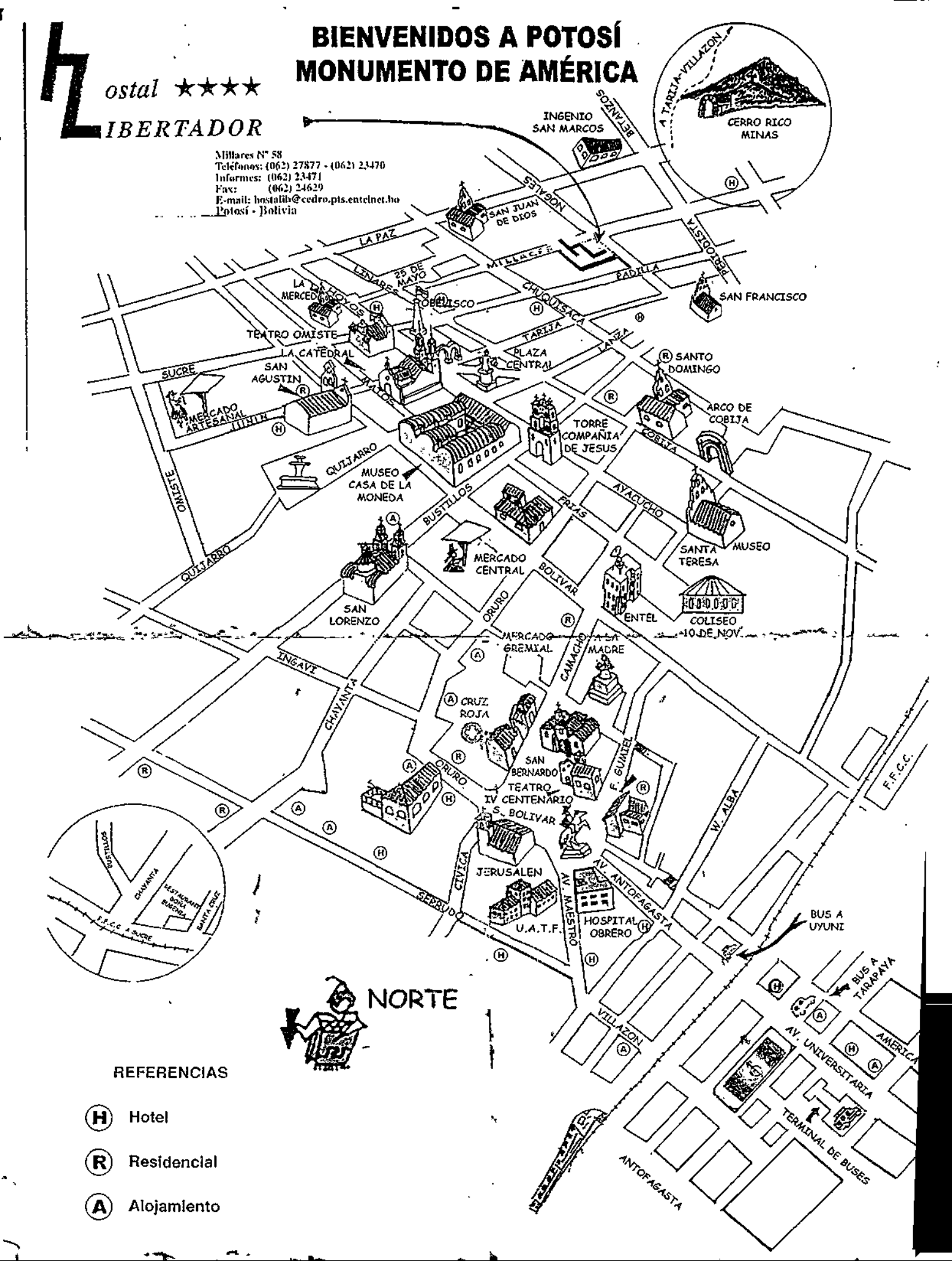
- Após o abate do animal, fazer a limpeza da pele, eliminando todo o sangue existente
- Retirar toda a gordura do carnal (lado interno da pele)
- Evitar danos à pele, durante a limpeza
- Proteger a pele contra predadores, principalmente ratos
- Não deixar a pele apanhar chuva
- Realizar a secagem à sombra e guardar logo que estiver seca
- Antes de guardar a pele seca, fazer tratamento da mesma contra pragas
- O tempo de secagem varia, conforme a região, de 5 a 10 dias

Fonte: Médico veterinário Amadeu Vasques de Quadros
Coordenador técnico da Emater-MG - Almenara ● emater.mg.gov.br

BIENVENIDOS A POTOSÍ
MONUMENTO DE AMÉRICA

Hostal ★★★★
LIBERTADOR

Millares N° 58
Teléfonos: (062) 27877 - (062) 23470
Informes: (062) 23471
Fax: (062) 24629
E-mail: hostalib@cedro.pts.entelnet.bo
Potosí - Bolivia



REFERENCIAS

- (H) Hotel
- (R) Residencial
- (A) Alojamiento

VIAGEM DA UFMT PELA INTEGRAÇÃO DAS UNIVERSIDADES NO CENTRO OESTE SUL-AMERICANO

Dia 18 de outubro - sexta-feira: SAIDA.

14 horas	Cuiabá – Cáceres	200 km CA
	Cáceres – Fronteira	90 km CA
	Fronteira – San Matias	10 km SA

20 horas – Jantar – San Matias

22 horas - San Matias – San Vicente		178 km SA
	San Vicente – San Ignácio	102 km SA
	San Ignacio – Concepcion	162 km SA

Dia 19 – Sábado: Café da Manhã em Concepción – Visita à Catedral. 8 horas -

Concepcion – San Javier	60 km SA
San Javier – San Ramon	40 km CA

San Ramon – Santa Cruz 192 km CA. Às 14 horas, almoço em Santa Cruz na Churrascaria Brasargent. Pernoite. **Hotel Continental Park**. Jantar de confraternização com professores locais. Cada um paga sua janta.

Dia 20 Domingo: às 8 horas, Santa Cruz – Cochabamba – La Paz = 468 km CA + 352 km CA.Pernoite em La Paz. Hotel Ichiban.

Dia 21 – Segunda-feira: às 9 horas, visita à Universidad Mayor San Andrés. Jantar de Confraternização com professores locais. Cada um paga sua janta.

Dia 22 – Terça-feira: outras visitas em La Paz. Visita à Embaixada do Brasil. Jantar de Confraternização com professores locais. Cada um paga sua janta.

Dia 23-Quarta-feira: às 8 horas, La Paz–Desaguadero/Fronteira Peru -115 km CA Desaguadero–Puno 150 km CA-Puno–Arequipa=412 km CA. – H. Posada Sonesta

Dia 24 – às 9 horas visita à Universidad Nacional San Agustín – UNSA. Jantar de confraternização com professores locais. Cada um paga a sua janta.

Dia 25 - Sexta-feira: manhã livre. Viagem às 12 horas para Arica 400 km CA. Pernoite. Hotel Azapla Inn

Dia 26 – Sábado: às 9 horas, visita Universidad de Tarapacá. Jantar de confraternização com professores locais. Cada um paga a sua janta.

Dia 27 – Domingo: às 8 horas, viagem para Potosi – 580 km CA. Hotel Libertador.

Dia 28 – Segunda-Feira: às 9 horas visita à Universidad Autônoma Tomas Frias. À tarde, vista à Mina. Jantar de confraternização com professores locais. Cada um paga a sua janta.

Dia 29 - Terça-feira: às 8 horas, Potosi - Santa Cruz, via Sucre ou Cochabamba. 750 km CA. Pernoite em Santa Cruz. Hotel Continental Park.

Dia 30 - Quarta-feira: às 9 horas, visita à Universidad Autônoma Gabriel René Moreno. Almoço de confraternização com professores locais. Cada um paga o seu almoço. Tarde livre. Saída para Cuiabá às 18 horas.

Dia 31 - Quinta-feira: às 18 horas, CHEGADA à Cuiabá. 522 km CA + 512 km SA

Obs.C A - com asfalto = 4.271 km; S A – Sem asfalto = 1.024 km. Total = 5295 km