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Pregnancy and Thyroid Gland

(II. Hyperthyroidism During Pregnancy)

Aydan Usman, M. D.*

Hyperthyroidism is less common in association with pregnancy (the incidence is about 0.04 %) than it is in the general population. This is possibly because hyperthyroidism is associated with menstrual irregalarities, anovulatory cycles and may decrease the likelihood of successful conception or gestation. Fertility is impaired and rates of spontaneous abortion, prematurity and perinatal deaths are higher in the untreated thyrotoxic than in the normal woman. On the other hand, pregnancy appears to ameliorate, to some extent, the severity of the hyperthyroidism so that clinical features may be mild. Many authors believe that hyperthyroidism is definitly ameliorated by pregnancy.[1,2]

Diagnosis and treatment of hyperthyroidism are difficult in pregnancy, because of the similarity between the normal hypermetabolism of pregnancy and symptoms of mild thyrotoxicosis. Diagnosis may be further comlicated by thyroid function tests that indicate altered thyroid function due to pregnancy.

Hyperthyroidism has several etiologies in pregnancy.[1] Diseases producing hyperthyroidism are:

1) Graves' disease
2) Multinodular toxic goitre
3) Single active nodule
4) Ectopic thyroid stimulating hormone (TSH) production (Hydatidiform mole)
5) Ectopic thyroxine (T_3) or triiodothyronine (T_3) production (Teratoma)

Graves' disease (or toxic diffue goitre) is the primary cause of thyrotoxicosis during pregnancy, because its incidence is highest in women of the third or fourth decade.[1-4] Plummer's disease (or toxic adenoma) as

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well as toxic multinodular goitre are relatively infrequent during the third and fourth decade and thus constitute relatively less common causes of thyrotoxicosis during pregnancy.

The most of the common signs and symptoms of hyperthyroidism also occur in a normal pregnancy. Pregnant women are often very nervous, emotionally labile, have warm extremities, manifest heat intolerance, have varying degrees of sinus tachycardia, paripheral vasodilatation with increased pulse pressure.

Total T_3, total T_4, PBI, BEI, radioactive iodine uptake (RAIU) and basal metabolic rate (BMR) will be found to be increased, although RAIU should not be performed in pregnancy.[5]

Elevated free T_3 and / or free T_4 levels are the most reliable tests to confirm the diagnosis of hyperthyroidism in pregnancy. The T_3 red cell or resin uptake test (T_3 RU) performed in vitro is also useful. In normal pregnancy, the T_3 uptake is in the hypothyroid range.[6] In the thyrotoxic pregnant women the values are usullay within the normal range.

In normal pregnancy, free thyroxine index (FTI: T_3 uptake/T_4 x 100) remains in the normal range, because of total T_4 is increased and the T_3 uptake is decreased. In hyperthyroidism the FTI will be elevated.

If the results of the tests are equivocal and clinical suspicion is strong, then an absence of TSH response to thyrotrophin-releasing-hormone (TRH) will confirm the diagnosis.

The development of a radioimmunoassay for T_3 has led to the discovery of increasing numbers of patients with "T_3 -thyrotoxicosis" in pregnant as well as nonpregnant states.[7] Accordingly, no patient with signs or symptoms of hyperthyroidims should be dismissed without serum T_3 measurement, if the serum T_4 is normal.

Therapy

Once the hyperthyroidism in pregnancy has been diagnosed clinically and confirmed by laboratory tests, treatment should be choiced between antithyroid drugs and surgery, since radioactiveiodine therapy is contraindicated during pregnancy.

The treatment of choice is genarally medical and consist of the smallest effective dose of antithyroid drug, propylthiouracil (PTU) or methimazole (MET), to keep the patient in slightly hyperthyroid state, in other words, to maintain the thyroid function tests at the higher levels

which are normally found in pregnancy. PTU is the drug of choice since it not only affects glandular synthesis of thyroid hormone but also blocks extrathyroidal deiodination of T_4 to T_3.[8] MET does not block conversion and has been led to scalp defects or aplaisa cutis in the off spring of mothers.[9] In addition, MET crosses the placenta more easily than PTU.[10]

These patients require frequent and meticulous follow up, since antithyroid drugs cross the placenta readily and block the fetal thyroid gland.[11-14]

The initial dosage, in severe forms of diesase, should be 100 to 150 mg of PTU and 10 to 15 mg of MET, every 8 hours; In milder forms, 50 mg of PTU and comparable doses of MET every 6 hours will suffice. When it is possible to monitor the response to treatment with sequential TSH estimations, any rise in serum TSH above normal indicates overtreatment and the need to reduce the dose of antithyroid drug. Once good control is achieved, the dose of drug must be reduced to maintenance dose.

The beta adrenergic blocking drug propranolol, can be given in pregnancy to control the peripheral manifestation of the disease. Even, it has been suggested as an alternavite to antithyroid drugs.[15] However, blockade of beta receptors also possess problems in pregnant women. In a double-blind study, the off spring of women who had received propranolol were more depressed at birth than the offspring of those who had received placebos.[16] In another study, the pharmacologic actions of propranolol on the fetus and neonate suggested with the observation of a small placenta, intrauterine-growth retardation, impaired responses to anoxic stress, depression at birth and postnatal bradycardia and hypoglycemia.[17] In addition, beta adrenergic blocking agents increase uterine irritability and may precipitate premature labor.[17]

These findings indicate that propranolol should not be primary agent for long-term treatment of hyperthyroidism during pregnancy.

The surgery (subtotal thyroidectomy) should only be considered in patients with antithyroid drug hypersensitivity, with large goitres causing obstruction, for cases of poor compliance and for those rare cases where reasonable doses of antithyroid drugs are ineffective to control thyrotoxic symptomatology or for those who are unable to follow the medical regimen correctly.[1, 2, 3, 18]

During the first two trimesters subtotal thyroidectomy performed after suitable preparation causes little risk to the fetus, but during the

last trimester an operation may precipitate the premature labour and for this reason antithyroid drug treatment is often preferred.[19] Whether or not operation is planned, the hyperthyroidism must be controlled initially with medical therapy and the patient should be clinically euthyroid at the time of surgery. Antithyroid therapy, in all cases, should be supplemented by small doses of iodides for 10 to 14 days.[5] Propranolol may be added to render the patient euthyroid. Prolonged treatment with iodides (more than two weeks) must be avoided because of the risk of goitre formation in the fetus.

The immediate postoperative complications for the pregnant hyperthyroid patient include premature labor and an increased incidence of abortion as well as a greater potential for thyroid storm.

Postoperatively it is advisable to put the patient on full doses of thyroxine replacement if the TSH level rises and to reassass the need for continuing therapy after delivery.[20]

Radioactive iodine is contraindicated in pregnancy as it is avidly taken up by the fetal thyroid gland after the 13 th to the 15 th weeks.[21, 22]

Antithyroid drugs are excreted in milk, so that babies born to mothers who are receiving them must not be breast fed.[19]

Hyperthyroidism in pregnancy has been reported to be associated with a slight increase in neonatal mortality and a significant increase in the frequency of low birth weight babies.[19] But it is uncertain if there is a real increase in the incidence of congenital abnormalities or if antithyroid drugs could be responsible for them. Some workers have expressed the possible adverse effect of antithyroid drugs on the development of the central nervous system of the fetus. However, it is apparent from the subsequent observations that the use of antithyroid drug in pregnancy had no injurious effect on physical and intellectual development of the children and there was no evidence of increased mental retardation in these children.[23, 24]

In the majority, if the mother has remained euthyroid or slightly hyperthyroid, the child will be normal at birth. Rarely the infant may have congenital thyrotoxicosis (neonatal Graves' disease).[25-28] This results from placental transmission of maternal LATS and /or other thyroid stimulating immunoglobulins. The course is usually self-limited and temporary. In mild cases, the condition remits spontaneously after 4 to 6 weeks when maternal immunoglobulins are eliminated from the infant's circulation. If therapy is required, it should consist of small doses of antithyroid drug, potassium iodide or propranolol.[29] In view of the

possibility of cardiac failure, many neonates may benefit from treatment with digoxin. Thyroid function tests carried out soon after birth may be misleading and the most reliable laboratory results can be obtained at the end of the first week of life.

Thyroid Storm

Thyroid storm is particularly apt to occur during labor or delivery. It is a life-threatening situation that requires immediate and skillfull management.

Specific control of thyroid hormone production involves the use of up to 1-2 gm. of intravenous iodine which prevents the release of thyroid hormones. Saturated solution of potassium iodide (SSKI) by mouth may also be used. PTU or MET should be started immediately in doses that range to 1 gm. of PTU or 100 mg. of MET per day. Cardiac symptoms may be treated with propranolol to control heart rate. A dose of 1-2 mg intravenously may be given with direct monitoring by ECG. It may be given orally and the dose adjusted to the patient's pulse, starting with 10-20 mg. every 4 hours and increasing the dose as needed. Reserpine or guanethidine are other alternatives to decrease the catecholamine effect seen in thyroid storm.

General supportive measures such as oxygen, glucose and adequate fluid and electrolytes, vitamin and glucocorticoid replacement are essential.[1]

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Invasive Carcinoma of the Vulva*

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Introduction

Total vulvar carcinoma accounted for 4 % of all female genital malignancies. Carcinoma in situ of the vulva is not uncommon. However, invasive cancer of the vulva is most frequently seen in our country. Treatment in situ lesion of vulva is conservative. Surgical procedure and its result is good. But radical vulvectomy with lymph node dissection was performed in invasive vulvar carcinoma. Prognosis is not good in advanced cases.

The methods of treatment used in invasive vulvar carcinoma and their results will be discussed in this study.

Material and Methods

Between 1964 and 1982 twenty cases of primary invasive carcinoma of the vulva were treated at The Department of Obstetrics and Gynecology in Hacettepe Medical School. This study was partially done retro and prospective. Histologic sections and medical records from all cases were reviewed.**** Age, symptoms, parity, lesion site, lymphatic invasion, treatment procedures used, survival rates, and complications were examined.

Results

Among the 270395 gynecologic cases, there were 20 cases with invasive vulvar carcinoma (7.37 in 100.000 cases). It has accounted for 3.7 % of all female genital malignancies. 5 % of all cases occourred in women under the age of 40 (Table I).

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**** Histologic examinations were done by the department of Pathology, Hacettepe University, Ankara, Turkey.

TABLE I
AGE DISTRIBUTION

Age Group	No. of Patients	%
40	1	5.0
41-50	4	20.0
51-60	6	30.0
61-70	6	30.0
71 +	3	15.0
Total	20	100.0

Only three cases were nullipare (Table II).

TABLE II
PARITY DISTRIBUTION

No. of Delivery	No. of Patients	%
Nullipare	3	15,0
Primipare	2	10.0
Multipare	15	75.0
Total	20	100.0

The most frequent presenting symptoms were pruritus, mass, ulceration and bloody discharge (Table III).

TABLE III
PRESENTING SYMPTOMS

Symptoms	No. of Patients	%
Pruritus vulva	10	50.0
Mass and ulceration	9	45.0
Bloody discharge	7	35.0
Pain (vulva, back, groin)	6	30.0
Dysuria and Dyspareunia	3	15.0
Mass in the Groin	2	10.0

30 % of all cases were in the menopause.

Many, such as diabetes, and hypertension, associated features were seen in patients with vulvar cancer (Table IV).

The primary disease in 65 % of the cases was seen on the labia (Table V).

TABLE IV

DISEASES ASSOCIATED WITH VULVAR CANCER

Diseases	No. of Patients	%
Diabetes	2	10.0
Hypertension	3	15.0
Obesity	3	15.0
Cervical Carcinoma	1	5.0
Total	9	45.0

TABLE V

THE SITE OF LOCALIZATION

Lesion	No. of Patients	%
Right labia majora	10	50.0
Clitoral area	3	15.0
Left labia majora	3	15.0
Posterior fourchette and perineal region	2	10.0
Multicentric (disseminated)	2	10.0
Total	20	100.0

Radical vulvectomy with lymph node dissection (inguinal, femoral, pelvic) had been performed in 11 (55 %) of the 20 cases while 9 (45 %) had had simple vulvectomy or wide local excision. Radiation therapy was used for five of the patients in the latter group (Table VI).

TABLE VI

THERAPEUTIC PROCEDURES USED

Procedure	No. of Patients	%
Radical vulvectomy plus inguinal and pelvic lymphadenectomy	11	55.0
Simple vulvectomy and biopsy	4	20.0
Biopsy + radiation	5	25.0
Total	20	100.0

The histological features of both the original biopsies and the operative specimens from all cases are given in Table VII.

Positive nodes were found in 54.5 % of the cases in which radical vulvectomy plus lymphadenectomy were performed.

TABLE VII

INCIDENCE OF VULVAR NEOPLASMS BY HISTOLOGICAL TYPE

Tumor type	No. of Patients	%
Epidermoid	18	90.0
Melanoma	1	5.0
Basal cell	1	5.0
Total	20	100.0

There was one operative death (5 %) from sepsis. The overall five year survival rate was 52.94 % (Table VIII).

TABLE VIII

THERAPY USED AND FIVE YEAR SURVIVAL

Therapy Used	Death / Total	%
Radical surgery	3 / 11	72.8
Radiation	3 / 4	25.0
There is no follow up	– / 3	–
Symptomatic	2 / 2	00.0
Total	8 / 20	

The five year survival rate was 66.6 % in cases with positive node (Table IX).

Postoperative complications are given in Table X.

TABLE IX

FIVE YEAR SURVIVAL RATES AND STATUS OF NODES

Status of nodes	Death / Total	% surviving
Positive	2 / 6	66.6 %
Negative	1 / 5	80.0 %
Total	3 / 11	72.8 %

TABLE X

THE POSTOPERATIVE COMPLICATIONS

Complications	No. of Patients	%
Wound infection and breakdown	10	90.00
Lymphocyst in groin	2	18.10
Lymphedema of the lower extremities	2	18.10
Failure of sexual satisfaction	2	18.10
Excessive scar	1	9.05
Local recurrence in the eleventh year after surgery	1	9.05

Discussion

Cancer of the vulva has accounted for 3 % to 5 % (average 4 %) of all female genital malignancies.[1,2,3] This state is 3.7 % in our series. During recent years it appears that this incidence has been increasing. This increase in incidence was due to the continued rise in average age of the female population, causing an increase in the number of eligible to develop the disease.

Vulvar cancer is seen most frequently in women in their mid-sixties, and in some series almost half will be 70 years of age or older. On the other hand, it is reported that about 15 % of all cases occur in women under the age of 40.[2,3,6,7]

In this study, patients range from 32 to 83 years of age and more than two thirds of these were in the age group between 51 to 83 years (Table I).

Primary disease can appear anywhere on the vulva, with approximately 70 % arising on the labia. It is more common on the labia majora (60 %), however it may also appear on the labia minora (20 %), clitoris (6.7-12.8 %), and perineum.[2,4,7] In our series, lesion in 65 % of all cases was on the labia (Table V).

The most common tumor of the vulva is squamous cell carcinoma (Table XI).

TABLE XI
INCIDENCE OF VULVAR NEOPLASMS BY HISTOLOGICAL TYPE

Tumor type	%[2,7]	Hacettepe %
Epidermoid	86.2	90.0
Melanoma	4.8	5.0
Sarcoma	2.2	–
Basal cell	1.4	5.0
Bartolin's gland		
Squamous	0.4	–
Adenocarcinoma	0.6	–
Adenocarcinoma	0.6	–
Undifferentiated	3.9	–

For many years pelvic lymphadenectomy was routinely performed along with radical vulvectomy and inguinal lymphadenectomy, irrespective of the size of the vulvar lesion or the presence or lack of the disease in the inguinal lymph nodes.[2,7]

In our study, radical vulvectomy plus inguinal and pelvic lymphadenectomy had been performed in 11 (55 %) of the 20 patients (Table VI).

In the early series of Way, the operative mortality approached 20 %, however in the last decade this has been reduced to 1 % or 2 %.[2, 3, 6] One operative death occurred in this study.

The complication encountered most frequently is wound breakdown, which occurs in well over 50 % of patients in most series.[2] In our serie, primary wound healing occurred only in one case. Careful debridement and vigorous care to keep wounds clean and dry will almost always result in adequate healing.

Lymphedema of lower extremities is another major problem.[2] This complication was seen in two of our cases. This complication can be reduced by routine use of custom-made elastic support hose during the first postoperative year while collateral pathways of lymph drainage are being developed.

The development of a lymphocyst in the groin area is an infrequent occurrence and it usually resolves spontaneously. In this series lymphocyst developed in two cases.

Removal of significant vulvar tissue, particularly the clitoris, can result in decreased sexual satisfaction. For this reason, two of our cases divorced.

Survival in cancer of the vulva is directly related to the extent of disease at the time that diagnosis and treatment are undertaken. In stage I and II diseases, the corrected five year survival rate should approach 90 %.

A 75 % corrected five year survival rate for all stages of vulvar cancer is not unusual, if however the lymph nodes are negative irrespective of stage, over 90 % of these patients will survive five years, whereas only one third will survive if the lymph nodes are positive (Table XII).

TABLE XII

SURVIVAL RATES FOR CARCINOMA OF THE VULVA

Series	Status of nodes	No. of Patients	% surviving	
			Positive	Negative
Way	Positive	45	42	–
(1960)	Negative	36	–	77
Franklin and	Positive	33	39	–
Rutledge (1971)	Negative	53	–	100
Morley	Positive	64	39	–
(1976)	Negative	130	–	92
Benedet and	Positive	34	53	–
associates (1979)	Negative	86	–	81
Hacettepe	Positive	6	66.6	–
	Negative	5	–	80

Recurrence may be local or distant, and over 80 % will occur in the first two years of the therapy, demanding close follow up. Over half of the recurrences are local and near the site of the primary lesions. Local recurrences can be successfully treated by local excision and by interstitial radiation. The patients with recurrent local diseases in the lymph node area or distant diseases are difficult to treat, and salvage rate is poor. In this study, local new tumor near the site of the primary lesion developed eleven years after the therapy. Local wide excision was performed in this area.

Summary

Twenty cases with invasive vulvar cancer were presented. Radical vulvectomy plus lymph node dissection has been performed in 55 % of all cases. The squamous cell carcinoma was found to be 90 %. Positive nodes were seen in 54,5 % of the cases. The five year survival rate was 72,8 %. Wound infection and breakdown occurred in ten cases.

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Treatment of Tinea Pedis

Fikret Kölemen, M.D.*

Dermatophytosis of the feet (tinea pedis), is the most common fungus infection and at times the most difficult to terat.[1] Survey of some population groups harve revealed an incidence approaching 30 percent of subjects having clinical evidence of disease and another five to six percent who are asymptomatic carriers of the causative fungi. The severity and extent of infection can vary from mild scaling to the toe webs to a severe inflammatory vesicular eruption.

Although rarely other organisms can be recovered from the skin of patients with tinea pedis, most infections are due to Trichophyton rubrum, Trichophyton mentagrophytes and Epidermophyton floccosum.[2] T. mentagrophytes and other dermatophytes have a saprophytic sexual phase in their life cycles and thus are widespread in dust and soil as well as on the surface of floors contaminated by persons with dermatophytosis. This fact, and the observed difficulty in infecting experimental subjects, suggest that factors other than mere exposure to the organism are important in the pathogenesis of tinea pedis. For example, the much higher incidence in population groups who wear more occlusive footwear and in those living in regions with warm humid climates illustrates the importance of environment in establishing and maintaning fungal infections of the skin of the feet. Warmth, and the hydration of the stratum corneum with sweat, provide excellent conditions for the growth of dermatophytes. Experimental infections result much more frequently when injured skin, inoculated with fungi, is occluded.[5]

In addition to exposure to the organism and environmental factors, differences in immunologic response also play a role in the pathogenesis of tinea pedis. Jones and his co-workers have shown that there is a hingh association of dermatophytosis of the feet with atopy and that patients with chronic infections often have reduced immune responeses to dermatophytes.

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Any approch to treatment of dermatophytosis is dependent upon accurate diagnosis of this condition. Dermatophytosis of the skin of the feet may be completely asmtomatic or manifested by only slight scaling of the webs between the third and fourth or fourth and fifth toes. More severe infection canbe divided in to two clinical types In one type there is more marked inflammatory reaction of the toe webs associated with vesicles of the instep of the foot. In general, this type of dermatophytosis is more easily treated than the other type, which is characterized by dusky redness and chronic scaling of the entire plantar surface of the foot.

Diagnosis

Since most treatments of tinea pedis involve the use of agents which act specifically on the causative fungi, it is important to establish a definite diagnosis, The most useful confirmatory test is the KOH or Amann's chloralactophenol.[3] Scale is removed from the involved skin with a scalpel blade, placed on a slide in 15 to 20 percent KOH or chlorallactophenol solution and then covered with cover slip. After slight heating the preparation is examined microscopically for the presence of fungal hyphae. If fungi are not found (and contact dermatitis is ruled out by the clinical pattern and negative patch tests to shoe components), a tentative diagnosis of dyshidrotic eczema can be made and treatment started with topical corticosteroids. Culturing of scale in fungal media is also useful to determine the presence of dermatophytosis.

Treatment

Once an accurate diagnosis of dermatophytosis is established, treatment can be started with antifungal medicetions. The most succesful early preparations for treatment of tiena pedis were those containing organic acids. Some of these preparations (e.g., whitfield's ointment and castellanis paint) were no doubt effective, but considerable irritation of the skin. Undecylenic acid preparations, were less irritating and were as effectiv. These because of their easy avalability as over the-counter preparations, are still probably the most widely used of all antifungal medications. Applied twice daily after cleansing and drying the involved skin, they will result clearing most mild and moderately severe infections. Tolanaftate, a never synthetic antifungal agent, is also available over-the counter, it is quite effective and even less irritating than undecylenic acid preparations.

Recently, there new synthetic antifungal agents have been introduced. These agents-haloprogin, miconazole and clotrimazole-appear to be somewhat more effective than the older medications and have the added advantage of possessing considirable activity against a number of bacteria and fungi other than dermatophytes.[6] Cure rates obtained with these agents approximate those obtained with oral griseofulvin. Side effects from the never topical antifungal agents are rare, although a few instances of contact senzitization have been reparted with tolnaftate and haloprogin and may possibly occur with the other two agents.

Alteration of the enviromental conditions conducive to the growth of dermatophytes has long been recognized to be useful in the managment of tinea pedis. Switching to less occlusive footwear (e.g., sandals) frequently suffices to bring mild infections under control. Socks of cotton or other loosely women fabrics result in less sweating and are also useful adjuncts to treatment. Foot powders consisting of talc are frequently used, but a recent study showed talc alone to be of little value in the management of fungal infections of the feet. Leyden and kligman have recently shown that efforts with aluminum chloride solutions are effective even if specific antifungal agents are not used. A 20 to 30 percent solution of aluminum chlorid is applied to the feet twice daily.[4]

Prevention

It may be possible sometime in the future to increase the immunologic response to the causative organisms and so treat tinea pedis in this manner. Until that time we must concentrate our efforts on eliminating the organisms and the environmental conditions whish enhance their growth. Such efforts would include measures, to reduce sweating and occlusion of the skin of the feet such as those discussed above, and prophylactic use of topical antifungal agents. The daily application of a powder containing tolnaftate, begining early in the warm season, will significantly reduce tinea pedis infections.

Most cases of dermatophytosis of the feet be eliminated effectively with the newer topical antifungal agents. However many patients who have chronic infections will improve while on therapy only to sustain recurence when the weather becomes warmer. We have found that many of these patients have to be retreated each spring and summer throughout much of their lives.

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Primary Echinococcal Infection of the Fallopian Tube*

(A Case Report)

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Introduction

Hydatid cysts in human have been well known since the time of Hippocrates.[3] Hydatid cyst is a parasitic disease caused by Taenia echinococcus granulosus.[2-5]

It is a common public health problem in many parts of the world. The mobility of world population has contributed to the wide spread of the disease.

Recent official statistical reports demonstrate an incidence of 17.5 per 100.000 patients who have undergone operation.[3]

The first and most important site is the liver. The organs usually affected by the disease are liver (60-70%), lung (30%), kidneys(22%), spleen (2%), bones (1%), brain (1%), and peritoneal cavity (4%).[2-4]

Hydatid cysts of female genital organs are very rare; they account for 0.2 % of all cases of hydatid disease. In the United States, the incidence of genital hydatid cyst is reported to be 2 in 658 patients who have undergone operation.[2, 3]

Echinococcus is an endemic problem in Turkey. A case with the primary echinococcal infection of the fallopian tube is presented and discussed.

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Case Report

The patient was 43 years old and had six children. She presented with complaints of vaginal bleeding and abdominal swelling in the last two months, on October 20, 1981.

On admission, physical examination demonstrated a left adnexial mass 10x3x3 cm. in size. The uterus could be felt separately, and was larger than normal.

Hemoglobin was 11.60 g/dl and white count was 4600/mL. The fasting plasma glucose was 68 mg/dL and blood urea nitrogen was normal. Results of the urine analyses were normal. Chest x-ray showed no abnormality.

Laparotomy was performed for the left adnexial mass. Exploration showed a mass measuring 15x4x4 cm in the left fallopian tube. There was no abnormality in peritoneal cavity, the liver, the spleen and the kidneys by palpation. Total abdominal hysterectomy and bilateral salpingo-oophorectomy was performed. Histological examination confirmed the presence of hydatid cysts in the left tube (Biopsy No.:B-7964-81)*

Discussion

Hydatid disease of the female genitalia is a rare problem in gynaecology. The incidence of genital involvement still remains very low.[2,6] Only 12 out of 532 patients with hydatid disease seen had pelvic infection.[1,2] Hydatid disease has been reported in the ovary, uterus, cervix, cul-de sac and broad ligament. This is the first case of fallopian hydatid cyst seen in our cilinic. Pelvic hydatid cyst is almost always secondary to a cyst elsewhere, resulting either from its rupture into the peritoneal cavity or its dissemination through the blood stream.

The symptoms of hydatid disease in genital organs are nonspecific. They are similar to those of ovarian cysts. Gynecologic examination reveals a soft tumor simulating ovarian cyst. The diagnosis depends on the patient's or her family's history of previous hydatid disease and specific serologic reactions, such as Casoni skin test or the complement fixation test for echinococcus. Eosinophilia is encountered in about 50 % of infected cases.[1,2,3] Occasionally, hydatid cysts of the genital organs calcify and produce characteristic x-ray patterns, which may be single or multiple.[3]

* Histologic examination was done by the Department of Pathology, Hacettepe University, Ankara, Turkey.

The treatment of hydatid cysts of female genital organs is surgical.[2,3] The best method in the perimenopausal period is total abdominal hysterectomy and bilateral salpingo-oophorectomy. However, conservative surgery is advised during the reproductive phase.[2-4]

Where removal is not possible, the contents of the cysts should be aspirated to reduce tension. 4 %-10 % formalin or absolute alcohol can be instilled for 4-5 minutes into the cavity to kill the scolices. If the contents are thick, the germinal membrane should first be removed and the cavity spooned or scraped out with saline to remove the formalin and the debris. Adrenocortical hormones have been used effectively during and after the operation to prevent anaphylactic shock.[1,2,3,5]

Summary

A patient with primary echinococcal infection of the fallopian tube is presented, and related literature is reviewed.

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Principal Health Problem and Morbidity in Students of Hacettepe University: (1976-1981)

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Introduction

The previous studies published by Demirtaş Kocaçitak in 1975, all statistical data during the period of 1969-1975 in our Student Health Center.[1]

This study was planned in order to evaluate principal health problems and morbidity in our students for the last 6 years (1976-1981).

In the center, an individual health cards has been filled out for each student who comes to center with any kind of health problem. All diagnosis have been coded, according to the International classification of Diseases (List A with 150 codes) All cases, diagnosed in a given code, have been collected on one disease index card annually. In order to evaluate results, all diagnosis have been classified in 18 groups (Table I).[2]

The distribution of diagnoses, during the period of 1976-1981, are presented in Table II. The total number of diagnoses is 38,831 in 6 years, including different diagnoses for the same person, except for repeated follow-up visits. The number of out-patient clinic visits has increased from 9353 in 1976 to 20,836 in 1981.

The annual total number of diagnoses from 3914 to 8122 indicating that the activities of the Student Health Center have been significantly increased in the last 6 years

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TABLE I

CLASSIFICATION OF DIAGNOSES IN DISEASE GROUPS

Disease Groups	Code Numbers
I. Upper Respiratory Infections	A 17,89,90,94,96
II. Gastrointestinal Diseases	A 5,98,99,100,101,103,104
III. Skin Diseases	A 29*,44,119,120
IV. Neuro-Psychiatric Diseases	A 69,70,74,79*
V. Musculoskeletal Diseases	A 23,80,121,122,123,125,130
VI. Eye Diseases	A 75,79*
VII. Urogenital Diseases	A 38,105,106,107,108,111
VIII. Intestinal Helminthiasis	A 43
IX. Traumas	AN (138-150)
X. Dental Diseases	A 97
XI. Ear Diseases	A 78,79*
XII. Cardio-Vascular Diseases	A 81,82,84,86,87,88
XIII. Endocrine Diseases	A 62,63,64,66
XIV. Respiratory Diseases	A 92,93,95
XV. Hematopoietic Diseases	A 59,67,68
XVI. Tuberculosis	A 6,8,10
XVII. Other Infections	A 2,3,4,15,18,25,29*,31
XVIII. Tumors	A 40,52,58,61,110

* Codes distributed into different groups.

Analysis of Morbidity Figures

The diagnoses have been analysed in the following 18 groups according to figures presented in Table II and case percentages were given in each group.

I. Upper Respiratory Infections include 45,58 % of total diagnoses established in 6 years. The annual percentages fluctuated between 42,99-49,13 % during this period. There were 1603 cases (9,05 %) of streptococcal angina (A 17), 13,383 (75,60 %) cases of various respiratory infection, such as acute pharingitis, tonsillitis, etc. (A 89); 1710 (9,65 %) cases of Influenza (A 90); and 156+850 = 1006 (5,68 %) cases with chronic upper respiratory infections (A 94 + A 96) (Table III).

II. Gastro-intestinal Diseases include 9,34 % of the total diagnoses with annual fluctuations between 8,82-9,89 %. There were 752 (20,72 %) cases with enteritis or gastroenteritis (A 5); 1481 + 529 = 2010 (55,38 %) cases with peptic ulcer or gastritis (A 98 + A 99); 24 + 52 = 76 cases (0,66+1,43 = 2,09 %) with appendicitis, hernia or cholecytopathy, (A 100 + A 101) and 791 (21,79 %) cases of various types of gastrointestinal disorders (A 104).

TABLE II

DISTRIBUTION OF DIAGNOSES IN HACETTEPE UNIVERSITY STUDENTS (1976-1981*)

Disease Groups	1976		1977		1978		1979		1980		1981		Total	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
I.	1803	46,06	2453	43,41	2396	42,99	3388	43,95	3864	49,13	3798	46,76	17702	45,58
II.	365	9,32	559	9,89	492	8,82	712	9,23	731	9,29	770	9,48	3629	9,34
III.	545	13,92	663	11,73	659	11,82	1154	14,97	1039	13,21	1205	14,83	5265	13,55
IV.	222	5,67	369	6,53	348	6,24	497	6,44	387	4,92	396	4,87	2219	5,71
V.	148	3,78	228	4,03	238	4,27	286	3,71	304	3,86	349	4,29	1553	3,99
VI.	65	1,66	217	3,84	271	4,86	226	2,93	304	3,86	342	4,21	1425	3.66
VII.	220	5,62	343	6,07	459	8,23	461	5,98	309	3,92	262	3,22	2054	5,28
VIII.	79	2,01	91	1,61	122	2,18	166	2,15	109	1,38	147	1,80	714	1,83
IX.	66	1,68	117	2,07	103	1,84	155	2,01	124	1,57	108	1,32	673	1,73
X.	31	0,79	44	0,77	86	1,54	153	1,98	149	1,89	150	1,84	613	1,57
XI.	114	2,91	169	2,99	61	1,09	155	2,01	117	1,48	146	1,79	762	1,96
XII.	51	1,30	81	1,43	72	1,29	112	1,45	110	1,39	118	1,45	544	1,40
XIII.	94	2,40	133	2,35	93	1,66	109	1,41	127	1,61	114	1,40	670	1,72
XIV.	58	1,48	88	1,55	89	1,59	79	1,02	78	0,99	120	1,47	512	1,31
XV.	11	0,28	22	0,38	34	0,61	14	0,18	112	0,15	26	0,32	119	0,30
XVI.	21	0,53	22	0,38	10	0,17	12	0,15	9	0,11	12	0,14	86	0,22
XVII.	19	0,48	34	0,60	23	0,41	15	0,19	85	1,08	53	0,65	229	0,58
XVIII.	2	0,05	17	0,30	17	0,30	14	0,18	6	0,07	6	0,07	62	0,15
Total Diagnoses	3914		5650		5573		7708		7864		8122		38831	
No. of Visits**	9353		12412		11646		16503		18975		20836		89275***	

* Various first diagnoses made at the same or different times in the same person, are grouped and percenteges are calculated in annual total diagnoses.

** All diagnoses are evaluated for university and college students in 1976-1981.

*** Total number of visits in 6 years (1976-1981).

TABLE III

		1976		1977		1978		1979		1980		1981		Total	
		No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
I.	A 17	115	6,37	202	8,23	125	5,21	2224	6,61	375	9,70	562	1,63	1603	9,05
	A 89	1503	83,36	1995	81,32	1854	77,37	2657	78,42	2794	72,30	2580	67,93	13383	75,60
	A 90	57	3,16	96	3,91	266	11,10	238	7,02	543	14,05	510	13,42	1710	9,65
	A 94	18	0,99	29	1,18	27	1,12	30	0,88	26	0,67	26	0,68	156	0,88
	A 96	110	6,10	131	5,34	124	5,17	239	7,05	126	3,26	120	3,15	850	4,80
		1803		2453		2396		3388		3864		3798		17702	
II.	A 5	60	16,43	132	23,61	122	24,79	128	17,97	154	21,06	156	20,25	752	20,72
	A 98	1481	40,81	209	37,38	244	49,59	280	39,32	293	40,08	310	40,25	1481	40,81
	A 99	87	23,83	67	11,98	92	18,69	120	16,85	76	10,39	87	11,29	529	14,57
	A 100	5	1,36	10	1,78	8	1,62	1	0,14	–	–	–	–	24	0,66
	A 101	12	3,28	11	1,96	13	2,64	7	0,98	5	0,68	4	0,51	52	1,43
	A 104	56	15,34	130	23,25	13	2,64	176	24,71	203	27,77	213	27,66	791	21,79
		365		559		492		712		731		770		3629	

TABLE III Continue

		1976		1977		1978		1979		1980		1981		Total	
		No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
III.	A 29	25	4,58	56	8,44	46	6,98	194	16,81	31	2,98	84	6,97	436	8,28
	A 44	110	20,18	163	24,58	140	21,24	256	22,18	218	20,98	209	17,34	1096	20,81
	A 119	50	9,17	84	12,66	108	16,38	124	10,74	113	10,87	112	9,29	591	11,22
	A 120	360	66,05	360	54,29	365	55,38	580	50,25	677	65,15	800	66,39	3142	59,67
		545		663		659		1154		1039		1205		5265	
IV.	A 70	189	85,13	259	70,18	319	91,66	470	94,56	360	93,02	354	89,39	1951	87,92
	A 74	9	4,05	12	3,25	11	3,16	12	2,41	14	3,61	18	4,54	76	3,42
	A 79	124	10,81	98	26,55	18	5,17	15	3,01	13	3,35	24	6,06	192	8,65
		222		369		348		497		387		396		2219	
V.	A 80	16	10,81	17	7,45	37	15,54	25	8,74	10	3,28	8	2,29	113	7,27
	A 121	10	6,75	7	3,07	7	2,94	15	5,24	28	9,21	34	9,74	101	6,50
	A 122	94	63,51	166	72,80	160	67,22	200	69,93	210	69,07	250	71,63	1080	69,54
	A 124	1	0,67	2	0,87	1	0,42	3	1,04	3	0,98	3	0,85	13	0,83
	A 125	27	18,24	36	15,78	33	13,86	43	15,03	53	17,43	54	15,47	246	15,84
		148		228		238		286		304		349		1553	

TABLE III Continue

		1976		1977		1978		1979		1980		1981		Total	
		No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
VI.	A 75	20	30,76	107	49,30	136	50,18	155	68,58	155	50,98	294	85,96	867	60,84
	A 79	45	69,23	110	50,69	135	49,81	71	3,09	149	49,01	48	14,03	558	39,15
		65		217		271		226		304		342		1425	
VII.	A 38	4	1,81	6	1,74	3	0,65	2	0,43	4	1,29	6	2,29	25	1,21
	A 106	–	–	–	–	–	–	–	–	1	0,33	–	–	1	0,04
	A 108	21	9,54	39	11,37	32	6,97	40	8,67	40	12,94	35	13,35	207	10,07
	A 111	195	88,63	298	86,88	424	92,37	419	90,88	264	85,43	221	84,35	1821	88,65
		220		343		459		461		309		262		2054	
IX.	AN 141	2	3,03	2	1,70	–	–	–	–	–	–	1	0,92	5	0,74
	AN 143	5	7,57	6	5,12	9	8,73	–	–	–	–	7	6,48	27	4,01
	AN 144	2	3,03	–	–	1	0,97	–	–	–	–	–	–	3	0,44
	AN 145	6	9,09	11	9,40	7	6,79	21	13,54	14	11,29	6	5,55	65	9,65
	AN 146	2	3,03	9	7,69	–	–	2	1,29	6	4,83	1	0,92	20	2,97
	AN 147	4	6,06	3	2,56	4	3,88	12	7,74	–	–	–	–	23	3,41
	AN 148	5	7,57	16	13,67	9	8,73	5	3,22	11	8,87	9	8,33	55	8,17
	AN 149	1	1,51	–	–	1	0,97	2	1,29	2	1,61	–	–	6	0,89
	AN 150	39	49,09	70	59,82	72	69,90	113	72,90	91	73,38	84	77,77	469	69,68
		66		117		103		155		124		108		673	

TABLE III Continue

		1976		1977		1978		1979		1980		1981		Total	
		No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
XI.	A 78	29	25,43	57	33,72	44	72,13	66	42,58	39	33,33	56	38,35	291	38,18
	A 79	85	74,56	112	66,27	17	27,86	89	57,41	78	66,66	90	61,64	471	61,81
		114		169		61		155		117		146		762	
XII.	A 81	14	2,74	6	7,40	6	8,33	5	4,46	11	10,00	7	5,93	49	9,00
	A 82	4	7,84	6	7,40	9	12,56	11	9,82	2	1,81	4	3,38	36	6,61
	A 84	3	5,88	5	6,17	5	6,94	5	4,46	–	–	3	2,54	21	3,86
	A 86	–	–	–	–	–	–	–	–	6	5,45	2	1,69	8	1,47
	A 87	–	–	3	3,70	1	1,38	–	–	1	0,90	–	–	5	0,91
	A 88	30	58,82	61	75,30	51	70,83	91	81,25	90	81,81	102	86,44	425	78,12
		51		81		72		112		110		118		544	
XIII.	A 62	69	73,40	112	8,42	72	77,41	95	87,15	118	92,91	101	88,59	567	84,62
	A 63	11	11,70	10	7,51	11	11,82	9	8,25	1	0,78	1	0,87	43	6,41
	A 64	8	8,56	7	5,26	9	9,67	2	1,83	8	6,29	12	10,52	46	6,86
	A 66	6	6,38	4	3,00	1	1,07	3	2,75	–	–	–	–	14	2,08
		94		133		93		109		127		114		670	

TABLE III Continue

		1976		1977		1978		1979		1980		1981		Total	
		No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
XIV.	A 92	14	24,13	10	11,36	14	15,73	9	11,39	18	23,07	14	11,66	79	15,42
	A 93	44	75,86	78	88,63	75	84,26	70	88,60	60	76,92	106	88,33	433	84,57
		58		88		89		79		78		120		512	
XV.	A 67	10	90,90	22		26	76,47	11	78,57	9	75,00	25	96,15	103	86,55
	A 68	1	9,09	–		8	23,52	3	21,42	3	25,00	1	3,84	16	13,44
		11		22		34		14		12		26		119	
XVII.	A 2	–	–	–	–	–	–	–	–	1	1,17	–	–	1	0,43
	A 3	2	10,52	5	14,70	2	8,69	2	3,39	5	15,88	4	7,54	20	8,73
	A 4	–	–	1	2,94	–	–	–	–	1	1,17	–	–	2	0,87
	A 528	2	10,52	7	20,58	14	60,86	7	46,66	8	9,41	6	11,32	44	19,21
	A 29	15	78,94	21	61,76	6	26,08	6	40,00	70	82,35	43	81,13	161	70,30
	A 31	–	–	–	–	1	4,34	–	–	–	–	–	–	1	0,43
		19		34		23		15		85		53		229	
XVIII.	A 61	2		15	88,23	15	88,23	14		6		6		58	93,54
	A 110	–		2	11,76	2	11,76	–		–		–		4	6,25
		2		17		17		14		6		6		62	

III. Skin Diseases include (13,55 %) of the total diagnoses with annual fluctuations between 11,73-14,97 %. There were 436 (8,28 %) cases with viral disease (A 29), such as herpes simplex, zona zoster, verrucas, etc; 1096 (20,81 %) cases with dermatomytomycosis or dermatophytosis (A 44); 591 (11,22 %) cases with skin infections (A 119); 3142 (59,67 %) cases with non-infections skin diseases (A 120).

IV. Neuro-psychiatric Diseases include 5,71 % of total diagnosis with annual fluctuations between 4,87-6,53 %. There were 1951 (87,92 %) cases with various types of psychoneuroses and psychoses (A 70); 76 (3,42 %) cases of epilepsy (A 74) and 192 (8,65 %) cases with various types of neurological disorders (A 79).

V. Musculoskeletal Diseases include 3,99 % of the total diagnoses with annual fluctuations between 3,71-4,29 %. There were 113 (7,27 %) cases with acute rheumatic fever (A 80); 101 (6,50 %) cases with arthritis (A 121); 1080 (69,54 %) cases with myalgia, lumbago and other so-called rheumatismal disorders (A 122); 13 (0,83 %) cases with deformities (A 124), and 246 (15,84 %) cases with various types of diseases related to bones, muscles and joints (A 125).

VI. Eye Disease include 3,66 % of the total diagnoses with annual fluctuations between 1,66-4,86 %. There were 867 (60,84 %) cases with eye infections (A 75) and 558 (39,15 %) cases with various refrection errors (A 79).

VII. Urogenital Diseases include 5,28 % of total diagnoses with annual fluctuations between 3,22-8,23 %. There were 25 (1,21 %) reported cases of acute gonorrhea (A 38); 207 (10,07 %) cases with urolithiasis and 1 (0,04 %) case with nephritis or pyelitis. (A 106 + A 108) and 1821 (88,65 %) cases with various types of urinary and genital diseases (A 111).

VIII. Intestinal Helminthiasis (A 43) have been found in 714 cases (1,83 %). The annual percentages fluctuated between 1,38-2,18 % in 6 years.

IX. Traumas include 673 cases (1,73 %) with annual fluctuations between 1,32-2,07 %. There were 5 (0,74 %) cases with luxation without fracture (AN 141); 27 (4,01 %) cases with intracranial trauma (AN 143); 3 (0,44 %) cases with intratorasic, intraabdominal, intrapelvic trauma (AN 144); 65 (9,65 %) cases with injuries (AN 145); 20 (2,97 %) cases with superficial trauma and echimose (AN 146); 23 (3,41 %) cases with foreing matters in the skin (AN 147); 55 (8,17 %) cases with Burns (AN 148); 6 (0,89 %) contraaffects of chemical materials and 469 (69,68 %) etc.

X. Dental Diseases (A97) have been found 613 cases (1,57 %). The annual percentages fluctuated between 0,77-1,98 % in 6 years.

XI. Ear Diseases makes-up 762 cases (1,96 %) of total diagnoses with annual fluctuations between 1,09-2,99 %. There were 291 (38,18 %) cases with otitis media or mastoiditis (A 78) and 471 (61,81 %) cases with other diseases (A 79).

XII. Cardio-Vascular Diseases include 544 (1,40 %) of the total diagnoses with annual fluctuations between 1,29-1,45 %. There were 49 (9 %) cases with chronic rheumatic heart disease (A 81); including mitral and aortic lesions; 36 (6,61 %) + 21 (3,86 %) + 8 (1,47 %) + 5 (0,91 %) = 70 (12,86 %) cases with hypertension, arrythmias or thrombophilebitis (A82), (A84), (A86), (A87) and 425 (78,12 %) cases with various diseases (A 88) such as hemorrhoids, varices, lymphangitis etc.

XIII. Endocrine Diseases include 670 (1,72 %) of total diagnoses with annual fluctuations between 1,40-2,40 %. There were 567 (84,62 %) + 43 (6,41 %) = 610 (91,04 %) cases with goiter and/or hyperthyroidism (A 62 + A63); 46 (6,86 %) cases with diabetes mellitus (A 64) and 14 (2,08 %) other cases (A 66).

XIV. Respiratory Diseases include 512 (1,31 %) of the total diagnoses with annual fluctuations between 0,99-1,59 %. There were 79 (15,42 %) cases with pnaumonitis (A 92); 433 (84,57 %) cases with bronchitis or bronchial asthma or empyema case (A 93).

XV. Hematopoietic Diseases include 119 (0,30 %) of the total diagnoses with annual fluctuations between 0,15-0,61 %. There were 103 (86,55 %) cases with anemias (A 67) and 16 (13,44 %) cases with lymphadenitis (A68).

XVI. Tuberculosis has been found in 86 cases (0,22 %). The annual percentages fluctuated between 0,11-0,53 %. (A 6).

XVII. Other infection sinclude 229 (0,58 %) of the total diagnoses with annual fluctuations between 0,19-1,08 %. There were 1 (0,43 %) + 20 (8,73 %) = 21 (9,17 %) cases with typhoid or paratyphoid fevers (A 2 + A 3); 2 (0,87 %) cases with shigellosis (A 4); 44 (19,21 %) cases with infections hepatitis (A 28); 161 (70,30 %) cases with various viral infections (A 29) such as mumps, chichen pox, etc. and 1 (0,43 %) malaria case (A 31).

XVIII. Tumor include 62 (0,15 %) of the total diagnoses with annual fluctuations between 0,05-0,30 %. There were 58 (93,54 %) cases with bening types of tumors (A 61) and 4 (6,25 %) cases with bening cysts. (A 110).

Discussion

This article shows that the Medico-social and Recreation of Student Hacettepe University activities have significantly increased in the last 6 years. (1976-1981). Diagnoses coded according to International classification Table A have been classified in XVIII groups. (Table I). Annual distribution of diagnoses in disease groups have been presented in table II. In this period of 1976-1981 the number of total diagnoses is 38,831. The most frequent diagnoses have been found to be upper respiratory infections 17702 (45,58 %); 5265 (13,55 %) skin disease 3629 (9,34 %) gastrointestinal diseases, neuro-psychiatric diseases 2219 (5,71%); urogenital diseases 2054 (5,28%) then other 13 groups remaining 7349 (18,92 %) similarly to a previous study done in the center by Kocaçitak.[2] The average distribution of diagnoses in 6 years have been shown in Table II and Table III. The annual percentages have been fluctuating in each disease group, but these fluctuations have not been very significant except second group. Now, we understand that morbidity have not been changed during this period.

There are a lot of health problems to be subject of further investigators. Evaluation of the surveys and laboratory examinations has been accepted very useful for the determination of these problems. The casting of the laboratory examinations has been seen in Table IV. The laboratory of Student Health Center of Hacettepe University have started to study on 1976. Micro-graphic apparatus had started to used on 1979. The distrubution of laboratory and micro-graphic x-ray examination during 1976-1981, are presented in Table IV. The total number of examinations is 49,126 in 6 years. The number of examinations has increased from 613 in 1976 to 11662 in 1981.

TABLE IV

	1976	1977	1978	1979	1980	1981	Total
Urine Analysis	200	1844	1982	2983	1577	1800	10386
Hemoglobin	166	2002	2251	3404	1573	2300	11696
Hematocrite	71	310	429	61	227	444	1542
Leucocytes	138	1928	2186	3558	1892	2165	11807
Sedimantation	38	424	293	497	269	444	1965
Blood in the feces	–	32	36	100	19	–	187
Formula	–	–	69	105	62	185	421
Parasite in the feces	–	–	69	381	187	524	1161
Micro-graphy	–	–	–	2315	3846	3800	9961
Total Examination:	613	6540	7315	13404	9592	11662	49126

According to these studies it seems that better determination of health problems in University students might be obtained by systematic surveys composed of complete clinical and laboratory screening.

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Obstetric Outcome Before and After Metroplasty in Women with Malformed Uterus*

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Congenital anomalies of the female genital tract can be associated with many problems in gynecology and obstetric.[1,4,6,7] However the incidence of congenital abnormalities of the vagina and uterus in the general population is difficult to determine since the vast majority of these anomalies are compatible with normal pregnancy.

Generally, the incidence of anomalies has been found to be between one in 15.000 deliveries and one in 500-700 deliveries.[1,3,4,6,7]

Anomalies of the uterus were divided into various groups based on faulty embryological development, functional uterine capability and anatomical forms.[1, 2, 3, 4, 6] Various gynecologists including H. W. Jones, Strassman, W. S. Jones. and Semmens have attempted to define functional or clinical classes of abnormal uterus.[6] A simple classification as follows was presented:

1. Agenesis
2. Problems of vertical fusion
   a) Obstructive
   b) Nonobstructive
3. Problems of lateral fusion
   a) Obstructive
   b) Nonobstructive

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Many previous reports have discussed anomalies with regard to their various proposed classification systems, their gynecologic symptoms, their relationship to infertility, their potentially serious impact on obstetric capabilities, and on indications for and techniques of surgical reconstruction.

Surgical reconstruction of uterine anomalies had been performed for the following indications (according to Strassman, based on 84 cases) :[8]

1. Menometrorrhagia 26 %,
2. Dysmenorrhea 39 %,
3. Dyspareunia 11 %,
4. Primary infertility 15 %,
5. Habitual abortion or premature delivery 46 %.

After assessing the anatomic defect, either the Strassman, Jones, Tompkins, Carapedyan or Mahgoub procedure was utilized as described.[2, 3, 5]

The purpose of this study is to relate the experience at the Department of Obstetrics and Gynecology, Hacettepe Medical School, with uterine anomalies, especially as it pertains to obstetric performance before and after surgical repair.

Materials and Methods

A total of 45 patients seen from 1964 to 1982 constitute the study group. Data were obtained from special records for each patient. The diagnosis was made by pelvic examination, hysterosalpingography, laparoscopy, laparotomy, and dilatation and curettage in women with malformed uterus. Assessing the anatomic defect, Strassman (on the bicorniate), Jones, or Tompkins procedure was used. Obstetric outcome before and after surgical repair in women with malformed uterus was examined.

Results

Surgical repair was performed in 45 cases with malformed uterus. Their ages varied from 19 to 37 (Table I).

TABLE I
AGE DISTRIBUTION

Age	No of patients	%
24 and below	19	42.22
25-29	20	44.45
30 and above	6	13.33
Total	45	100.00

The clinical complaints of cases are given in Table II.

TABLE II
CLINICAL COMPLAINTS

Complaint	No of patients	%
Repeated pregnancy loss (RPL)	33	73.33
Infertility*	9	20.00
RPL + pain	3	6.67
Total	45	100.00

* Wedge resection and metroplasty together were performed in 5 patients, and 2 of these had term delivery.

The surgical procedures used are seen in Table III.

TABLE III
TYPES OF SURGICAL PROCEDURES

Type	No of patients	%
Jones	24	53.33
Strassman	19	42.22
Tompkins	2	4.45
Total	45	100.00

Before unification 93.6 % of 157 conceptions in these 45 cases resulted in fetal wastage (prematurity and abortion). Outcome of pregnancies before unification is shown in Table IV.

TABLE IV
OUTCOME OF PREGNANCIES BEFORE UNIFICATION

Anomaly	No of patients	Total conception	Fetal wastage	Successful delivery No	Successful delivery %
Septate	24	106	99	7	6.60
Bicorniate	19	46	43	3	6.52
Didelphys	2	5	5	–	–
Total	45	157	147	10	6.36

There was no follow up in four cases after surgical procedure. Peritubal adhesion and block occurred in 5 cases. 14 cases have not conceived yet. Obstetric outcome after surgical correction is given in Table V.

TABLE V
OUTCOME OF PREGNANCIES AFTER CORRECTION

Anomaly	No of patients	Total conception	Fetal wastage	Successful delivery No	Successful delivery %
Septate	10	10	–	10	100.00
Bicorniate	12	26	6*	20	
Didelphys	1	1	–	1	100.00
Total	23	37	6	31	

* Wanted termination of pregnancy.

Successful term pregnancy occurred in 83.78 % of total conceptions after unification.

Term delivery occurred in 33.4 % of total infertile cases.

Discussion

A literature review by Strassman revealed several commonly accepted indications, namely abnormal bleeding, dysmenorrhea, dyspareunia, primary infertility, and repeated pregnancy loss.[8] Current concept agrees with reproductive failure being the primary indication for surgery, and unification for pain, abnormal bleeding, and dyspareunia should rarely be done.[4] Primary infertility should rarely, if ever, be an indication. In our clinic, metroplasties are done for repeated pregnancy loss only after other obstetric, medical, and endocrinologic causes have been ruled out.

In unification, if patient selection is made properly, the obstetric outcome is good.

As mentioned above, 83.78 % of our postoperative pregnancies resulted in successful term pregnancies, as compared to only 6.36 % in the same patients preoperatively.

In the literature, successful term pregnancies vary from 50 % to 86.4 % postoperatively, as compared to only 1.5 % to 26 % in the same series preoperatively.[3] In addition, Rock and Jones have reported that 77 % of the patients after this precedure can be expected to have a term delivery.[2] Other authors have reported similar results.

Summary

Obstetric outcome before and after metroplasty in women with malformed uterus is discussed.

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Acute Lymphocytic Leukemia in Pregnancy

(A Case Report)

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Introduction

Pregnancy complicating acute lymphocytic leukemia is uncommon. There are very few case reports in the literature with successful outcome of the pregnancy.[1,2] The chemotherapy presents some particular problems during the pregnancy because of their known teratogenic effects on the fetus.[3,9] It would seem that the chemotherapy may cause either interruption of the pregnancy or will cause potential fetal damage or death of the fetus when used during the first trimester of pregnancy.[9,10] It seems the fetal damages are less or negligible with the chemotherapy if it is used during the second or third trimester.[1,2,11,13]

Case Report

This 35 years old woman sought medical attention because of stabbing loin pain, excessive sweats, malaise, nonpleuritic chest pain, dyspnea on exertion of 3 months duration. She was hospitalized in another hospital and was found to be anemic and transfused 7 units of whole blood. The bone marrow aspiration was attempted several times for the diagnostic purposes, without success. She was referred to the University hospital for further work-up of the anemia. Meanwhile she experienced oozing blood from her gums and intermittent fever, weight loss in spite of a good appetite. Her past medical and family histories were unremarkable except for the absence of menses for 8 months. Physical examination revealed several petechia and ecchymoses over both arms and legs and a small drained abcess on right arm. The tem-

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perature was 37,3°C. There was herpes simplex of lower lip. Mucous membranes were pale, both tonsils were hyperthorphic. There was yellowish-white exudate over tonsils and soft palate as well. Multiple small, discrete nontender bilateral anterior, posterior cervical lymph nodes were present. There was a short systolic murmur at apex. The abdomen was distended and uterin fundus was felt 3 cm below the umbulicus and fetal heart tones were positive. The liver was palpable 7 cm below the right costal margin (total liver span was 18 cm) and the spleen was palpable 10 cm below the left costal margin at the midclavicular line. Pretibial (+) edema was present. Rest of the physical exam was unremarkable.

Laboratory data showed normocytic normochromic anemia with hemoglobin value of 5,3 gm/dl. The white blood cell count (WBC) was 1600 / cu mm with 20 percent segmented neutrophils, 54 percent lymphocytes, 26 percent lymphoblasts. The platelet count was 120 000 cu.mm. The erythrocyte sedimentation rate was 180 mm/hr. The serum uric acid was 6,1 mg/dl. Total serum protein was 6,9 gm/dl with 2,8 gm/dl albumin.

The bone marrow aspiration was diagnostic for acute lymhocytic leukemia with predominance of lymphoblasts.

The patient was transfused 2 units of fresh whole blood and chemotherapy was started with oncovin 2 mg I.V./weekly and prednisone 40 mg/m²/daily.

Her lymphadenopathy dissappeared, liver and spleen size decreased 2 and 5 cm respectively with this therapy. The bone marrow aspiration was repeated when the peripheral blood smear showed no lymphoblasts. However, no marrow aspirate could be obtained in spite of several attempts, hence bone marrow was biopsied. Bone marrow biopsy showed a normocellular marrow in remission. At this point, her steroid dosage was decreased gradually. Her pregnancy remained uncomplicated clinically with a normal growth rate of the fetus. Fetal heart tones were within normal limits and there was no clinical evidence of intrauterine hemorrage. Nevertheless, her blood pressure went up to 180/110 mm with prednisone treatment which was controlled by a beta bloker and diuretic therapy. There was no proteinuria. By reducing steroid dosage blood pressure returned to normal.

The patient went into natural labor at the time when the gestation was determined to be 36 ∓ 2 weeks by ultrasonic examination and a live male infant, weighing 2050 gr was delivered. The infant's apgar

scores were 7. A CBC of the baby revealed a Hb level of 20,44 gr/dl., WBC of 7000/cu mm with 66 percent segmented neutrohils, 8 percent band forms and 26 percent lymphocytes.

The patient's postpartum course was uneventful. A bone marrow aspiration on the fourth postpartum day showed a bone marrow remission, a moderately hypocelluler marrow with less than 5 percent blast cells. The patient was scheduled for cranio-axial radiotherapy and remission therapy with methotrexate and purinethol was planned at discharge.

The patient and her baby were in good condition at the time of this writing and baby is due for a chromosome analysis.

Discussion

The literature is scant of cases with the pregnancy complicating acute lymphocytic leukemia. Because those patients with ALL either never reach to the reproductive age or they do not easily conceive.[14, 15] But the prognosis of ALL has very much improved since the introduction of multiple agent chemotherapy. So it was expected that the number of reports will increase eventually in the literature. There is no evidence that pregnancy has any deleterious effect on leukemia.[2, 20] On the other hand leukemia has deleterious effect on pregnancy because of increased risk of infection, hemorrage from thrombocytopenia, disseminated intravascular coagulation or hypofibrinogenemia. It has been suggested that a pregnant leukemic might be managed without termination of pregnancy and the patient should be treated as though she was not pregnant.

However, the management of acute leukemia during pregnancy is difficult because of the potential hazards of the chemotherapy on the fetus. While the chemotherapy during the first trimester carries a very high risk of fetal malformations,[3–9] cytotoxic drugs whether given alone or in combination in the second or third trimester, do not.[1, 2, 10–13]

Acute leukemia associated with pregnancy has been treated with 6 MP and prednisone, vincristine, cytarabine, thioguanine with uneventful course of pregnancy and birth of alive normal infants. Mc Lain documented 256 cases of acute leukemia complicated by pregnancy of which 63 patients had acute lymphocytic leukemia. 60 percent of those had full term live births.[16]

Corticosteroids given to rats during pregnancy altered maxillary process fusion and cleft palate resulted. However Nicolson reported no fetal malformations due to corticosteroid administration during pregnancy.[17]

Animal studies showed that vincristine passes the placental barrier but it stays to be determined, if it passes placenta and causes malformations of fetus.[18]

Our patient was in her second trimester of her pregnancy when her leukemia was diagnosed. Termination of pregnancy was not considered at this time because of the potential hazards of hemorage and infection. She and her family were informed by the hazards of chemotherapy. She insisted on having the baby. It was decided to treat her with conventional vincristine, prednison combination and both clinical and marrow remission were achieved by this mode of therapy. She tolerated the therapy well except the development of a steroid dependent hypertension which was controlled easily and dissappeared when the dosage was reduced. She was delivered a normal live infant at the term, the baby neither showed any of the side effects of aggressive chemotherapy, nor the signs of leukemia.

It was our purpose; by reporting this case, to stress again the importance of chemotherapy of a pregnant leukemic in order to achieve maternal survival until the fetus becomes viable and there after. And at least two of the major drugs for ALL, vincristine and corticosteroid, did not seem to cause apparent malformations of the fetus when they are used after the first trimester, as in our case.

Summary

Pregnancy associated with leukemia is relatively uncommon and majority of the reported cases have had acute granulocytic leukemia. The high occurence of granulocytic rather than lymphocytic leukemia is somehow expected; because the incidence of granulocytic leukemia is higher during the childbearing age of women. The present case is one of those rare cases of the acute lymphocytic leukemia associated with pregnancy who was succesfully managed with chemotherapy and delivered a live normal infant. This report is also another proof to the previous reports stressing that the chemotherapy has little or no teratogenic effect on the fetus, if used during the second or third trimester.

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Endemic Fluorosis

(Clinical, Roentgenological and Biochemical Study of Chronic Fluorine Intoxiation in Kızılcaören)

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Introduction

Chronic fluorine intoxication, as manifested by mottled enamel and diffuse osteosclerosis of the skeleton, has been observed in areas where the drinking water contained fluoride in concentrations higher than 3-4 parts per million (ppm).

This form of chronic intoxication, was first described in India, in the state of Madras as early as 1937[26] and was designated as "Endemic Fluorosis". Subsequently, cases of endemic fluorosis have been described as occuring in other parts of India[14, 15, 27] and sporadically from almost all parts of the world, particularly in China,[19] Japan,[13] South Africa,[22] North Africa,[23] Argentina,[3] Saudi Arabia,[10] United States,[7] Canada[16] and certain parts of the Turkey.[28, 29, 30]

Investigation of toxic effects of fluoride in humans have evoked a lively interest because public health programs of fluoridation for the prevention of dental caries have always considered the risk of a remote cumulative intoxication. However, the indices of early intoxication are poorly defined. A number of biological effects have been ascribed to fluorides. Although many reports of such effects are unsubstantiated, several have been studied sufficiently to deserve careful summarization including the effects on bone, kidney, teeth, thyroid and growth in general.

Our interest in the problem was aroused when we observed a number of cases of skeletal sclerosis and mottled enamel in the Kızılcaören area. All these cases came from area of Kızılcaören. These observation led to an extensive epidemiological survey of the Kızılcaören area.

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Material and Method

The data to be presented are based upon the study of 323 cases of endemic fluorosis over a 2 years from Kızılcaören, one of the endemic areas of the Turkey. Most of these patients were studied there while epidemiological surveys were being carried out by a team of experienced workers which included Orthopedist, pediatrist and biochemist. In the epidemiological study only these cases which had a definitive radiological osteosclerosis were included. Twenty of these cases were hospitalised for comprehensive study. The physical examination was recorded on a special form with particular emphasis, on examination of teeth, goniometry, skeletal examination. The biochemical determination included calcium, inorganic phosphorus, alkaline phosphatase. Fluoride estimations were done on the drinking water.

Kızılcaören is one of the middle Anatolia village. This area of Eskişehir, has a hot summer, the temperature reaching 35-40°C, and has a dry and sandy soil. The chief sources of water supply for domestic and drinking purposes, are water wells located in or near the village.

The fluoride content of this water varies from 3,9 to 4.8 ppm. More than % 95 of its male population are farmers. This involves strenuous work in the hot sun with consequent excessive sweating and copious intake of water. The general hygenic standards are poor and the diet of most of population is deficient, particularly lacking in animal proteins and green vegetables.

Dental Fluorosis

Mottled enamel is a well-recognized entity.[2, 7, 8] It has been shown that if a person is born and reared in an area having a fluoride content of more than 1 ppm in the water supply, he will probably developed mottled enamel. This mottling is one of the first and earliest visible signs of an excessive intake of fluorine in childhood. It is usually regarded as a suggestive diagnostic criterion.

In our survey work in the Kızılcaören, 157 children were examined, of whom 58 % showed typical changes of dental fluorosis.

Teeth affected with mild fluorosis have the appearence of being hard, lustrous and polished; with minute opaque flecks scattered irregularity, with a greater degree of fluorosis, pits, grooves and depressions of irregulear area, and depth appear with intrinsic discoloration involving the major portion of the crown. This discoloration is a characteristic feature with variation in the shade of brown from light to dark.

Skeletal Fluorosis

The changes in the skeleton are the most distinctive and characteristic feature of endemic fluorosis.

Radiological Changes: Roholm,[25] divided the degree of skeletal involvement as seen radiologically in to 3 stages.

1 st Stage: The spinal column and the pelvis show roughening and blurring of the trabeculae,

2 nd Stage: The trabeculae merge together and the bone has a diffuse structureless appearence. The bone contours become uneven. These changes are most marked in the pelvis, spine and ribs. The medullary cavities may be narrowed and the ligaments show early calcification.

3 rd Stage: The bones appear as marble white shadows, this being most marked in the axial skeleton. The bones of the extremities show irregular periosteal thickening with calcification of ligaments and muscular attachments. The cortex of long bones is dense and thick, and the medullary cavity is diminished. The interosseous membranes also show calcification.

The grade I stage of Roholm was rarely seen, most of the cases showing grade II and III changes.

The most pronounced change were seen in the vertebral column, osteosclerosis and irregular osteophyte formation were noted in the vertebral body.

Next to the spine, osteosclerosis was most evident in the pelvis, along with calcification of sacrotuberous and sacrospinous ligaments. Irregular periosteal bone formation was observed along the tendons and the fascial and muscular attachements, including interosseous membranes of forearms and legs, linea aspera, the deltoid tuberosity, the lower margins of the ribs, the attachement of the Achilles tendons, the tibial tubercules, and the greater trochanter of femur. Chest x-rays revealed a peculiar contrast of the marble white, bony cage with radiolucent lungs (Figures 1-4).

Histopathology: Although there are many histopathological reports on experimental fluorosis.[1,18,25,33,34] The data in human intoxication are scanty.[12, 24, 35]

In the present investigation, a bone biobsy was obtained from the iliac crest in one case. The compact bone showed disordered lameller orientation and an enlarged, poorly formed Haversian system. In the spongy bone, areas of osteoid tissue were found among well-formed trabeculae (Figure 5).

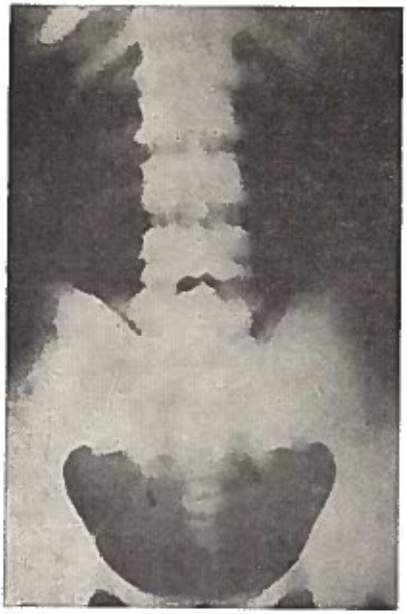

Figure 1
X-Ray of the pelvis showing osteosclerosis and sacrotuberous ligament calcification.

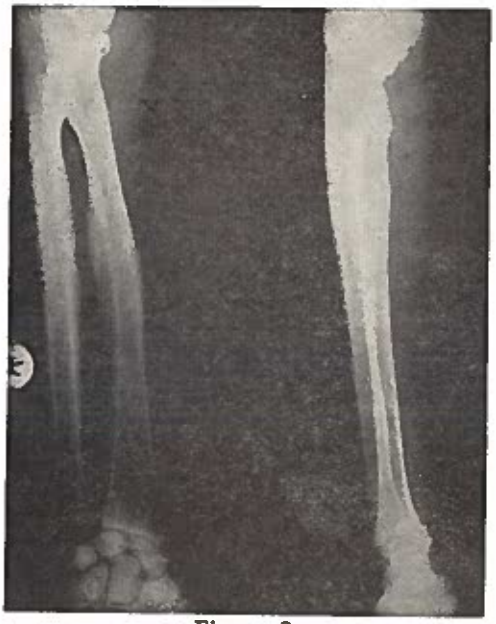

Figure 2
X-Ray of the forearm showing marked interosseous membran calcification.

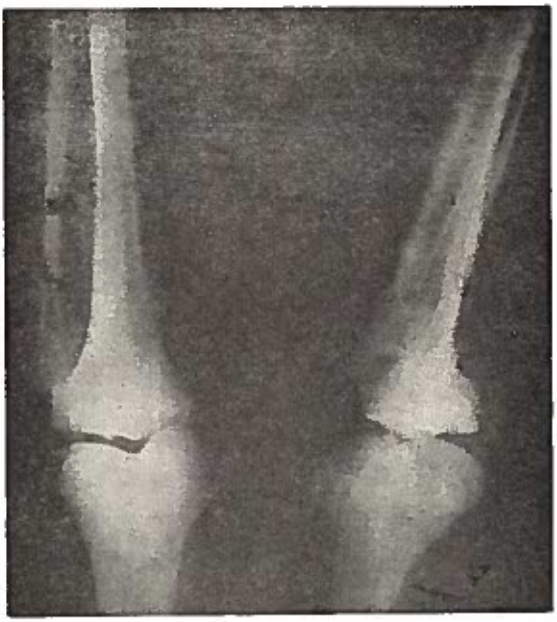

Figure 3
X-Ray of the leg showing interosseous membran calcification.

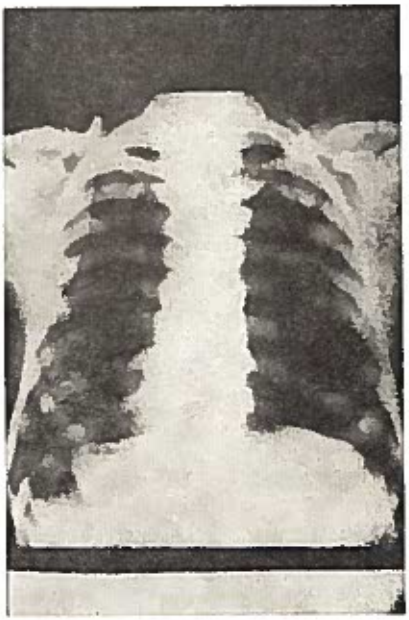

Figure 4
X-Ray of the chest showing the contrast of chalky white bony cage with radiolucent lungs.

Figure 5
Histopathological picture of bone biobsy showing disordered lameller pattern. (H. E., x 75)

Diagnosis of Fluorosis

Dental fluorosis is easly recognized, but the skeletal abnormalities are not so obvious until the advanced stage of crippling fluorosis. Such cases are frequent in the endemic area and may be misdiagnosed as rheumatoid or osteoarthritis.

The advanced stage of fluoride intoxication has resulted from the continuous exposure of an individual to high fluoride ion daily over a period of 10-20 years. The advanced picture of crippling fluorosis was strikingly uniform. The quadriplegic bent with kyphosis, markedly restricted movement of his spine, contractures and flexion deformity of hips and knees provided a grim picture of the result of excessive fluoride intake (Figure 6). The chest was usually fixed, with minimal expansion. Due to the extreme fixation of the spine, the body moved as a single unit with each attemp to straighten any portion of it.

Endocrine and Metabolic Effects

Fluoride has an inhibitory effect on many enzyme systems.[11] It has been demonstrated,[9, 11] that the fluoride ion at certain concentrations will inhibit the activity of such enzymes as lipase, bone phosphatase, urease, various esterases, and those engaged in glycolysis. While the

Figure 6

The kyphotic deformity and flexion contractures of crippling fluorosis are quite obvious in one of the our patient.

toxicity of the fluoride ion for these enzymes is universally recognized, it is suprising that such an important in vitro effect is associated with so few recognizable clinical manifestations other than the dental and skeletal abnormalities.

Calcium and Phosphorus Metabolism in Fluorosis: Many author,[2, 22, 34] in describing the bone changes in fluorosis, pointed out that in many respects fluorosis and hyperparathyroidism exert a similar action on bone and that the final picture may be a combination of fluorosis and hyperparathyroidism.

The clinical manifestations in both conditions, depending as they do on the mobilisation of calcium and phosphorous excretion, with a tendency to the formation of renal calculi, have features in common. Differential diagnosis, however, can be easily made on the history and the serum concentration of calcium, inorganic phosphorus and alkaline phosphatase. Radiological examination reveals a predominant osteosclerosis in fluorosis while there may be a generalised decalcification of bones in parathyroid disease.

We have studied serum calcium, inorganic phosphorus, and alkaline phosphatase in 20 patients with advanced fluorosis. Serum calcium

ranged from 9 to 12 mg/100 ml compared to 9.2 in normal controls. Inorganic phosphorus was between 2.5 and 4.8 mg/100 ml as compared to normal controls of 3.2-5 mg/100ml.

Alkaline Phosphatase activity varied from 10.4 to 11.8 King-Armstrong units (Mean 10.8). Weidmann et all,[34] noted an increased in alkaline phosphatase activity and suggested a close relationship between the degree of fluorosis and enzymatic activity. In our cases, alkaline phosphatase did not show significant variation from normal.

Hematopoietic System: Various observers have recorded the hematological findings in patient with fluorosis.[6, 20, 30] It has been alleged that fluorosis results in anemia. Roholm,[25] thought that the anemia was due to an accompaying nutrituonal imbalance; others that it was due to encroachment on the bone marrow by the osteosclerotic deposits. In our series of 241 cases, no significant differences were observed between the fluorotic and nonfluorotic subjects (Table I).

TABLE I

HEMOGLOBIN AND HEMATOCRIT VALUES IN HUMANS

Sex	No	Hemoglobin gm %	Mean	Hematocrit %	Mean
Men	51	11.40–14.15	13.18	35–47	42
Women	62	10.50–13.20	11.92	32–45	41
Boys	68	9.12–12.56	11.26	33–42	38
Girls	60	10.10–13.08	12.07	33–40	38

Estimations of Fluoride in Water Samples

A total of 4 samples of water were analysed from the different regions of the endemic area, and the range was between 3.9 and 4.8 ppm. Owing to the extremely high temparature in summer and the strenuous type of work done by the farmers, the water intake of the population is considerable. Considering an average of 5 liters daily, it will provide as much as 20 to 30 mg of fluoride to the individual from the water alone and when it is realized that a good quality of water is used in cooking, it is obvious that the total fluoride intake is enormous.

Preventive Aspects

There is no doubt that, if measures could be adopted to give fluoride-free water to the people of this endemic area, the crippling effects of this chronic intoxication would vanish. Various methods have been suggested to defluorinate the water. However, defluoridation of water

by chemical methods has been found to be impracticable because of cost and because of the vastly scattered areas. Deep drilling of wells has been suggested because fluoride rocks are supposed to be present near the surface. In the village of Kızılcaören, drinking water was supplied from the village near by. The fluoride content of this water was between 0.4 and 0.7 ppm. We have, therefore, recomended that drinking water be supplied to the affected villages from this source.

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Labelling and Biodistribution Studies of Some ^{131}I-Dipeptides

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Introduction

Amino acids and peptides have been labelled with a variety of radioisotopes in attemts to visualise pancreas.[1-9] ^{11}C labelled DL-valine is the only promising agent introduced so far, but the cyclotron produced radioisotope (^{11}C) used has limited application due to availability and short physical half-life of 20 min. ^{99m}Tc is an ideal radioisotope for scintigraphy ($T_{\frac{1}{2}}$ =6h, E_γ=140 keV), however the complexes prepared with it show different biological properties than the original compounds[6,8] Iodone is a better label, since it is incorporated into the molecule and may not change the biological behavior to the same extent.

In this investigation four dipeptides (l-tyrosyl-l-valine, l-tyrosyl-l-alanine, l-tyrosyl-l-leucine and l-histidyl-l-leucine), one tripeptide (l-valyl-l-tyrosyl-l-valine) and α – methyl tyrosine were labelled with ^{131}I ($T_{\frac{1}{2}}$ =8.08 d, E_γ = 364 keV) using a modification of the chloramine-T method.[10] Only those peptides containing tyrosine or histidine were chosen, because of the ease in labelling the rings and the stability of the I bond on the ring compared to aliphatic linkage.

Materials and Methods

The following compounds used for labelling were obtained from Sigma Chemical Co., U.S.A.: l-tyrosyl-l-valine (T-V), l-tyrosyl-l-alanine (T-A), l-tyrosyl-l-leucine (T-L), l-valyl-l-tyrosyl-l-valine (V-T-V), l-histidyl-l-leucine (H-L) and α-methyl-tyrosine (M-T). ^{131}I (in NaOH solution, for protien iodination) was purchased from Radiochemical Centre, Amershan, England.

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1. Radiolabelling: All the peptides were labelled according to the following procedure:

To 2 mg peptide in a glass vial, 200 µl phosphate buffer (pH=7.4, 0.05 M), 5 µl ^{131}I (1 mCi) and 200 µl chloramine-T (24 mg/10 ml phosphate buffer) were added. The reaction mixture was vortexed for 10 min. The reaction was stopped by the addition of 1 ml sodium metebisulphite (40 mg/10 ml phosphate buffer). 100 µl KI (100 mg/10 ml buffer) was then added to provide iodode carrier for the unreacted ^{131}I.

α-Methyltyrosine was labelled by the same method but an ethanolic solution was used to dissolve the compound, because of its spare solubility in water (100 µl phosphate buffer and 100 µl ethanol were mixed to dissolve 2 mg α-methyltyrosine at the beginning). After completion of the reaction 500 µl more ethanol was added.

After labelling, ^{131}I-histidyl leucine was passed through a column (1x1.5 cm) of Dowex 2x8 (50-100 mesh, Cl^-form) to remove free unreacted ^{131}I. This step was not necessary for the other labelled compounds.

2. Chromatography: Paper electrophoresis was used to determine the labelling efficiency and the amount of free $^{131}I^-$. Five microliters of each of the reaction mixtures was spotted on a 59x2 cm strip of Whatman No: 3mm chromatography paper at a point 6 cm from one end. On a separate strip $^{131}I^-$ was spotted and they were electrophoresed together in a H.V. electrophoresis apparatus (Hormuth-Vetter, pherograph Model: 64) in barbitone buffer (0.06 M, pH=8.5) at 1000 volts for 1 h. Then the strips were removed, dried and cut into 1 cm segments and assayed for radioactivity in an automatic γ-counter (Berthold, Model: BF 5300). In the case of ^{131}I-H-L electrophoresis was performed both before and after column chromatography. Electrophoresis was repeated at daily intervals up to 3 days to check the stability of the label.

3. Animal Experiments: Each labelled compound was diluted with phosphate buffer to a specific activitiy of 10 µl/0.1 ml. A total of 18 mice were used. 0.1 ml (10 µCi) of each of the labelled compounds was i.v. injected into 3 mice through the tail vein. They were sacrificed at 30 min after injection. The following organs were removed: heart, lungs, liver, spleen, pancreas, stomach, intestines, kidneys and some blood. They were weighed and counted in the automatic gamma counter against a standart prepared from a dilution of the injection solution. The percentage dose taken up by each organ and the percent of the injected dose/g organ were calculated.

Results

On electrophoresis the labelled peak appeared at 4-5 cm from the origin towards anode. Free $^{131}I^-$ moved 14-15 cm towards anode. The labelling efficiency was greater than 99 % for all the tyrosine containing compounds. For histidyl leucine the yield was 66 % before passage through column. Free $^{131}I^-$ was completely removed after column chromatography. The amont of free $^{131}I^-$ was 0.3-1.0 % on the day of preparation increased to 1.1-2.9 % the next day and 5.0-8.8 % two days later. All the animal experiments were performed on the same day of labelling so that the amount of free $^{131}I^-$ in the injected solution was lowest.

The results of the biodistribution of ^{131}I labelled peptides are shown in Table I. ^{131}I-α-methyltyrosine was also included for comparison. There was no appreciable difference in organ distribution of the first four peptides: tyrosyl valine, tyrosyl alanine, tyrosyl leucine and valyl tyrosyl valine. All the tyrosyl contatining dipeptides and a tripeptide showed a similar pattern of distribution. The stomach was the target organ with highest uptake followed by the intestines. The percent stomach uptakes were 14.25∓2.09, 9.51∓2.81, 9.37∓0.21 and 12.33 ∓ 1. 16 % for iodinated T-V, T-A, T-L and V-T-V respectively. The difference in % uptake per g of stomach tissue was more striking compared to other tissues. The stomech uptake of ^{131}I-α-methyltyrosine was high (7.50∓2.55 %), however due to kidney excretion kidney accumulation was higher (13.9∓2.12) with this agent. ^{131}I-histidyl leucine showed a homogenous distribution pattern without any target organ as is observed in % dose/g tissue values.

Discussion

All the tyrosine containing compounds studied were labelled with high efficiency using the well-known chloramine-T method. All the peptides were labelled with radioiodine for the first time. α-methyltyrosine was labelled before with ^{123}I by Tisljar et al[11] and its biodistribution in mice was studied in an attempt to visualise pancreas. They used a different method of labelling and obtained 66 % labelling efficiency. Our method is simpler and faster and the reaction goes almost to 100 % completion. With histidyl leucine a lower labelling efficiency (66 %) was obtained, which might be attributed to the difficulty in labelling a five membered ring compared to a six membered ring.

Our results in tissue distribution of ^{131}I-α-methyltrosine is comparable to those of Tisljar et al.[11] Small differences observed might be attributed to the specific activities of the preparations. The pancreas

TABLE I

DISTRIBUTION OF ^{131}I LABELLED PEPTIDES IN MICE

Organ	^{131}I-T-V	^{131}I-T-A	^{131}I-T-L	^{131}I-V-T-V	^{131}I-H-L	^{131}I-M-T
			% Administered dose per whole organ			
Heart	0.11 ± 0.01	0.15 ± 0.04	0.14 ± 0.03	0.15 ± 0.02	—	—
Lungs	0.38 ± 0.01	0.50 ± 0.06	0.42 ± 0.08	0.48 ± 0.06	—	—
Liver	2.46 ± 0.12	2.88 ± 0.15	3.13 ± 0.39	2.73 ± 0.32	3.33 ± 0.42	3.39 ± 0.94
Spleen	0.16 ± 0.00	0.21 ± 0.01	0.21 ± 0.04	0.15 ± 0.01	0.17 ± 0.05	0.17 ± 0.04
Pancreas	0.42 ± 0.03	0.42 ± 0.02	0.40 ± 0.08	0.44 ± 0.01	0.98 ± 0.02	1.22 ± 0.13
Stomach	14.25 ± 2.09	9.51 ± 2.81	9.37 ± 0.21	12.33 ± 1.16	0.96 ± 0.19	7.50 ± 2.55
Intestine	7.35 ± 0.35	6.08 ± 0.32	5.63 ± 0.88	6.94 ± 0.12	6.55 ± 0.16	5.38 ± 1.05
Kidneys	1.43 ± 0.16	1.40 ± 0.04	1.60 ± 0.14	1.42 ± 0.35	1.53 ± 0.19	13.90 ± 2.12
			% Administered dose per g tissue			
Heart	0.75 ± 0.01	1.21 ± 0.40	1.06 ± 0.21	0.94 ± 0.11	—	—
Lungs	1.83 ± 0.13	2.05 ± 0.28	2.41 ± 0.66	2.22 ± 0.04	—	—
Liver	1.24 ± 0.06	1.44 ± 0.06	1.55 ± 0.12	1.25 ± 0.01	1.55 ± 0.39	1.70 ± 0.42
Spleen	1.15 ± 0.11	1.35 ± 0.05	1.46 ± 0.50	1.26 ± 0.20	1.49 ± 0.10	1.43 ± 0.46
Pancreas	1.48 ± 0.01	1.71 ± 0.13	1.61 ± 0.28	1.51 ± 0.28	3.34 ± 0.08	4.03 ± 0.01
Stomach	11.68 ± 1.73	16.65 ± 1.48	13.38 ± 1.10	19.93 ± 0.75	1.54 ± 0.11	11.93 ± 2.54
Intestine	1.75 ± 0.10	1.62 ± 0.00	1.64 ± 0.08	1.68 ± 0.15	1.59 ± 0.21	1.40 ± 0.27
Kidney	2.29 ± 0.10	3.32 ± 0.91	2.91 ± 0.47	2.44 ± 0.62	2.62 ± 0.35	23.88 ± 3.85
Blood	2.63 ± 0.20	3.14 ± 0.11	3.05 ± 0.27	2.88 ± 0.24	2.97 ± 0.12	2.37 ± 0.13

uptake of all the iodinated compounds are too low to be considered for pancreas visualization. The significant finding that the stomach concentrates more of injected radioactivity compared to the other organs in tyrosyl containing peptides deserves further attention. In one dog study we were able to visualize the stomach scintigraphically using Pho/Gamma IV Camera 1-2 h after i.v. injection of 1 mCi ^{131}I-T-L. In our distribution studies stomach was counted with its contets. Scintigraphically observed image showed radioactivity within stomach as well as on the walls. A further study is needed where the stomach and its contents are assayed for radioactivity seperately and the stomach juice is electrophoresed in order to see whether radioactivity is secreted from the stomach and if so in what chemical form. It is probable that the labelled peptides are de-iodinated in vivo and free ^{131}I- (iodide) is secreted rather than intact molecules.

Summary

Four di-, one tri-peptide containing tyrosine or histidine and α-methyltyrosine were labelled with ^{131}I in the rings using cholramine-T method. >99 % labelling yields were obtained in tyrosine containing compouns, and 66 % in histidyl leucine. The biodistribution studies in mice showed a very high uptake in stomach with tyrosine containing peptides. This is a significant finding deserving further investigation. Pancreas uptake was not sufficient in any of the iodinated peptides to be of value for imaging studies.

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Electrical Activity (Spike) Alterations on the Wall of the Small Intestines Due to Obstruction

(Experimental Study)

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Introduction

There is an electrical activity in the small intestines which starts from the longitudinal muscles of the duodenum and proceeds downwards. This is called electrical rhythm and expressed by BER (Basic Electrical Rhythm). BER has no relation with the nerve plexus and the motor activity inside of the intestines.[10, 15, 30]

Another electrical activity starts mainly with the excitation of the mucosa and causes construction in the longitudinal and circular muscles. Thus it sends the contents of the intestine to distal. The nerves coming from outside to the intestines do not start this operation but only regulates it.

The electrical events which occur on the wall of the intestine are measured in milliseconds (msec) and the potential variations are measured in millivolts (mv). Amplitude values are expressed in mv and frequency values are expressed in msec. For measurements special instruments are needed. Electrical events can be amplified by a factor of 1000 or more by using amplifiers, and can be recorded.

There is a negative potential difference inside the intestine with respect to the outsite. This is called "The membrane potential in relax condition" (Relax potential) or stable (balance potential). Its magni-

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tude varies between -10 and -100 mv. In human beings the average amplitude at the specific relax period is -50 mv. and the frequency is 50 msec.[15]

It is possible to measure the potential of a membrane or wall in the relaxed condition. For this purpose a microelectrode is needed. This microelectrode can make all types of extracellular measurements. The relax membrane potential values are found out to be -75 and -95 millivolt. The average value can be assumed to be -85 millivolt.[10, 15]

All potential variations are named as "Action Potential". A sudden increase and rapid decrease in potential which is rarely seen is called: Spike Potential (Peak or sharp potential). The major membrane potential change at the start in Figure 1 is the spike (sharp) potential.

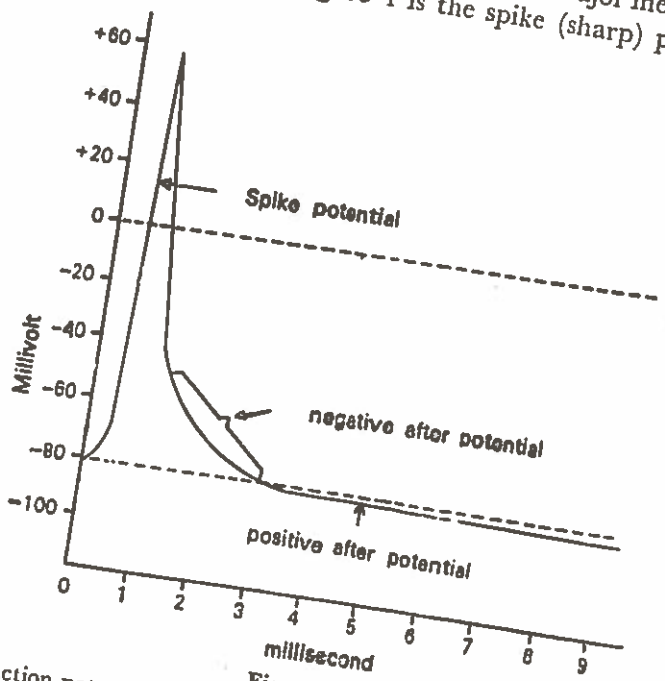

Figure 1
An idealized action potential showing: The initial spike followed by a negative after-potential and a positive after potential.[15]

Spike potentials were first observed by Berkson et al as follows: "just after the sharp rise (of the BER) at begining of contraction. there is rapid oscillation of the string at the rate of about 10 per second. These oscillations are not always observed, but are seen so frequently that we are inclined to belive that if they are absent, it is because of a lack of sufficient sensitivity in the recording devices "Berkson tended to relate

these "rapid oscillations" with tetanic-like contractions, leaving it for later workers to properly correlate the spike potantial with motor function.

Spike potentials in the rabbit duodenum are 0,9 mv and occur in bursts of three to eight spike at a frequency of 27 cycles per min.

Stretching or distanding to bowel initiated spike potentials which could not be blocked by atropine. Stimulation of the vagus nerve in the rabbit initiated spike potentials without influencing the BER. Stimulating the longitudinal muscle of rabbit gave a repeated series of spike potentials.

In contrast to the BER, which is propagated in a cauded direction, there is no apparent propagation of spike potentials. When two recording electrodes are placed 5 cm. apart, the lack of propagation is thus evidence: First, spike potentials are associated with only one-third the complexes in the BER in fasted control animals. Second, spike potentials are recorded from one site while the adjoining area is quiescent third, spike potentials generated by two adjoining sites can be different.

Spike Potentials Related to Bowel Obstruction and Anoxia: Muscle activity induced by procedures causing obstruction or anoxia of the bowel can be monitored by electrode techniques. Serosal monitoring has the advantage of not influening the intraluminal alterations induced by experimental procedures.

Mechanical Obstruction of the Intestine: In anesthetized rabbits, ligating the ileum increased the number and amplitude of spike potentials and the duration of brusts orad to the ligature for appoximately 5 hours. This was followed by a descrease in activity and muscular paralysis that lasted 20 hours postligation.

When the ligature was removed after 3 hours, electrical activity gradually returned to normal. When the ligature removed after 10 hours, no recovery occurred and the animal soon died. These observations have been confirmed.

Occlusion of Mesenteric Vessels to a Segment of Bowel: This procedure led to an increase in the number and amplitude of spike potentials and an increase in the duration of the brust of spike potentials for 1 hour, followed by a decrease of activity and finally disappearance of spike potentials by the fourth hour. If the occlusion was removed in 15 min. or even after 2 hours normal activity returned occlusion for 3 hours led to irreversible damage.

Stangulation Obstruction: A 360-degree rotation bowel leads to obstruction with circulatory occlusion. The effects on electrical activity orad to the site were similar to those of occulsion of the mesenteric vessels. Acute peritonitis induced by perforation of the small intestinal wall produced a vigorous discharge of spike potentials for approximately 5 hours followed by paralysis and disappearance of spike potentials.[10]

The initial very large change in membrane potential shown in Figure 1 which is called the spike potential.

The Negative After Potential: At the termination of the spike potential, the membrane potential fails to return all the way to its resting level for another few milliseconds, as shown in figure. This is called the negative after potential. It is believed to result from a buildup of potassium ions immediately outside the membrane; this causes the concentration ratio of potassium across the membrane to be temporarily less than normal and therefore prevents full return of the normal resting membrane potential for a few additional milliseconds.

The Positive After Potential: Once the membrane potential has returned to its resting value, it becomes a little more negative than its normal resting value; this excess negativity is called the positive after-potential. It is a fraction of a millivolt to, at most, a few millivolts more negative than the normal resting membrane potential, but it last from 50 milliseconds to as long as many seconds.

This positive after-potential is caused principally by the electrogenic pumping of soduim outward though the nerve fiber membrane which is the recharging process. If the active transport processes are poisoned, the positive after-potential is lost, though both the action potential and negative after-potential continue to occur.

The student might wonder why greater negativity in the resting membrane potential is called a positive rather than a negative after-potential, and likewise, why the so-called negative after-potential is not named positive. The reason for this is that these potentials were first measured outside the nerve fibers rather than inside, and all potential changes on the outside are of exactly opposite polarity, where as modern terminology expresses membrane potentials in terms of the inside potential rather than the outside potential.[15]

The duration of Spike (Sharp) potential is about 0,4 msec. (0,9 msec for rabbits). As the spike lasts the membrane potential does not reach to its own level, as can be seen from the figure, it delays a few milliseconds. Summarily the continuity at this stage is called "Negative after

potential". While the membrane potential is getting back to normal relax value first it is observed that it exceeds it. This excees negativity is called "Positive after-potential". According to the normal relax values it performs an excees negativity not more than 1 millivolt; or sometimes just above 1 mv. The duration of this is 50 milliseconds, sometimes a few seconds.[15, 26]

The reason of naming the excees negativeness of the membrane potential is "Positive after Potential" is because first its written from outside of the nerve fibre and its being named at that stage. If the records are taken from out of the nerve fibre and named according to the potential inside all the polarities would be inverse. In modern terminology as the other hand, the recording, which are taken inside are accepted as reference and the new concepts are because of this. This is the difference between them.[15]

In our experiments, as the "Action potential" was plotted in a more rapid manner with respect to figure 1, only the spike potentials are considered and the evaluations are made accordingly. Negative and positive after potentials were not taken into consideration.

The vessels and nerves inside the intestine wall show a uniform distribution. Both vessels and nerves lack the tissue layers that would prevent the effect of, all possible changes, on their surfaces. According to this the measurement of electric potentials are easily made and they be analysed.

Material and Method

Extremely precise electrodes are produced for measuring the intra- and extra-cellular electric potentials in the intestines. Some investigators have prepared very thin (1 mm. in diameter) Multi-electrodes.[5,9,10,12,14,20,21,28,29,31] Each electrode, despite its size of 50 or 100 micron is liable for intracellular measurements. The idea behind the producing of these electrodes so thin is not to damage the intestine very much. By means of such electrodes, many measurements are carried out and results are obtained in gastro-intestinal system.[2, 3, 6, 10, 13, 20, 23, 26] Some examples may be given such as; electrical potential changes after vagotomy, the effect of various drugs on electrical potential and even normal physiological changes.[11, 19, 21, 26, 30, 31]

Special "Contact Electrodes" were used for measurements. These electrodes are sensitive and cheap and can be prepared easily. Silver wires with 0,5 mm. in diameter, their surface were coated with silver chloride are placed into glass pipes with on inside diameter of 5 mm.

Silver chloride is coated on these silver pipes by electrolysis. Inside the glass pipe was filled with 2 % hot-agar Ringer solution. A piece of cottonwool wetted with 2 % agar Ringer solution, was place to the front end; and from the other end conductor wires which are soldered to silver wires are taken out. At the ends of these conductor wires plugs are placed. By means of these plugs the connection to the recording system was maintained. At the end of the measurements the electrodes are preserved in the Ringer solution which does not contain Calsium ions and glucose, which is kept at (+6) - (+4) °C in refrigator in the dark.[16]

As a recording system, Grass model polygraph was used. The electrodes are brought into contact with the desired points and the graphs are plotted by the polygraph. At the same instant pulse and blood pressure curves are plotted and reliable values are obtained.[16]

For the experiment 20 rabbits of 2-3,5 kg weights are used. No discrimmation between male and female rabbits were made. The experiment animals have been left hungry one day prior to the experiment and no other preparation has been made. Anesthesia was started by injecting 25 mg. nembutal per kg. to the ear vein. In this manner, the animal could be kept under a smooth anesthesia during the experiment period (5-8 hours). After the animal slept, a canule was placed into the trachea and it was connected to "bird" apparatus for artificial respiration as need. At the same time for blood pressure and pulse control, entry to artery was made which is connected to the polygraph. In order to keep the vein open during the experiment period, a canule was placed to one of the neck veins and serum glucose or serum physiologic of about 100-250 cc was fed.[15]

After, the animal has been fixed to the surgery-table, the abdomen was opened by median insicion by electro-cutter. The intestines have been examined starding from the stomach. From somethere about 10 cm. far from the stomach, the intestine segment was taken out of the abdomen and electrodes are placed to maintain contact with intestine surface. First the normal intestine electrical potential was plotted by Grass polygraph. Afterwards by taking into consideration the vessels feeding this intestine segment; the intestine only was tightly fixed from two sides, at just above the entry points of the vessels entering to the intestine. By this the intestine passage was cut, but the feeding was continueing by vasa recti (Figure 2). In this position the plotting of the intestine was made at the polygraph. This time, the main vessel coming to the intestine was connected and cut at the entry point. By this, the bleeding of the intestine segment was avoided (Figure 3), the plott was repeated at the polygraph. By this, a vasospasm with a paleness was

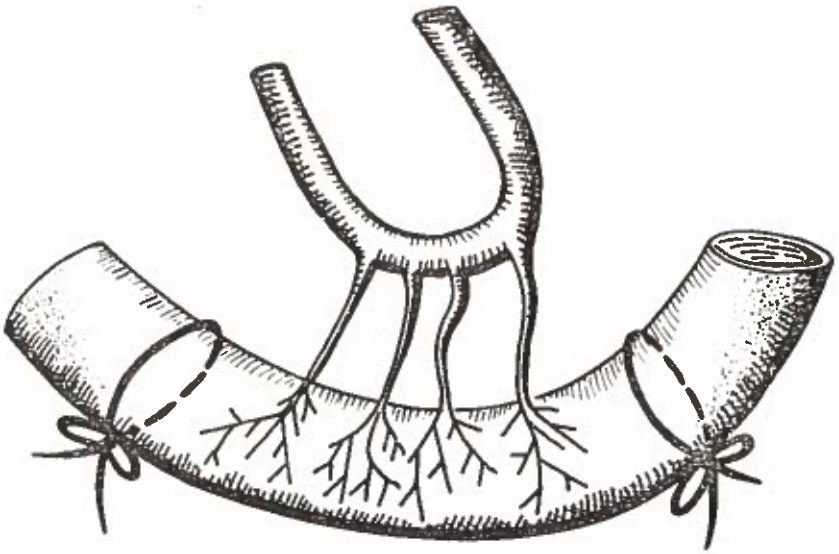

Figure 2
The schematic view of the ligatured intestine segment from both sides.[16]

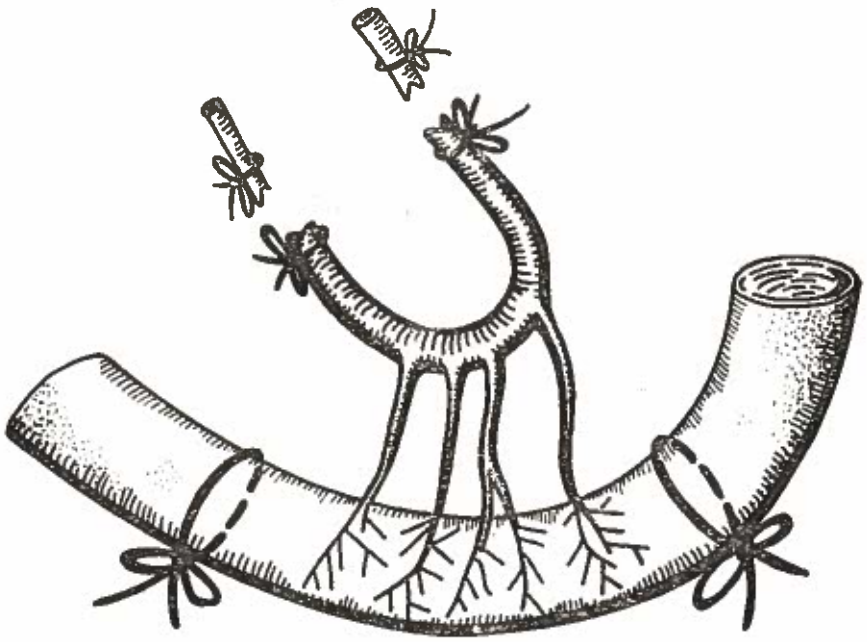

Figure 3
The schematic view of the ligatured intestine segment and its vessels.[16]

TABLE I

THE RATES OF SPIKE AMPLITUDE (mv)

Experiment No	Normal Intestine	Ligatured Intestine	Ligatured Vessels	5. min.	10. min.	20. min.
1	200	200	100	100	50	50
2	200	200	100	50	25	25
3	200	200	100	60	60	50
4	200	200	100	50	25	25
5	100	100	50	50	50	25
6	200	200	100	50	25	10
7	100	100	50	50	25	25
8	200	200	200	100	50	50
9	200	200	100	50	25	10
10	200	200	200	100	50	25
11	100	100	100	50	25	25
12	50	25	25	10	10	5
13	50	100	50	25	25	25
14	200	100	100	50	25	10
15	100	100	50	25	25	10
16	200	200	150	100	80	50
17	100	100	50	25	25	20
18	100	100	50	50	50	25
19	200	200	100	50	25	25
20	200	200	100	50	25	25
21	200	200	100	50	50	25
22	200	100	100	100	50	25
23	100	100	50	50	25	25
24	200	200	100	100	100	50
25	200	100	100	50	50	25
26	100	100	50	50	25	10
27	200	100	50	50	25	10
28	200	200	100	100	50	50
29	100	100	50	25	25	10
30	100	100	100	50	50	25
31	100	100	50	25	20	10
32	200	200	100	100	50	25
33	200	200	100	100	50	25
34	200	200	100	50	50	25

observed, on the intestine which its bleeding was obstructed. After this, the same plotts were carried out in 5th, 10th and 20th minutes respectively. The intestine segment was placed in the abdomen, another segment was chosen and experiments are continued as above. Thus, an experiment animal became at the same time the control of itself. During the experiments arterial blood pressure and pulse were closely observed and it was seen that none of the animals were subjected to shock until

end of the experiment. Thus the experiments were implemented and the animals were killed at the end of the experiments. No complications were observed in the experiment animals. The "bird" apparatus was applied to only 4 of the animals for artificial respiration and the "bird" apparatus was disconnected as soon as the respiration return to normal and the experiments were continued.[16]

The Findings Obtained From The Experiment

From these experiments made on rabbits, the amplitude and frequency value variations of the Spikes were observed.

Spike amplitude values were stated in 34 observations[16] (Table I). After the amplitude value is spike activities was taken in normal intestine (Figure 4), the intestine was tied (Figure 5) and again a decrease was observed (Table II). This decrease confirmed on 5th, 10th, and 20th minutes on bounding the vessels. (Figure 6,7,8,9,10,11,12). The differences in these decreases, in normal intestine and after the intestine was tied were statistically found to be unimportant ($p > 0{,}050$), but the others were important ($p < 0{,}001$) (Table III).

TABLE II

Variable	Mean	Standart Errors
1. Normal Intestine	158.82352	9.3148972
2. Ligatured Intestine	147.79411	9.3438726
3. Ligatured Vessels	88.970586	6.7742412
4. 5. Min.	57.205882	4.5334510
5. 10. Min.	38.823529	3.2365082
6. 20. Min.	25.147058	2.3075215

TABLE III

Variable	Variable	Rate of "T"	
1. Normal Intestine	Ligatured Intestine	1.8710	P > 0.050
2. Normal Intestine	Ligatured Vessels	10.2387	P < 0.001
3. Normal Intestine	5. Min.	13.8115	P < 0.001
4. Normal Intestine	10. Min.	14.2202	P < 0.001
5. Normal Intestine	20. Min.	15.4572	P < 0.001
6. Ligatured Intestine	Ligatured Vessels	8.6115	P < 0.001
7. Ligatured Intestine	5. Min.	11.7722	P < 0.001
8. Ligatured Intestine	10. Min.	12.9546	P < 0.001
9. Ligatured Intestine	20. Min.	14.7656	P < 0.001
10. Ligatured Vessels	5. Min.	6.6443	P < 0.001
11. Ligatured Vessels	10. Min.	8.4384	P < 0.001
12. Ligatured Vessels	20. Min.	10.8459	P < 0.001
13. 5. Min.	10. Min.	5.7578	P < 0.001
14. 5. Min.	20. Min.	9.8005	P < 0.001
15. 10. Min.	20. Min.	6.4051	P < 0.001

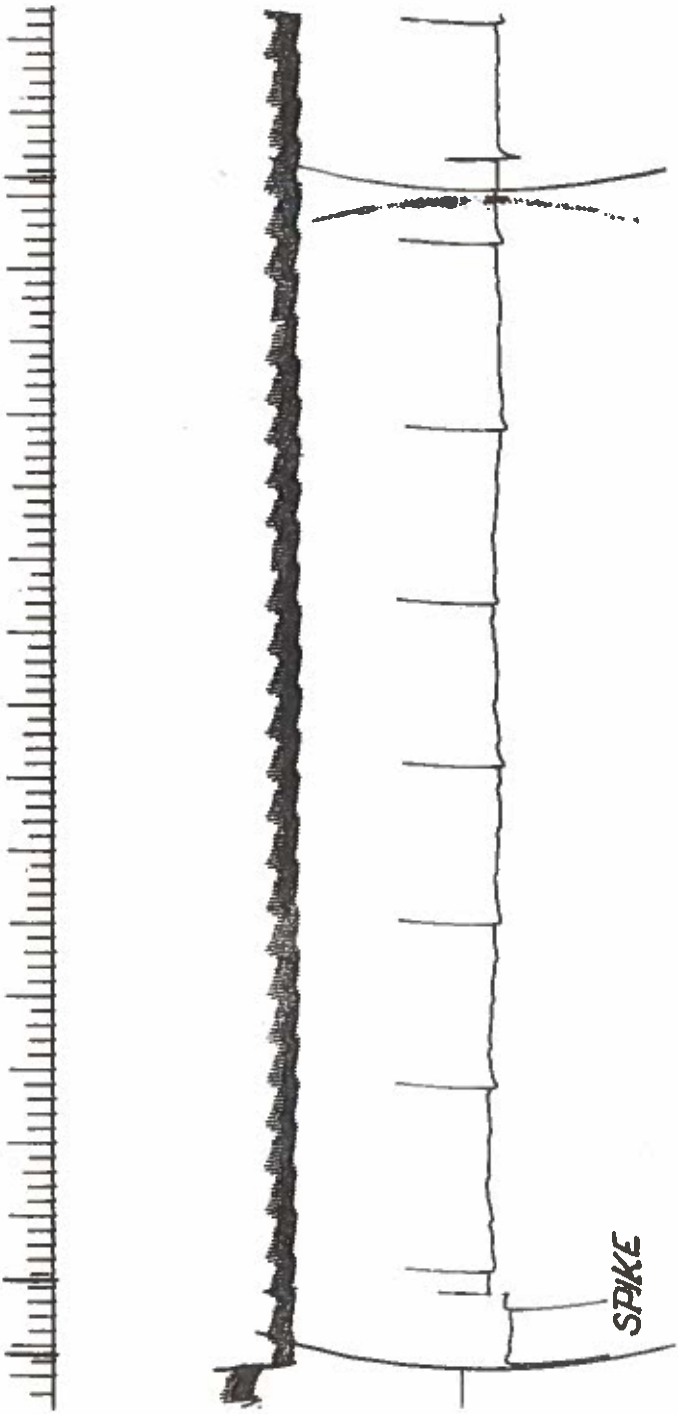

Figure 4
Normal Intestine (2 kg. Rabbit ♂).

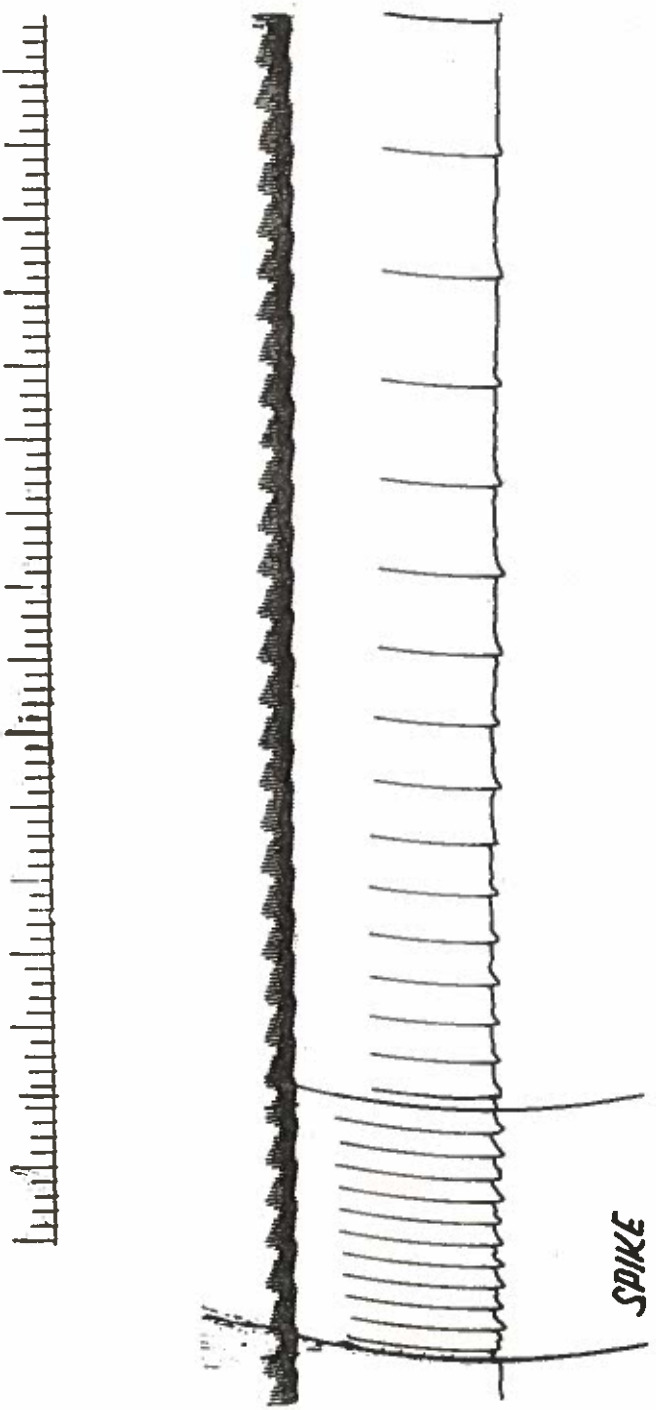

Figure 5
Ligatured Intestine.

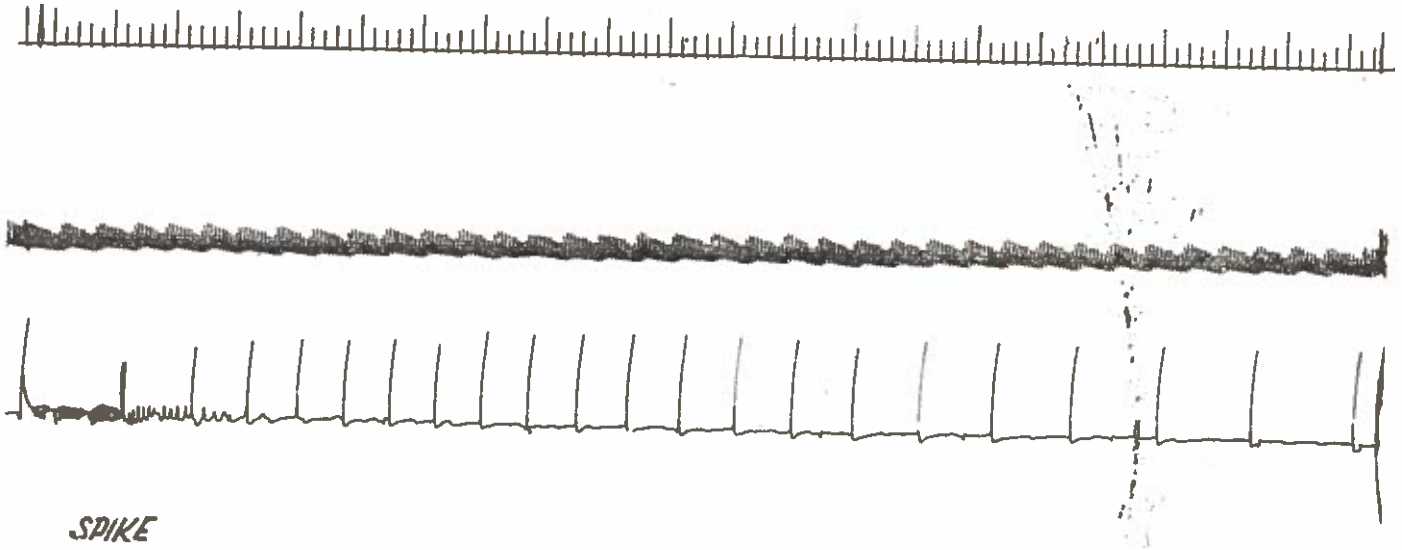

Figure 6
Ligatured Vessels.

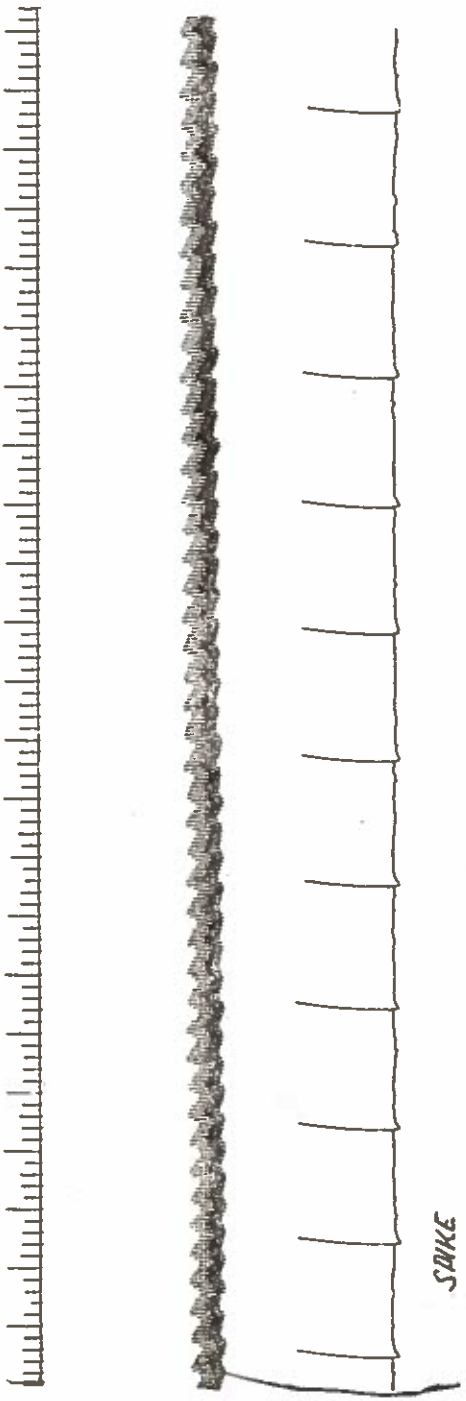

Figure 7
5. minute

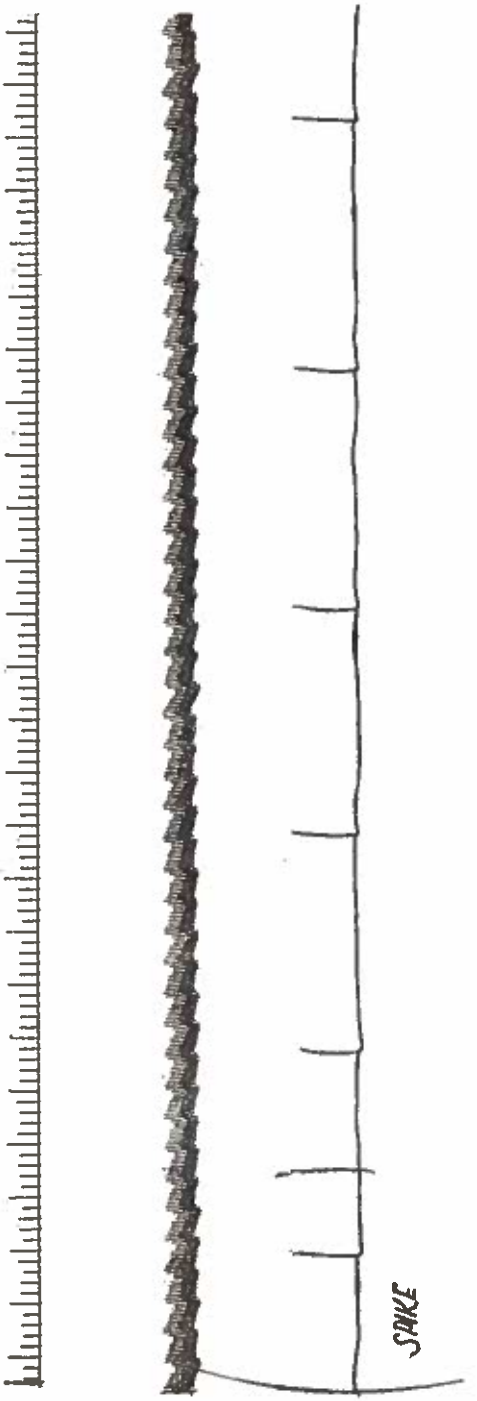

Figure 8
10. minute

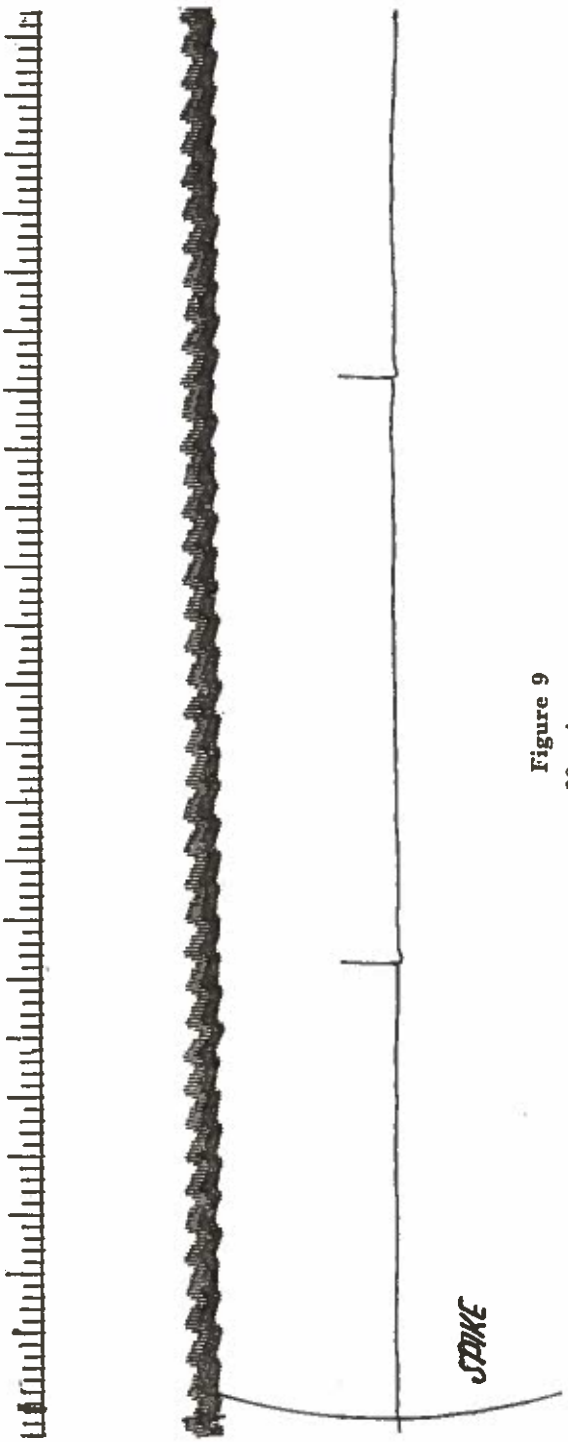

Figure 9
20. minute

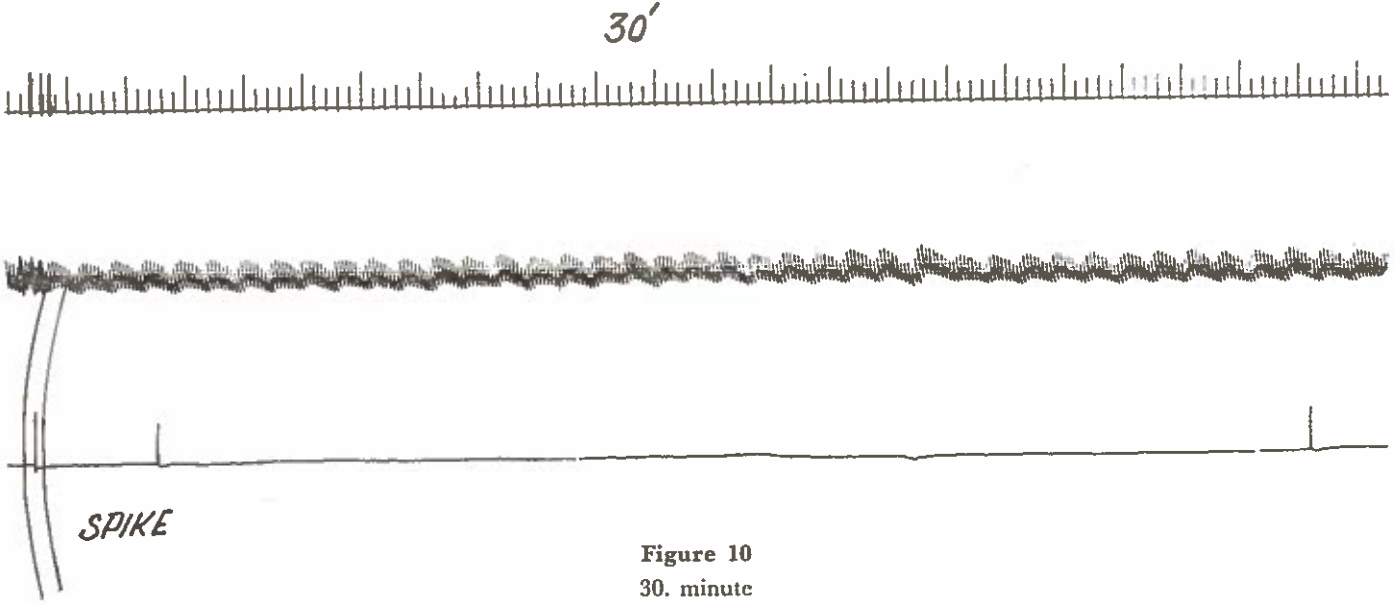

Figure 10
30. minute

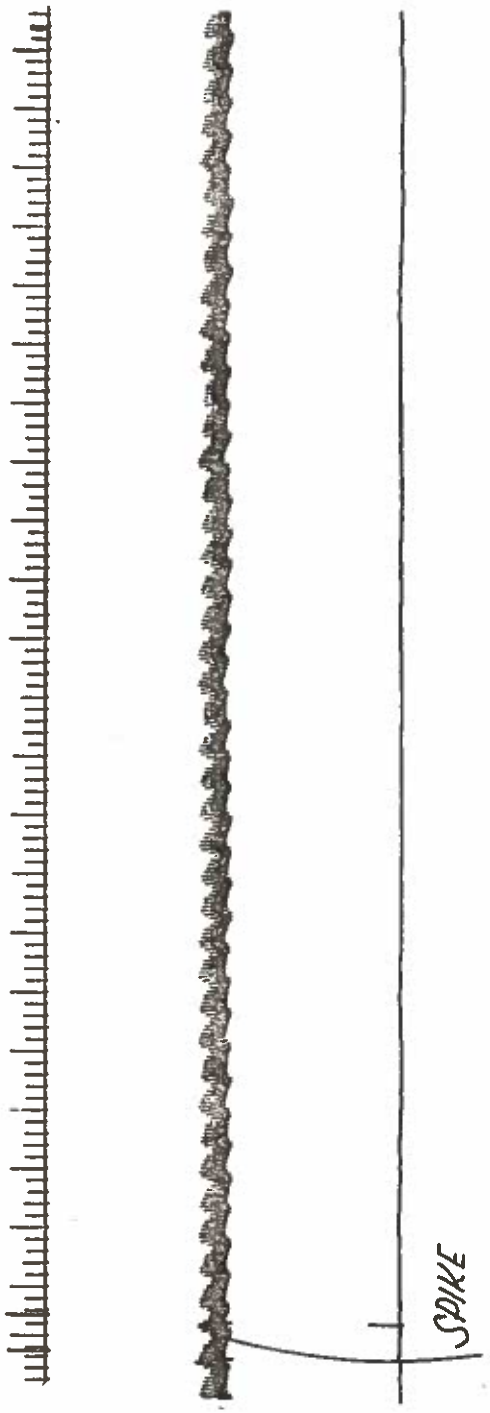

Figure 11
40. minute

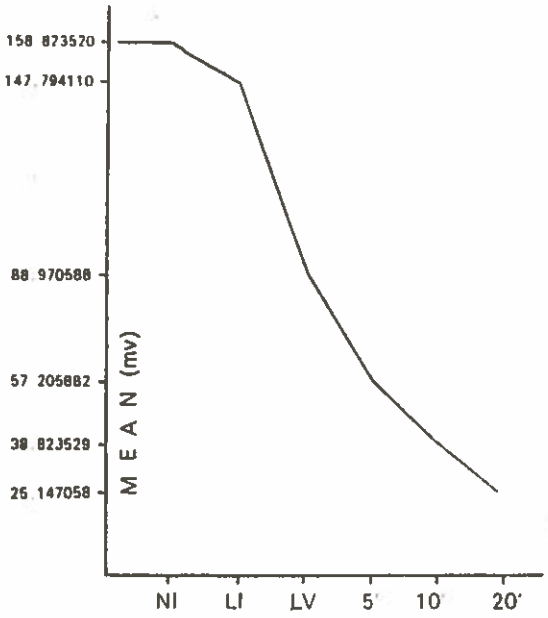

Figure 12
The rates of Spike Amplitude. (NI: Normal Intestine, LI: Ligatured Intestine, LV: Ligatured Vessels)[16]

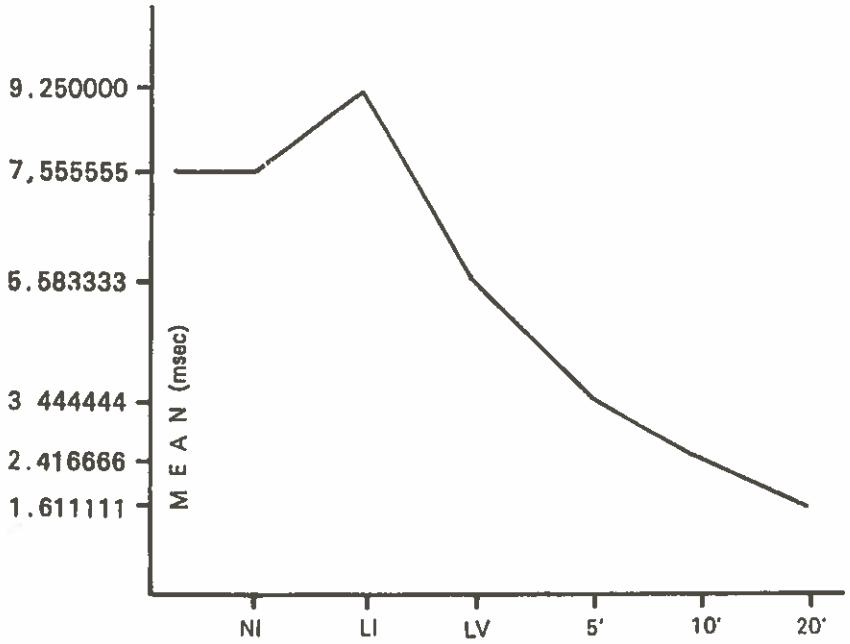

Figure 13
The rates of Spike Frequency. (NI: Normal Intestine. LI: Ligatured Intestine, LV: Ligatured Vessels)[16]

TABLE IV

THE RATE OF SPIKE FREQUENCY (msec)

Experiment No	Normal Intestine	Ligatured Intestine	Ligatured Vessels	5. Min.	10. Min.	20. Min
1	8	9	7	5	5	5
2	9	14	10	2	1	1
3	9	14	10	6	4	3
4	9	10	8	4	3	2
5	9	10	6	6	3	2
6	9	12	10	5	2	2
7	6	6	4	2	3	1
8	9	15	4	2	2	1
9	9	9	5	4	3	2
10	9	9	14	4	3	2
11	6	9	6	4	4	3
12	8	10	8	6	4	2
13	4	4	2	2	1	1
14	5	12	6	5	3	2
15	4	10	10	5	2	1
16	9	9	5	4	2	1
17	4	5	2	1	1	0
18	9	15	10	8	4	1
19	9	9	5	3	2	1
20	9	9	5	3	2	1
21	9	9	5	2	2	1
22	3	4	1	1	1	0
23	9	15	3	2	2	1
24	6	13	2	2	2	1
25	5	5	4	2	1	0
26	8	9	5	4	4	2
27	7	8	4	2	1	0
28	5	6	3	2	2	1
29	9	9	4	2	2	1
30	9	9	5	5	2	2
31	9	8	5	3	3	2
32	9	9	4	3	2	1
33	9	7	6	3	2	1
34	5	5	4	4	3	2
35	8	8	4	4	3	1
36	9	9	5	3	2	1

The spike frequency values were stated in 36 observations (Table IV). After the normal intestine spike frequency was taken as the intestine was tied an increase in frequency was observed (Table V). After this as the vessels were tied a decrease occured (Figure 13). At 5th, 10th and 20th minutes this decrease continued. The differences between these values were statistically found important (Table VI) ($p < 0{,}001$).

TABLE V

Variable	Mean	Standart Errors
1. Normal Intestine	7.5555555	0.32719198
2. Ligatured Intestine	9.2500000	0.50138696
3. Ligatured Vessels	5.5833333	0.47035098
4. 5. Min.	3.4444444	0.27442416
5. 10. Min	2.4166666	0.17536805
6. 20. Min	1.3611111	0.13305193

TABLE VI

Variable	Variable	Rate Of "T"	
1. Normal Intestine	Ligatured Intestine	4.0220	P < 0.001
2. Normal Intestine	Ligatured Vessels	4.3671	P < 0.001
3. Normal Intestine	5. Min.	11.7764	P < 0.001
4. Normal Intestine	10. Min.	16.1039	P < 0.001
5. Normal Intestine	20. Min.	19.9366	P < 0.001
6. Ligatured Intestine	Ligatured Vessels	7.2987	P < 0.001
7. Ligatured Intestine	5. Min.	12.6440	P < 0.001
8. Ligatured Intestine	10. Min.	14.2682	P < 0.001
9. Ligatured Intestine	20. Min.	16.4564	P < 0.001
10. Ligatured Vessels	5. Min.	5.9595	P < 0.001
11. Ligatured Vessels	10. Min.	7.4606	P < 0.001
12. Ligatured Vessels	20. Min.	10.0089	P < 0.001
13. 5. Min	10. Min	5.4402	P < 0.001
14. 5. Min.	20. Min.	9.6481	P < 0.001
15. 10. Min.	20. Min.	10.0539	P < 0.001

Discussion

The acute stop of intestine bleeding by various reasons cause very important problems.[7, 8, 25, 32] These problems are spontanously or due to surgical operations of surgeons, artificially.[4] Some anomalies can result in some changes because of arteriosclerosis in old age-or some vessels inadquacies can cause an acute or subacute ischemi.[17, 24] At the field, which is fed by the vessels which are suffocated because of this, ischemia and even a pathology lasting in necrose can form.

The liveliness of the intestine segment which has bleeding stopped, during the surgical operation could not be definitely stated, at the same time diagnosis is very difficult and genarally late treatment is made. Some segments are taken out unnecessarily by subjective measurements. Although the artery chainging surgeries can be carried out successfully today still the results are subjected to subjective decisions.

In cases of emergency, as the taking out of the intestine remained bloodless is risky, in those cases the surgeon cannot decide easily. In old times, some surgeons used the method of openning the abdomen for the second time in suspicious cases (Second look). We seek the existance of a scientific criteria for not making such an attempt. Urgent diagnosis is important from the treatments point of veiw. The suffocations obstructing the bleeding of intestine generally are emergency cases and most of the time the surgery is made without definite diagnosis. That is no preoperative preparations are made. Sometimes while the intestines were observed during the surgery operation. It is seen that the bleeding hold at a very short segment. The very bad situation of the patient result in surgical errors such as the leaving of the intestine in its place by the thought of "This intestine can bleed". This may result in very heavy complications.[16]

In the large number of implantation surgeries today, blood-stop may form without being aware of and in future some complications may form.[1, 18, 22, 27]

In that case, the colour, intensity and peristhaltism of the intestine are incapable of giving information to us about bleeding capacity during the disorder of intestinal bleeding.

In this field many investigators were made and many methods were searched to prevent this error. Some investigators tried, to inject dye substance into the vein and separate the bleeding segments. By the same thought Phluorescein was given and a visible method was obtained. But as these substances do not exist in our country. The use of them is unthinkable, and this dye substances stay in body for a long time.

The extracellular electrical potential variations at the intestine wall contain our main study. We didn't coincide with a study in this field, in our went to through the literature. The temperature and electrical potentials measurements by using pin shaped electrodes are made for different purposes. The electrical variations of some drugs on intestine, pharmacologically, were analysed. The extracellular measurements were only used in physiological searches.[2, 3, 6, 10, 13, 20, 23, 26, 30]

As the electrodes we use work only in contact manner and therefore give no harm to the intestine, there is no negative effect of them on the properties of the intestine. The measurements could be accomplished in various stages of the intestine by repeating the artificial blood stop formed in different segments, in each animal.[16]

Thus, every animal was happened to be its own control. The experiments done on each animal gave the same results and an accord was recorded in electrical variations.

As the electrical values can be measured at once by bringing the electrodes into contact with the intestine wall, and no damage would be given to the body and at the same time as it can be used easily in all conditions and is very cheap, I recommended this method. It can be easily used after the surgical attempts as a control.[16]

Conclusion

The results obtained in this study can be collected as follows:

1. As the methodical stages are applied respectively, a continuous decrease in Spike Amplitude values were recorded.

2. As the intestine was tied an increase in Spike Frequency occured and after as the vessels were tied a rapid decraese started. In certain, time intervals it decreased to a minimum.[16]

By these results obtained, as the bleeding stops in the intestine due to any reason there occur variations in electrical potential. It is easily seen that although some increases recorded at first in the end a decrease definitely occurs. By making advantage of this it can be easily stated whether an intestine piece is dead or alive.[16]

Summary

The electrical potential variations, due to artificial blood stop at the intestine wall, were observed and analysed in full detail. First an intestine segment was chosen and, after its electrical potential has been measured, it was suffocated by tying it at a certain distance with respect to the vessel satisfying bleeding. It this position, again, measurements were taken; this time the vessels were also tied and both artificial intestine bleeding and the intestine passage were cut. Under these conditions, electrical variations were investigated, plotted in Grass polygraph and determined, in certain time intervals.

With respect to the normal intestine a considerable decrease were observed in Spike amplitude values as the intestine and the vessels were

tied. In Spike frequency variations, however, an increase occured as the was tied and after the vessels were tied considerable decreases were observed.

By this method the capacity of bleeding of the intestine could be determined. And it was found that by the help of this method the surgical intestine complications could be avoided. The application of this method which its results can be scientifically defined, is recommended.

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Cystic Tuberculosis of the Phalanx

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Introduction

Tuberculous dactylitis is now uncommon. The metacarpals, metatarsals or phalanges may be affected. It may involve several digits, which become swollen and fusiform or spindle-shaped. Disability is minimal and pain is little. A history of trauma is common. Shortening and contracture of the affected digit will result. Roentgenograms disclose expansion by cystlike rarefaction of the infected short tubular bone with some subperiosteal new bone formation.

Case Report

A five year old girl presented to the hospital with tenderness and pain of the second phalanges of both hand on April 3,1979. There were swelling of the second phalanges and X-ray examination showed a cyst inthe second phalanges of two hand (Figure 1).

The swelling of the right hand was explored on the 9th May 1979 with a tentative diagnosis of a spina ventosa. The operation note is as follows, "Longitudinal lateral incision along the shaft of the second phalanx. Cortex was found soft friable. The large cavity in the phalanx was curetted, white-yellow material removed, Keflin 50 mg was placed in the cavity and closure of skin with collagen 4/0. Biobsy sent for culture and for histology".

The wound healed solidly with one week. An histology report on 20th May 1979 showed a positive Ziehl-Nielson stain for acid fast bacilli, and on 11th June 1979 acid fast bacilli were reported cultured. The histology specimen shows a celluler apperence consistent with tuberculosis.

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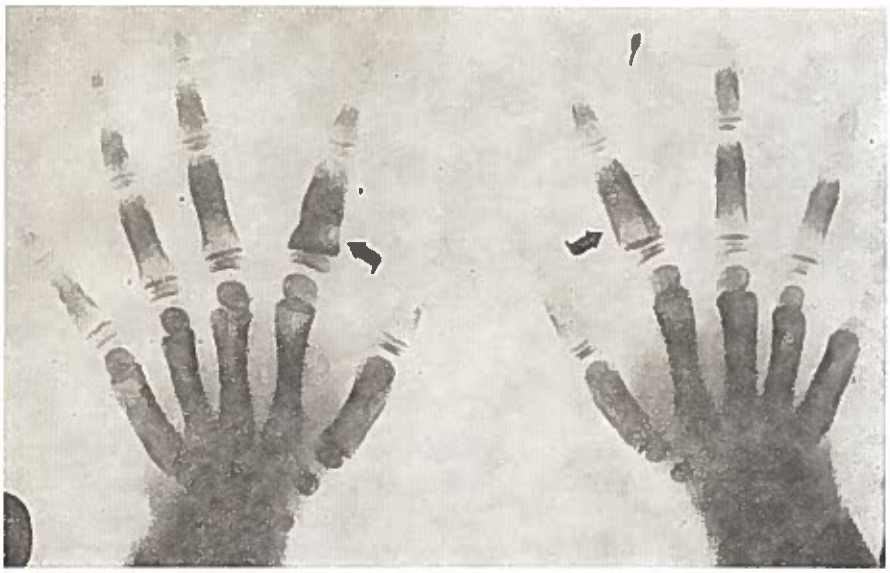

Figure 1

X-Ray of Hand, April 1979, showing cavity in the second proximal phalanges.

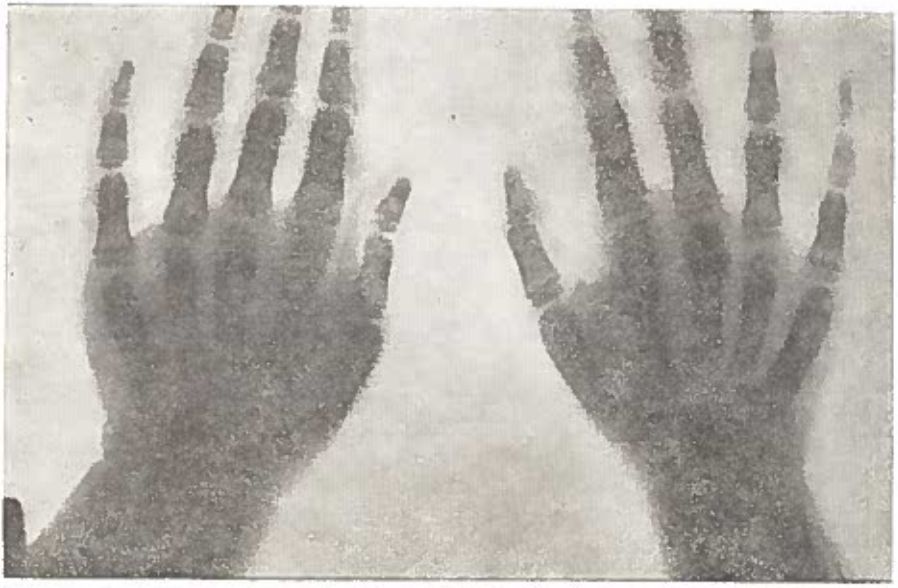

Figure 2

Healed lesion, May 1980.

Mantoux test strongly positive
Erythrocyte Sedimentation Rate, 30 mm/hr
W.B.C. count 10.400 / mm^3
Hgb. 12.92 %
Chest X-ray showed no pulmonary tuberculosis.
No family history was obtained.

She was referred for anti-tuberculosis therapy, she was reviewed on 4th May 1980 after her anti-tuberculosis therapy had been terminated. The hands and second phalanges shows no functional impairment and the X-rays (Figure 2) shows the healed lesions.

Discussion

Tuberculosis of the phalanx, rare of very rare appearence, and of these the most common locations are the vertebral bodies, hips and knees. Tuberculosis of the phalanx, also called Tuberculous dactylitis or spina ventosa consist in the appearence of a thin and expanded cortex.

Tuberculosis in bone tissue are though to arise from tuberculous emboli, presumably from pulmonary or other visceral sources.

Tuberculosis of the bones of the fingers and toes, seems to appear almost in early childhood, and the condition is observed about 5 times as often in the hands as in the feet.[2] From half to thirds of the cases also show other foci of skeletal tuberculosis.[4, 6] An affected phalanx usually reveals a thin and expanded cortex, which may even be perforated. Johansson reported that spina ventosa was present in about one fifth of the cases of skeletal tuberculosis appearing before the age 15.[2]

The diferenteal diagnosis of the radiographic changes in tuberculous dactylitis; Soliter enchondroma, syphilis and pauci articular arthritis.[1, 3, 5]

The Mantoux test is said to be positive in all cases of osseous tuberculosis,[5] the E. S. R. is expected to be elevated.

Histological and bacteriological confirmation requires biobsy before chemotherapy is commenced. Chemotherapy with anti-tuberculous drugs usually will clear the lesion in children.

In the present case, tuberculous dactylitis is observed second proximal phalanx of both hand. The exact reason, why an infected embolus does infect the same phalanx of both hand, is not known.

Summary

A girl of five years presented with tuberculosis of the second proximal phalanx of both hand. The clinical picture of the case, gradual swelling of the proximal phalanges and pain, the treatment was conservative and the result was good.

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Pigmented Villonodular Tenosynovitis

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Introduction

Villonodular synovitis of the tendon sheaths are not uncommon in the fingers. Etiology of the villonodular synovitis is unknown. Most often it is observed as encapsulated, firm, multicolored, lobulated compact tissue mass.

Villonodular synovitis, is a benign tumor, which may arise from the tendon sheaths. The lesion occurs chiefly in the fingers, palm and ankles.[1, 2, 6, 7, 8]

In the series of Jaffe,[4] great majority of the cases, the lesion is to be observed in the finger. The lesion may be located on the flexor or the extensor surface.[1, 3, 7]

Case Reports

Between 1977-1980 seven patient admitted our hospital due to swelling and pain in either hand. Three of them were female and four of them were male. The distrubition of the villonodular synovitis in the fingers showed Table I.

TABLE I
DISTRUBITION OF THE VILLONODULAR SYNOVITIS IN THE FINGERS

No.	Sex	Age	Right Hand	Left Hand	Finger
1	Woman	48	−	+	Thumb
2	Woman	30	−	+	Index
3	Woman	50	+	−	Middle
4	Man	38	+	−	Index
5	Man	52	+	−	Middle
6	Man	40	−	+	Index
7	Man	54	+	−	Thumb

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In two of the cases, which villonodular synovitis are located in the thumb, radiographic examination showed the bones of the first distal phalanx eroded (Figure 1).

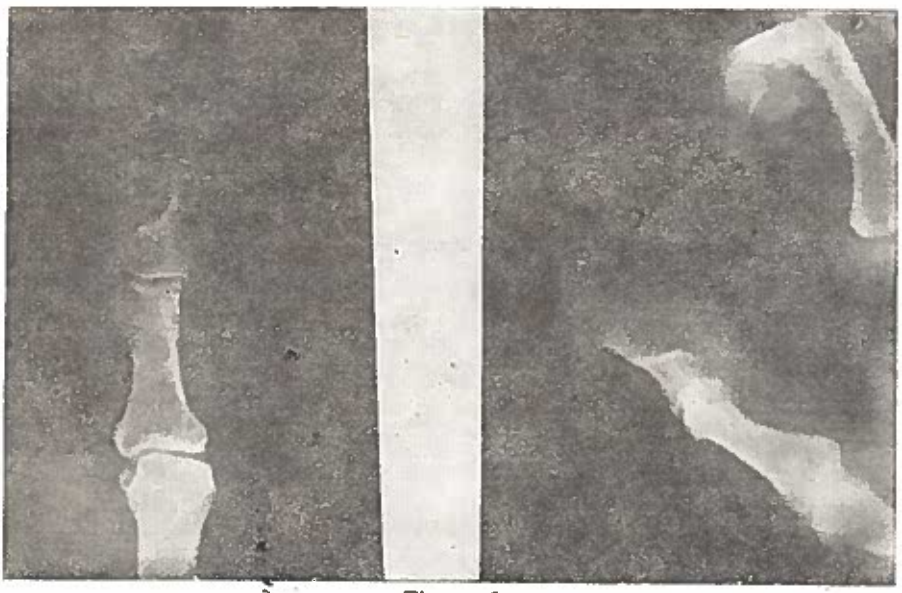

Figure 1

Radioluscent lesion in the distal phalanx caused by extrinsic pressure from a giant cell tumor.

Biobsy were performed in all of the cases, and tumours removed completly. That was appeared to originated from the sheaths of the flexor tendons and no connections to the neurovascular structure.

The microscopic examination revealed a villonodular tenosynovitis.

Discussion

Villonodular synovitis of the finger are benign and tumour located flexor or extensor surface. All of our cases were observed in the flexor surface.

Phalan, Mc Cornach and Gazale[1, 3] in their analysis of 56 tumour of this type found that most of the lesions occured in person between 40 and 60; the sex incidence was almost equal.[3] The tumor occured equally in the right and left hands, most often in the index and middle finger.

From the study of the literature, it seems that the local erosions of the bone are a rare condition.[2, 3, 4, 6] Two of the seven our cases, the tumor eroded the bone (Figure 1). This erosion most probably is due to local pressure of the tumor on the bone itself.

Choice of treatment of these lesions is local excision of the tumor,[1, 3, 5, 7, 8] if the removal of lesion is incomplete, recurrence is normal.

Summary

Seven cases of pigmented villonodular tenosynovitis in the fingers are presented. The clinical picture of all cases are essentially the same, gradual swelling and pain.

Two of the cases, the tumour erodes the bone. This is a rare condition.

Treatment was operative and complet excision of the tumor.

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