SUMMARY

Tranylcypromine, a potent antidepressant agent, has been associated with a syndrome dominated by exceedingly severe, pounding cephalgia.

Our experience with this syndrome is presented, and the literature is reviewed.

Associated symptoms and signs may include chest pain, paroxysmal hypertension, pallor, cold and collapse.

The possibility of confusion with subarachnoid hemorrhage or pheochromocytoma is pointed out, and some severe complications of the syndrome are noted.

Possible mechanisms of action are discussed, and attempts at treatment are outlined.

The syndrome is regarded as a serious and not uncommon complication of tranylcypromine treatment of depressive illnesses; physicians using this agent should be aware of this effect.

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The Diagnosis and Treatment of Tuberculosis of the Breast

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TUBERCULOSIS of the breast is a strange disease, confusing alike to the surgeon, pathologist, bacteriologist and sanatorium doctor. Fortunately it is extremely rare, so that many family doctors have never seen a patient with this disease. Drawing from a population of half a million people, with four University teaching hospitals, a Federal Indian and Eskimo hospital, and a large provincial sanatorium, we have been able to find only five proved cases over the past 15 years. In this period, three times as many cases were tentatively diagnosed by a pathologist as tuberculosis of the breast or "granulomatous infection in keeping with tuberculosis". However, after a hard second look at these cases, employing all of the clinical, pathological, and particularly bacteriological material at hand, we have labelled them "comedomastitis". This syndrome of dilated ducts, toothpaste-like material within the ducts, a foreign-body reaction surrounding the ducts, and even abscess formation, has previously been called "plasma cell mastitis"[1] and "chronic breast abscess".[2] The diagnosis of tuberculosis of the breast applied to many cases in the world literature has been a misnomer; in reality, these were cases of comedomastitis. At the present time we hesitate to diagnose mammary tuberculosis without bacteriological proof; that is, without cultures and/or guinea-pig inoculation *positive* for tuberculosis. Such proof has been obtained in the five cases presented here.

ABSTRACT

Tuberculosis of the breast is a rare disease. It may be primary—confined to the breast, or secondary to tuberculosis elsewhere. Five cases are reported of which three were primary.

The clinician confuses the disease with pyogenic breast abscess and cancer. The pathologist may confuse the disease with comedomastitis. Definite diagnosis must rest on bacteriological proof, that is, positive tuberculous culture and guinea-pig inoculation.

Treatment of the disease may be either medical or surgical. Medical treatment in our hands has been long and expensive, and the disease tends to reappear in further pregnancies. Surgical treatment, which usually consists of simple mastectomy, is preferable.

Besides the confusion existing between tuberculosis of the breast and the syndrome of dilated ducts, it is difficult for the clinician to differentiate the former disease from pyogenic breast abscess and cancer. We feel very humble in this respect, for most of our initial diagnoses have been wrong.

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The breast appears to be peculiarly resistant to tuberculosis. Workers in sanatoria rarely see it. Nagashima,[3] who performed 34 autopsies in patients with miliary tuberculosis, did not find involvement of the breast in a single case; indeed it was the sole part of the body never affected. Morgen,[4] who reviewed the literature to 1931, found only 439 cases, but in only one-quarter of these was bacteriological proof obtained.

The breast was thought to be immune to tuberculosis until Sir Astley Cooper in 1829 described the first case, calling it "scrofulous swelling of the bosum". He felt that the breast was secondarily involved by lymphatic spread from infected cervical and axillary lymph nodes. Most writers still believe that the common mode of infection is retrograde lymphatic extension from primary foci in mediastinal, para-sternal, cervical and axillary lymph nodes.[4-8] However, of the reported cases, 60% have been primary (isolated) cases of tuberculosis of the breast; the remainder secondary to generally widespread tuberculous foci elsewhere. Students of tuberculosis sometimes express the opinion that "most people carry tubercle bacilli which are ever ready to settle out when a suitable nidus is provided and the natural immunity is lowered";[7] such a nidus is provided in the syndrome of dilated ducts of the nipple. In one of the present cases (Case 1—S.T.) the pathologist described the lesion as comedomastitis and was surprised when the presence of tubercle bacilli was later demonstrated. The diagnosis of tuberculosis of the breast was confirmed when guinea-pig inoculation gave positive results. The lactating breast is probably more susceptible to invasion by tubercle bacilli, and three of our other four cases developed in women just before or after delivery.

Other modes of infection have to be considered, such as through the milk ducts by way of the nipple, through abrasions of the skin, by direct extension from the lungs and chest wall, and by the blood stream. In any single case, proof of the mode of infection is often lacking; in our five cases, three were primary—confined to the breast, and two had tuberculosis elsewhere in the body. The three patients with primary disease had had direct contact with patients suffering from tuberculosis.

In our experience, tuberculosis of the breast presents in two ways: (1) As a hard, non-tender lump with perhaps some fixation of the skin and retraction of the nipple. This lesion simulates a carcinoma. (2) As a subacute or chronic breast abscess close to the nipple, particularly in a lactating breast.

In Morgen's[4] review, 75% of the patients presented with a painless lump; in our five patients, only one presented in this fashion, the other four with breast abscesses.

Young women are most often affected, and the common age-group is 20 to 40 years. In the older women, the disease generally presents as a hard mass simulating cancer; in the younger women, more commonly as an abscess. It is nearly always unilateral, only 3% of reported cases being bilateral;[9] and 96% occurred in women, the male breast hardly ever being involved.[4]

CASE REPORTS

CASE 1.—Mrs. S.T., a 52-year-old French Canadian woman, was admitted to the University of Alberta Hospital on April 15, 1961, with a history of a mass in the right breast of one month's duration. The lump had gradually increased in size and was not painful. There had been no discharge from the nipple and no history of trauma.

Examination showed a healthy-looking middle-aged woman with pertinent findings confined to the right breast. Extending outwards from the right nipple, which was moderately indrawn, was a large hard mass, 4 cm. in diameter, which was very slightly—if at all—tender. There was some puckering and adherence of the skin over the mass, but it was deeply mobile. A movable, non-tender, firm lymph node, 1.5 cm. in diameter, could be palpated in the right axilla. Preoperatively, all of the clinicians and the pathologist agreed that the lump was a carcinoma with questionable metastases to the axilla. A radiograph of the chest was negative.

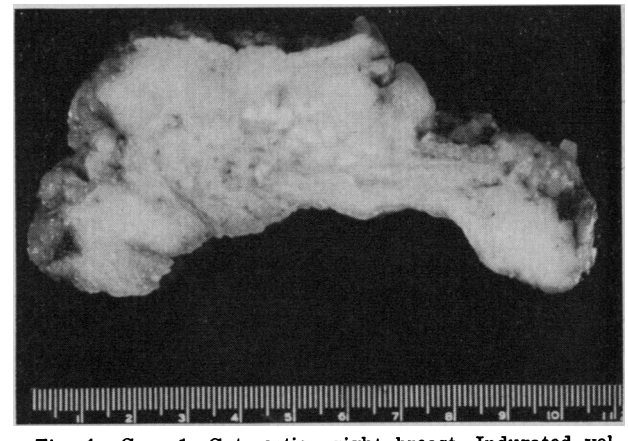

Fig. 1.—Case 1. Cut-section right breast. Indurated yellowish mass with cystic spaces from which toothpaste-like material could be expressed.

The past history was interesting, though unrelated to this illness. In August 1956, one of the authors (T.S.W.) had performed a wide colon resection plus distal pancreatectomy and splenectomy on this woman because of a large carcinoma of the splenic flexure involving the tail of the pancreas. There had been no evidence of recurrence up to the present admission. In 1959, in another hospital, a hysterectomy had been performed for a malignant hydatidiform mole, and since then this woman had been well.

She had never had tuberculosis, nor had any members of her family. However, a cousin had been a visitor in their house for a few days just before being admitted to the sanatorium with active pulmonary tuberculosis.

Surgical treatment for the presumed breast cancer was carried out on April 17, 1961, when a radial incision was made directly over the mass for biopsy purposes. Immediately on incision a considerable amount of greenish fluid was released. The affected

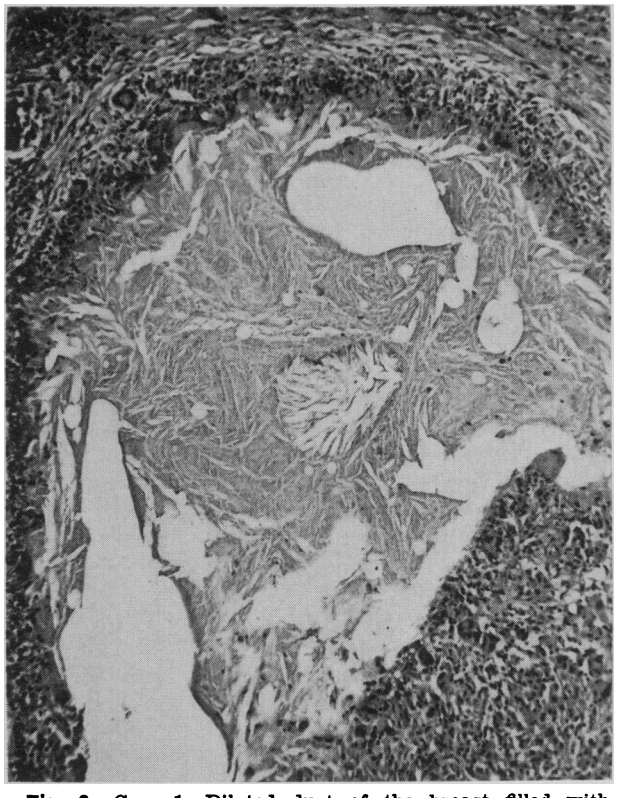

Fig. 2.—Case 1. Dilated duct of the breast filled with amorphous debris. Around the dilated duct, there is considerable inflammatory cell infiltration (× 50).

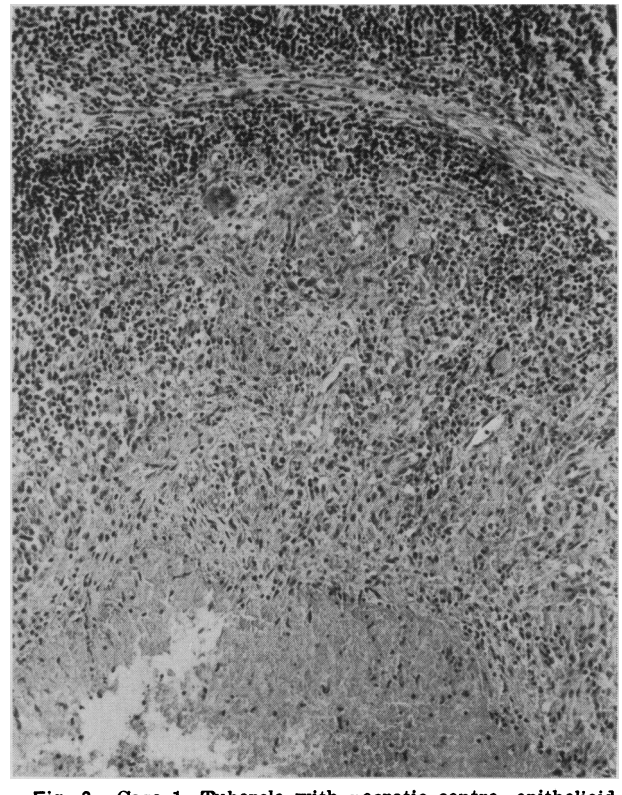

Fig. 3.—Case 1. Tubercle with necrotic centre, epithelioid cells, giant cells, and a fringe of lymphocytes (× 50).

tissue was hard and no definite abscess cavity was encountered. Quick section was carried out in several areas, and the pathologist reported the presence of a chronic inflammatory process localized around the dilated ducts. Because this process involved all of the lateral half of the breast and extensively undermined the nipple, a simple mastectomy was carried out.

The patient did well and was discharged to her home in the Peace River district after 11 days, with primary wound healing. Follow-up by letter on September 19, 1961, revealed that the wound had remained healed and she felt well.

Pathology.—The cut-surface of the breast revealed a firm, indurated, yellowish mass (Fig. 1). There were several cystic spaces from which a moderate amount of thick greenish material with a yellow tinge could be expressed. Further section through the breast revealed a cystic space 1 cm. in diameter containing thick yellowish-green material, situated beneath the nipple. Sections showed the presence of numerous dilated ducts, the lumina of which were filled with amorphous debris. Around the dilated ducts there was considerable inflammatory cell infiltration, leukocytes and plasma cells. Also prominent were many pseudotubercles with necrotic centres, epithelioid cells and giant cells. The centre of these pseudotubercles contained necrotic debris similar to that seen in the dilated ducts (Figs. 2 and 3). Acid-fast stains were carried out as a routine, but no acid-fast organisms were demonstrated. In the pathologist's opinion these were the features of a comedomastitis and the pseudotubercles were sites of foreign-body reaction to the lipoid material which had escaped from dilated ducts. There was no evidence of malignancy. His diagnosis was comedomastitis.

However, at the time of operation some of the murky fluid was sent for direct smear, routine culture and culture for tuberculosis. No acid-fast bacilli were seen on direct smear, and the ordinary culture was sterile. However, acid-fast bacilli were isolated after eight weeks from the culture for tuberculosis. A guinea-pig inoculated from the culture and killed on August 4, 1961, was positive for tuberculosis. The final diagnosis in this case must therefore be tuberculous comedomastitis.

CASE 2.—Mrs. C.Y., a 29-year-old Indian woman, was near term with her eighth child when she was admitted to the University of Alberta Hospital on December 17, 1958, with a history of a painful lump developing in the nipple region of her right breast over the previous month. There was an indefinite history of trauma—a bump on the breast—just before the enlargement was noticed.

On examination, there was a fluctuant, moderately tender mass 3 cm. in diameter under the nipple and just to the lateral side, which was considered to be an antepartum breast abscess. She was afebrile and did not look ill; examination of the axilla was negative. Both breasts were engorged, as one would expect near term. A radiograph of the chest was negative.

This patient had never suffered from tuberculosis herself, but there was an extensive family history. Her mother, two sisters, two daughters and a father-in-law had recently been patients in the sanatorium.

The resident surgeon* very promptly obtained all of the necessary smears and cultures. On December 18, 1958, the abscess was aspirated with a needle and

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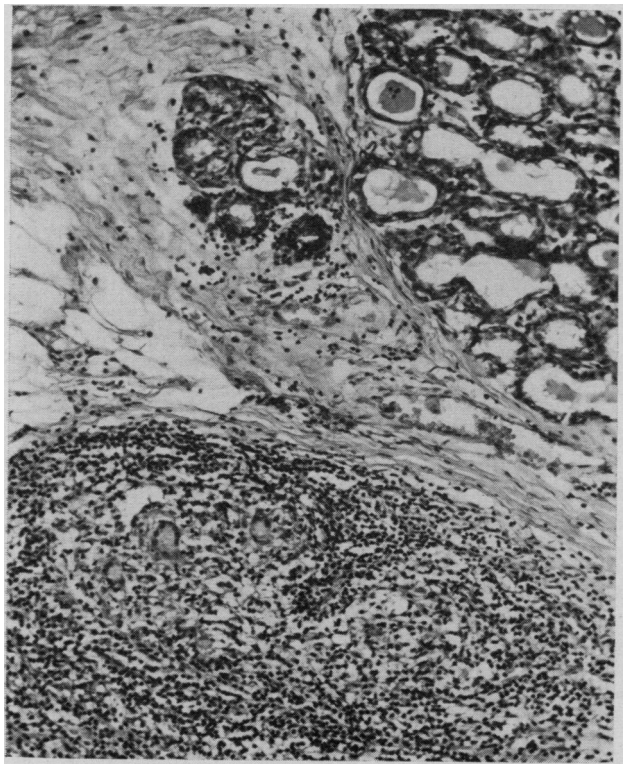

Fig. 4.—Case 2. Small tubercles in abscess wall (× 100). Physiological hyperplasia (pregnancy change) of breast.

syringe, and 20 c.c. of greenish pus was obtained. Acid-fast bacilli were demonstrated on direct smear; culture for *M. tuberculosis* and guinea-pig inoculation were afterwards positive for tuberculosis. Ordinary culture yielded *Staph. albus* only. The abscess cavity was then unroofed and part of the wall was sent to the pathologist.

Pathology.—Sections of the wall abscess cavity contained skin and subcutaneous tissue overlying lobules of female breast tissue which showed physiological hyperplasia. The skin surface was covered by an intact layer of squamous epithelium. No significant inflammatory changes were present in the skin or subcutaneous fat. Breast lobules showed considerable physiological hyperplasia and early secretory activity in keeping with late pregnancy. Tissue comprising the abscess wall was heavily infiltrated with lymphocytes, plasma cells and polymorphonuclear leukocytes. Present in the abscess wall and in the adjacent breast tissue were scattered, small miliary tubercles composed of epithelioid cells, fibroblasts, multinucleated giant cells of Langhans' type and lymphocytes (Fig. 4).

The diagnoses were those of (1) a subacute abscess of the right breast, probably tuberculous, and (2) physiological hyperplasia and secretory activity (pregnancy change).

The patient was delivered of a normal healthy infant on January 7, 1959, and was transferred on January 13 to the Aberhart Memorial Sanatorium, where she was retained for four weeks. Therapeutic doses of para-aminosalicylic acid (PAS), isoniazid (INH) and streptomycin were administered and the drainage ceased. When she returned home she neglected to take these drugs and the abscess began to drain again. It was still draining on July 3, 1959, when she was re-admitted to the University of Alberta Hospital for subacute appendicitis and appendectomy. Following this operation, she was sent to the Aberhart Sanatorium and retained there from July 13, to October 7, 1959. A radiograph of the chest again was negative, the sputum was negative and on several occasions urine culture and guinea-pig inoculation were also negative. The antituberculous drugs, INH and streptomycin, were again administered because she was unable to tolerate PAS. The patient was instructed to take them for three months. At the time of her discharge from the sanatorium the drainage had stopped.

At home she remained well until May 1960, when the breast became painful and drained spontaneously for one week. Pain and swelling in her right breast recurred on August 12, 1960, and she was again sent to the Aberhart Sanatorium and remained there from August 19, 1960, to January 11, 1961. On admission, there was a diffuse tender mass deep to the nipple, but no fluctuation. A chest radiograph and sputum and urine cultures with guinea-pig inoculation were again negative. She was about two months' pregnant. She was again placed on INH, streptomycin and PAS; this time she was able to tolerate the last-named drug. On this regimen the mass became smaller and less tender and there was no drainage. The total administered dose of drugs was at least 252 g. of PAS, 58 g. of INH and 59 g. of streptomycin.

The patient has not been seen since discharge. A tuberculous process had been present in her breast, in various states of activity, for over two years despite fairly intensive medical treatment. She also occupied a bed in the sanatorium for nine months, the breast being the *only* focus of tuberculosis, as far as could be determined. She may or may not be cured of disease at the present time.

CASE 3.—Mrs. L.T., a 20-year-old woman, first noted a lump in her right breast in August 1958, shortly after delivery of her first baby. It was not bothersome and she did not seek medical attention until March 1959, when she was in the sixth month of her second pregnancy. At that time she was admitted to the Royal Alexandra Hospital because of this mass. The lesion was under and medial to the right nipple, measured 3 cm. in diameter and was fixed to the skin but not to the deep fascia. She was afebrile; the mass was not warm and only moderately tender. The axilla was negative. Biopsy of the mass was carried out on March 25, 1959.

Pathology.—The specimen had been cut in half and revealed a focus of granulation tissue in relation to a cyst wall which measured 2 cm. in diameter. Further sectioning revealed numerous other areas of cyst formation with a shaggy, variegated yellowish-red granulomatous tissue. Microscopic examination of the cyst showed a lining of granulomatous inflammatory debris, including large numbers of giant cells with epithelioid proliferation but no typical caseation, and questionable tubercle formation (Fig. 5). Special stains failed to show acid-fast bacilli. The pathologist assumed that the granulomatous reaction was secondary to duct ectasia and called the lesion "granulomatous inflammation of the breast". However, 10 weeks later, guinea-pig inoculation was positive for tuberculosis.

The patient was admitted to the Aberhart Sanatorium on May 29, 1959, with a discharging sinus medial to the nipple at the site of the biopsy. A 2-cm. mass was present deep to the sinus. A radiograph of the chest and sputum and urine culture with

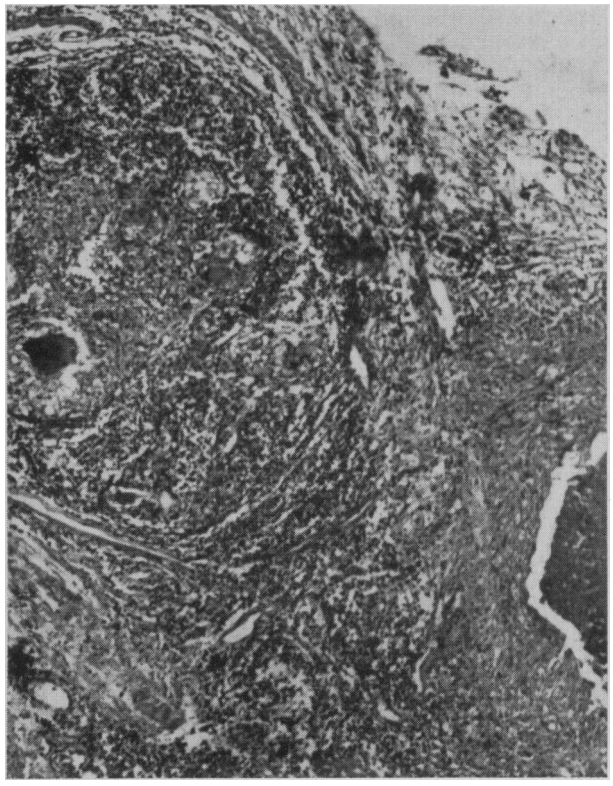

Fig. 5.—Case 3. Giant cells, epithelioid cells, and questionable tubercle formation (× 100).

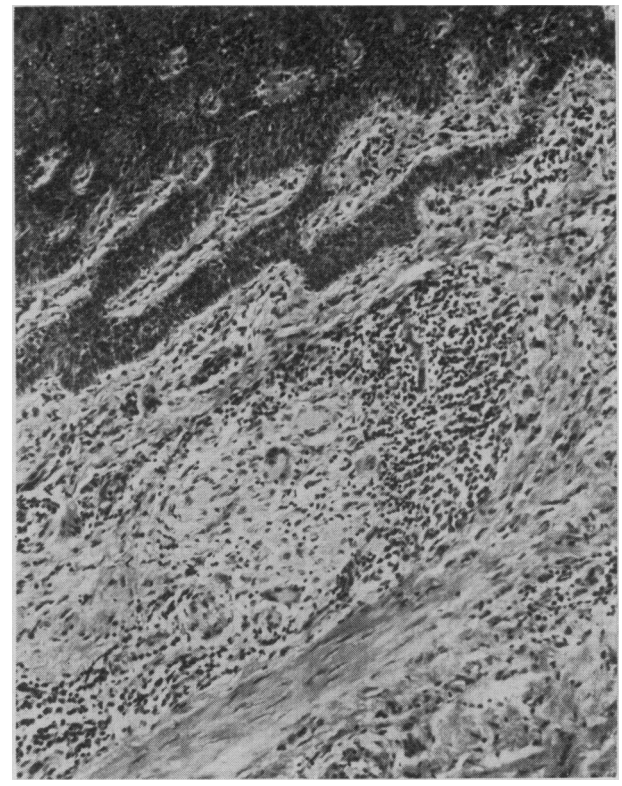

Fig. 6.—Case 4. Chronic granulomatous reaction beneath skin with giant and epithelioid cells and lymphocytes (× 100).

guinea-pig inoculation were all negative. She had never had tuberculosis, but her mother had pulmonary tuberculosis and was in the sanatorium. The patient was given INH and PAS in therapeutic doses. She was delivered of a normal child on June 8, 1959. She was finally discharged from the sanatorium on July 10, 1959, at which time the sinus had healed but a large mass was still present in the breast.

She was readmitted to the sanatorium on March 31, 1960, again five months' pregnant, with a history that the mass had enlarged, broken down and drained one month before admission. She was given INH in a total dose on both admissions of 17 g., and PAS, a total dose of 660 g. At discharge on June 17, 1960, the sinus had healed and the mass was smaller. She delivered a normal child, her third, on July 2, 1960.

As far as is known, she has had no complaints relative to the breast since, but she was a difficult patient who signed herself out of hospital. It is known that she had an active tuberculous process of 18 months' duration confined, as far as could be ascertained, to her breast, and that she spent five months in a sanatorium under adequate medical treatment. It is not known whether she is cured. When last seen in June 1961, the mass was small and there was no discharge.

CASE 4.—Mrs. S.T., a 31-year-old Indian woman, six months' pregnant with her sixth child, was admitted to the Fort Simpson Hospital in April 1960, with an abscess of the left breast, close to the nipple. It was incised and drained. Acid-fast bacilli were present on direct smear, and afterwards tuberculous culture and guinea-pig inoculation were positive. She was placed on INH and PAS, and the drainage ceased after one month. She had a normal delivery July 27, 1960, and was transferred for assessment to the Charles Camsell Indian Hospital in Edmonton on August 18.

At this time there was a nodular mass under the left nipple but no drainage. One surgeon advised simple mastectomy, but the weight of opinion favoured medical treatment and she was returned to the Fort Simpson Hospital for six months' treatment with INH and PAS. A radiograph of her chest was negative.

Her past history was interesting because she had had three separate postpartum abscesses in her left breast in 1956, 1957 and 1959. *Staph. aureus* had been cultured but no tubercle bacilli. In August 1959, a chronic sinus which developed following a breast abscess was biopsied at the Charles Camsell Hospital. This was reported as "chronic granuloma—possibly T.B.—with superadded pyogenic infection". The biopsy contained skin and subcutaneous tissue and showed giant cells, epithelioid cells and acute and chronic inflammatory cells but no true tubercles (Fig. 6).

This patient had pulmonary tuberculosis in 1949, but was presumed to be free of tuberculosis since that time, except for the lesion in her breast, described above. An exceedingly strong family history was elicited: four of her children, a brother and a sister-in-law had had pulmonary tuberculosis.

The patient underwent cholecystectomy for gallstones in July 1961 and made an uneventful recovery. At this time there was no obvious mass in the left breast and no discharge; presumably her mammary tuberculosis had healed.

CASE 5.—Mrs. D.S., a 22-year-old Indian woman, had a fusion of the right hip in June 1948, for presumed tuberculosis of the joint. Unfortunately, the diagnosis was never proved by bacteriological means. While still in hospital, she developed an abscess in the

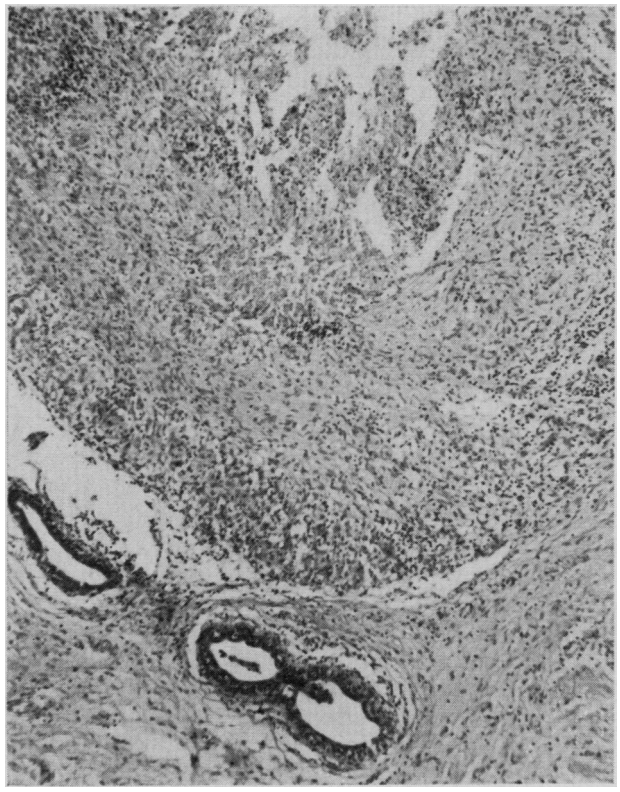

Fig. 7.—Case 5. Tubercle showing caseation, epithelioid cells and, at the periphery, lymphocytes. In the bottom left-hand corner ducts of the breast are seen (× 50).

right breast which extended from beneath the nipple upwards and outwards, the whole mass measuring 2.5 cm. in diameter. This abscess was unroofed on November 1, 1948. No acid-fast bacilli were identified on direct smear but subsequent guinea-pig inoculation was positive for tuberculosis. Pathological examination of the abscess resulted in the report of "acute inflammation".

In September 1949, because of excessive menstrual flow, a diagnostic curettage was performed; the material so obtained gave positive evidence of tuberculous endometritis. From October 26, 1949, to February 13, 1950, she was in the Aberhart Sanatorium and received two therapeutic courses of streptomycin of 42 g. and 44 g. each. At that time a radiograph of the chest, an intravenous pyelogram, and sputum and urine cultures were all negative.

In January 1953, she was admitted to the University of Alberta Hospital with a history of a mass in the right breast of one month's duration. The mass was close to the nipple and undermined it. It measured 1.5 cm. in diameter, was very slightly tender and was questionably fixed to the skin. It was quite hard and extended from the nipple upwards and outwards, similar to the previously described mass. The lump was removed on January 13, 1953. Some fluid material in the centre of the mass was examined and acid-fast bacilli were seen on direct smear. Guinea-pig inoculation was afterwards positive for tuberculosis.

Pathology.—Microscopic sections showed a tubercle of the breast with caseation, epithelioid cells and lymphocytic infiltration at the periphery. In the bottom left-hand corner of Fig. 7 are seen the ducts of the breast.

The surgical incision healed but broke down and began to drain on July 1, 1953. She was readmitted to the sanatorium on July 3, 1953 and remained until November 14, 1953. During this time she received 29 g. of INH and 1396 g. of PAS. The mass, 2 cm. in diameter, deep to the previous incision subsided to a small indurated area and the drainage ceased.

This patient has not been seen since that time and it is not known whether she is cured or not. She was in the sanatorium for eight months—half of this time because of mammary tuberculosis.

DISCUSSION

Judging from our own records and from a perusal of the world literature, tuberculosis of the breast is a rare disease. It may be primary and confined to the breast, or secondary to tuberculosis elsewhere. In a period of 15 years, we have seen only five proved cases, of which three were primary. The mode of infection is unknown, but tubercle bacilli may settle out in the breast if a suitable nidus of lowered resistance is present. We propose that such a nidus is provided in a lactating breast, or in one with the diseased and dilated ducts of comedomastitis.

Diagnosis is extremely difficult. An awareness of the rarity of the disease may make any clinician hesitate to name it, and the pathologist loath to confirm it. Indeed, the pathological picture of the syndrome of dilated ducts, with its giant, epithelioid and chronic inflammatory cells, may mimic tuberculosis so closely that bacteriological confirmation of the diagnosis is imperative; this is provided by positive culture for tuberculosis and/or guinea-pig inoculation. However, in our experience the commonest way in which the disease presents is as an abscess, close to the nipple, particularly in a lactating breast. If a woman with such a lesion also gives a history of tuberculosis or has been exposed to tuberculosis, a search should be made for acid-fast bacilli by direct smear following a Ziehl-Neelsen stain, and culture and guinea-pig inoculation for *M. tuberculosis*. Most "chronic" breast abscesses close to the nipple are caused by a chemical or comedomastitis, secondary to dilated and diseased ducts. In most cases these abscesses are sterile.

Mammary tuberculosis is not a particularly serious disease. Our first patient was cured in 11 days after a simple mastectomy. The other four patients had long periods of sanatorium care, averaging seven months, during which considerable amounts of antituberculous drugs—streptomycin, para-aminosalicylic acid and isoniazid—were administered. On this regimen, drainage stopped and the masses became smaller. The disease in such patients may not be cured but may recur, particularly if the patient becomes pregnant, as in Cases 2, 3 and 4 in this series. Therefore we believe that the proper treatment of tuberculosis of the breast is surgical; in most cases simple mastectomy. If the disease is localized to a small segment, a wedge excision might be curative. However, since in most cases the disease is close to and undermines the nipple,

the nipple and areola should be removed. In the much commoner chronic breast abscess due to dilated ducts, we believe that such wedge excision of the nipple, areola and dilated major ducts, with the small abscess in continuity and as a block, is the proper treatment.

SUMMARY

Some of the problems encountered in the diagnosis and treatment of mammary tuberculosis are discussed. Diagnosis must rest on bacteriological proof. Five cases are presented in some detail.

Once the diagnosis is confirmed, the treatment is surgical, and consists of simple mastectomy.

We wish to thank Dr. H. H. Stephens, Director of the Aberhart Memorial Sanatorium, Dr. S. Hanson, Pathologist, Charles Camsell Indian Hospital, Edmonton, and Dr. P. W. Davey, Pathologist, Royal Alexandra Hospital, Edmonton, for their help and interest.

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The Metabolism of the Volatile Amines:

V. The Spontaneous Formation of Ammonia in Shed Blood on Standing

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ONE OF the major problems associated with the measurement of the blood ammonia levels is that the ammonia content of whole blood, termed "free" ammonia in order to differentiate it from the ammonia produced by the alkali reagent, increases rapidly after it is shed.[8] It is thus necessary to measure the blood ammonia levels as soon as possible after the blood is drawn if a useful determination of the ammonia content is desired. It is the purpose of this paper not only to discuss some of the factors which appear to influence this ammonia formation and to suggest a means of partially inhibiting the reactions involved but also to present some preliminary data which introduce the hematological significance of this phenomenon.

Conway[1] was the first worker to investigate and discuss the nature of the formation of ammonia in shed whole blood. Although many investigators have not been able to duplicate his findings,[2, 4] others[5] agree with his theory that there are at least two phases in the formation of ammonia in shed whole blood. He termed the first the "alpha phase" and said that it was very rapid, was due to the evolution of carbon dioxide from the blood, and took place over the first three to five minutes after the blood is drawn. He said that the second or "beta phase" was slower, and was probably associated with the enzymatic breakdown of adenyl pyrophosphate and adenylic acid. Conway also described the possibility of a third or "gamma phase" which Archibald[6] suggested was derived from the breakdown of glutamine-containing compounds.

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ABSTRACT

The spontaneous formation of ammonia which takes place when shed whole blood is allowed to stand was investigated and was found to consist of a complex series of reactions. The rate of ammonia formation was initially rapid but gradually slowed, and the maximum amount of ammonia was formed after a period of about seven days. Both the type of anticoagulant used and the availability of oxygen influenced the rate of ammonia formation. This reaction was inhibited when the blood was kept frozen but it was found that the measurement of the ammonia content of frozen and thawed blood was both difficult and inaccurate. Dilute solutions of zinc bromide partially inhibited this reaction.

Compounds which give rise to ammonia were found to be present in both plasma and erythrocytes, although the deamidation reactions took place solely within the erythrocytes. The total amount of ammonia formed depended on the hemoglobin content of the blood and varied in certain patients suffering from erythrocyte disorders.

METHODS AND MATERIALS

The blood ammonia levels in the present study were determined initially by the microdiffusion technique,[1, 7] although the microaeration technique was used exclusively after it had been developed.[8] Since certain aspects of this work were completed before the method