REVIEW OF LITERATURE
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History:

Phlyctenulosis is an old disease. Crude description of it are to be found in the Greek and Arabic literature and in Byzantine times. It was given considerable study by Paul of Aegina (c. 625 - 690). C. de Saint Yves (1722) was first to define the modulator conjunctivitis with characteristics of disease in his classical book.

Wardrop (1808) depicted the typical clinical picture with a plate in his Essay on the Morbid Anatomy of the Human eye.

Beer in 1813 attempted to give an aetiological classification of ocular diseases, scrofulous ophthalmia come to stand for a variety of conditions, of which a scrofulous diathesis was assumed to be the cause of phlyctenulosis.

Ivanoff (1869) was first to investigate the pathology of phlycten. Later histological examination of conjunctival phlyctenule was done by (Hartel, 1969; Hochel, 1900; Liver, 1901; Hayashi, 1909; Wecker, 1910; Fiesberger, 1923; Stargardt, 1925).

The conflict between the aetiological and the anatomical approach to the eye disease led on the one hand to the histological study of the phlycten by Ivanoff and on other, to the assumption of diathesis other than
scrofula as the cause of the affection. It is thus that
esoma was suggested by Morner in (1880) as the cause of
eye condition.

With the advent of bacteriology many observers
tried to isolate a hypothetical causative organism, but
failed. Almost every one of the organism commonly
present in the conjunctival sac, was incriminated and
for a time staphylococcus-aureus almost gained
acceptance.

Towards the end of century, general feeling was
once more turning towards endogenous factor as cause of
the phlycten, the scrofulous diathesis once again come
to the forefront, but meanwhile bacteriology had
demonstrated that the scrofulous joints and glands were
tuberculous in origin and scrofulous assumption of
phlycten as tuberculous likewise, could not, however,
be verified.

With the introduction of the tuberculin test by
Van Pirquet in 1907, the significance of tuberculosis
in phlyctenuisis again become apparent and was emphasised
by frequent occurrence of phlyctenule in the kerato-
conjunctivitis produced by the ophthalmic tuberculin test
of calmette and wolff esner. It was suggested that
phlyctenule was an allergic response to circulating tuber-
culous product in a patient with minimal tuberculosis and
this is the theory of etiology, which has to date received
the widest acceptance.
At the beginning of century (20th), after the search of tubercular bacilli in the phlycten had proved vein, many workers tried to produce tuberculous lesion by injecting phlyctenular material (Lever, 1901; Muller, 1901), but fruitless, while other hand phlycten was produced by injection of tuberculin in non-immunised rabbit (Guillery, 1921).

At-Hassan et al (1977) gave association of phlycten with helminths as given by other observers. Laurell, 1926; Jeffery, 1955) and even antibodies against M. Nana (in 1979) has been demonstrated with great association of phlycten with M. nana.

Recently workers have experimentally developed the phlyctenular and catarrhal infiltration in rabbit immunised with a preparation of staphylococcus aureus cell walls mixed with complete freund's adjuvant. (Mardine, 1982)

Though a lot of work have been carried from the day of notification to present days still, we have not come to anexact etiology, while tubercular protein, as an endogenous, factor has top of acceptance.

**Incidence**

Phlyctenulosis showed a great decline in incidence as noted by Walker (1928); Golden berge (1930); Balantyne (1936); Golden (1936) and Barretta (1938) in their countries.
Warner (1928) has found a progressive decline from 13.4% in 1901 to about 4% in the period 1923-26, while there was reported stationary.

Rolet (1931) reported that in the period of 1906-10, the incidence of a phlyctenulosis was 8.2% of total number of patients and it was only 3.6% in 1926-30.

Rochem (1932) found incidence of phlycten between 1914-30 declined from 8.7% to 1%.

Redding (1935) found a steady decline during a period of 1912-32. While Burgin and Higgins (1938) reported a continuous decline over a period of 25 years. The 384 cases were seen between 1910-19 and only 54 were seen between 1930-34.

Essen Moller (1936) in his report gave decreased incidence of phlyctenulosis for period of (1909-33) from 9.8% to 1.5%. While Meinonen (1936) found it from 1.5% to 0.5% during a period 1928-34.

A graph produced by Redding (1912-33) shows a marked decline of cases and particularly in 1925-23. Number of cases falling from about 575 in first year to about 375 in last year. Graph given by Freminopoulos revealed decline of number of cases from 400 in 1924 to 40 in 1937.

Boshkott (1939) saw a decline from 1359 cases in 1920 to about 250 in 1925.
In contrary to the decline incidence of phlyctenulosis, there has been reported an increase in the number of cases in period from 1912 to 1932, from Hôpital Bicêtre of Paris and consistently higher incidence of it during 1914 war and aftermath.

Though Rochat (1932) reported steady decline incidence of phlyctenulosis (8.7% to 1%) for period of 1914 to 1930, but it was not applicable for period of 1914 to 1917, when number of cases remained stationary and slightly increased in end of 1918.

Warner noted an increase number of cases for period of 1918-22. Similar observation was found by Kassner (1921) and recorded a rise of 4% in pre war year to 7% in 1919.

Though phlycten has been reported decline in incidence in developed countries but can be found sporadically and still a serious problem of developing countries because of corneal scarring after phlyctenulosis which gravely affects the visual acuity, being a factor of blindness.

It has also been reported parallel incidence to the tuberculosis (Thygeson, 1951).
Thygeson (1948) noted the report of Fields, who stated that 20% to 50% of children in many Alaskan native village had corneal scar seen due to phlyctenulosis.

Marshall reported higher incidence of corneal scar due to phlycten affecting in Indian and Eskimos.

Duggan et al (1958) reported incidence of 17.2% as evidence of past of present phlyctenulosis.

Clyde Farsen (1961) reported in a series of 166 individual 19% an established phlyctenulosis and less well established about 40%.

Age

Phlyctenulosis is essentially a disease of children and young adult age group. Most commonly occurring in first and second decade of life (Duke Elder).

Statistical evidence of various observers reveals that the peak period is between the age of 2 year and 15 years (Gutmann, 1939; Krasse, 1928; Granholm, 1928; Rolet, 1931; Essen Muller, 1936; Sorsby, 1942; Mathieu, 1947), but the disease may occur before the third and after 80th years of life.

Phlyctenulosis in tropical countries appears to have clinically and possibly also histologically different from those seen in Europe and United States.
In India Herbert (1898) noted that more than 33% of cases occurred in patients over 20 years of age. In Japan Kubuki (1924) found the affection predominantly in adults. Yamaguchi (1937) gave the peak age as 16-20 years.

Thygson (1951) in Alaskan series observed peak age at 16 years. Youngest patient at 4 years of age and oldest 27 years of age. The earliest age at which he noticed active phlyctenulosis was a 4 month old white child in California.

Milo H. Fritz et al (1951) observation reveals the development of phlyctenulosis in older children and in adults. Besides the pre-school children two youngs of age groups10 years, two oldest of age 18 years and 19 years.

At-Hassaini et al (1979) in the series of 417 patients suffering from phlyctenulosis found maximum incidence under 10 years of age group than 11-30 years and least alone it, as 56.48%, 31.63% and 11.86%.

All observers agree that phlyctenulosis is more common in female than male. Incidence of phlyctenulosis ranges from 60% to 70% as given by Carrell, 1929; Wechser, 1929; Trenimopoulos, 1940; Sorsby, 1942; Set et al, 1963.
Culimen (1898) noted that the difference in sex incidence becomes apparent at about the fifth year of life and increases with age. He produced elaborate evidence about sex incidence and gave fact that affection of phlyctenulosis in female is twice common as in male, eg. 69.2% in female and 30.8% in male of 3973 patients.

Cohen (1909) also supported same in series of 121 cases of phlyctenulosis seen in patients over 15 years of age, gave sex ratio as 37 to 63 males to females.

Sersby (1942) reported an observation of study of a period between 1928-1940 as 60.9% in girls and 39.1% in boys.

Thygesen (1951) has also reported the sex incidence in the favours of older observers. He found only 3 male cases out of 10 cases of active phlyctenulosis.


Seasonal incidence:

The incidence throughout year is not alike as noted by observers. There was increase number of cases in spring (Mossely, 1919; Schwann, 1937). Maximum
incidence was reported in April to June by Kassner (1921), March - May by Savin and Preston (1925), January - April by Harmen (1925) and Rylett April by Carvill (1929), whilst Kenney (1932). The peak period was in July and September as month of lowest incidence.

Zanker et al (1964) reported that there is no co-relation between occurrence of phlycten and weather of the same day. 40% appeared on one day after a change of warm air and the appearance of high pressure area.

Etiology:

Tuberculosis:

The cause of phlycten has long been disputed. No specific organism has ever been recovered from the lesion to show a specific type of lesion. A number of etiological factor have been stated, but allergy to bacterial protein of tubercle bacilli has got most acceptance. Even this concept has been questioned and claims have even been made from the experimental production of phlycten by ordinary protein such as horse serum and pollen and cell wall proteins of bacteria eg. (Staphylococcus auris).

It is known fact that tubercle bacillus has not been isolated from the lesion and its implantation in conjunctive produces tuberculcar lesion, rather producing the phlycten a negative evidence.
There are some supportive findings in the patients of phlyctenulosis as high incidence of positive tuberculin test, high incidence of radiographically demonstrable tuberculous chest lesion, high incidence of a history of past or present tuberculosis, positive family history of tuberculosis, high incidence of subsequent tuberculosis. Significant incidence of after tuberculosis, worldwide parallelism between the incidence of tuberculosis and phlyctenulosis. (Well response to anti-allergic therapy) go in the favour of accepted theory that it is an allergic response to the protein of tubercle bacillus.

**Positive Tuberculin Test:**

Since introduction of Van Pirquet test 1907 and its subsequent modification, a high percentage of positive tuberculin reaction has been reported in phlyctenular cases. It varies from 60% - 100% with an average 80%.

Data of various observer from 1907 to 1940 presented by Sorsby (1942). There were about 6000 cases with a positive tuberculin reaction minimum 60% (Burgin and Higgins, 1938) (Mx. test) and maximum 100%. By (Walker, 1910; Stevenson and Janieson, 1910; Redner, 1911; Wood, 1918; Casparis, 1927; Lemoine, 1927; Kamke, 1930; Towbin and Rauvic -Scarbo, 1930; Franinospeules, 1940). Exceptional report of series reported by Burgin and Higgins (1938). The case (7 of pseudophlycten) given by Been.
Lion (1930), the early series of Burn (1912) and small series of 27 cases reported by Elder (1931), no observation found an incidence of less than 70% positive reaction whilst most gave a higher incidence.

This finding remains same for a sub-series of 960 cases of children under 6 years of age. Here the mean percentage is 78.3%. If the series of Burgin and Higgins, who gave an incidence of 60%, is excluded. The percentage of positive result ranges between 74 and 94, a statistically significant after comparing with normal.

Self study of Sorby (1942) in which tuberculin test in 592 cases of phlyctenulosis he found tuberculin positivity in 84.4% against 15.3% in 900 cases of blepharitis as control.

Phygen, P (1931) has also reported a constant positive tuberculin test in phlyctenulosis. From the observation of tuberculin test in Eskimo and Indian school children (1949) 100% positive test was found whether phlycten was active or inactive.

Forsen (1961) in a group of 164 Eskimo aged ranging from 6.5 years to 10.5 years studied the correlation between phlyctenulosis and tuberculin skin reaction. Of 110 tuberculin positive children 19% had established phlyctenulosis and 48% less well established case.
Srivastava et al (1983) conducted an immunological study of phlyctenulosis at T'cell level. Simultaneously PM test was done and found 13 were mantoux positive and 8 were mantoux negative out of 21 cases.

Radiological evidence:

Weekers and Calmant (1922) reported the radiological evidence of active tuberculosis in 36 cases and Roser in 50 cases.

Stalder (1926) studied 100 cases and found 64 with active tuberculosis against definite negative 6 cases.

Carvell (1929) found evidence of active tuberculosis radiologically in 48.5% of a series of 350 cases.

Greener (1931) in a series of 150 cases evidence of tuberculosis in all cases, 31.8% showing fresh lung lesion and 69.2% inactive lesion.

Sive (1934-1935) recorded high incidence in children under 4 years of age and decreasing incidence with advancing age. In series of 140 cases active tubercular lesion was found in 75% of children under 4 years, 50% in age group of 4-7 years, and 20% in 7-13 years.

Data presented by Burgin and Higgins (1938) shows decreased incidence. On 502 cases of phlyctenulosis, they found 109 "clinical tuberculosis", 94 of whom were cases of tuberculosis of hilus, 11 of other glands 2 of
peritoneum and meningeal. All cases were of "primary" or "childhood" tuberculosis and subsequently were not immediately series only 3 patients were critically ill with tuberculosis. Colume (1933) in series of 31 cases mostly adult of about 20 years of age found radiological evidence in all cases, 7 showing inactive lesions and remainders were active cases.

Pascheff (1935) gave hilus changes in 91% of his cases.

Urbank and Roschott (1939) in a series of 160 cases found that only 59 were negative both radiologically as well as clinically.

Fremopoulos (1940) in a series of 61 cases radiological evidence of tuberculosis in 30 cases of which 5 were showing clinically too.

Sorsby (1942) analysed 510 cases and found 358 or 71.2% with radiological evidence of tuberculosis and only 60 or 11.7 percent, definitely negative.

Thysen (1951) stated that demonstrable radiological evidence of primary tuberculosis was found in all cases of phlyctenulosis in Alaskan series of his study without a control series.
Clyde Fasson (1961) in his series of 169 Inhime children, found none of entire group was with extensive scarring infiltrates on chest X-ray examination. All were reported negative, primary inactive or primary arrested except two.

**Tonsils and Adenoids:**

Gold bach (1977) observed 6 times tubercle bacilli in extirpated tonsils of series of 16 cases.

Mann (1920) reported 10 cases of phlyctenulesis which were affected by removal of tonsils and adenoid. Off these 10 cases 3 were examined histologically. Tonsils showed tuberculous lesion in one, adenoids in another and remaining two cases no tuberculous could be found.

Von Toth (1930) reported the result of operation on 80 cases. In four out of seven cases in which the tonsils were studied histologically tuberculous.

Sorsby (1944) during period between 1936 - 1938 examined 184 cases of phlyctenulesis and 414 cases of other affections for the evidence of a difference in incidence of nasopharyngeal septis in 184 cases of phlyctenulesis. 35 cases showed Tonsillar septis against 70 in controlled group of 414. Tonsils removal was made in 20 cases of phlyctenulesis but tubercle bacilli could not be detected.

**History of Tuberculosis (personal):**

Suggestive history of tuberculosis in the patient of phlyctenulesis has been found by many observers, even
Cohen (1909) in the series of 123 cases in adult found evidence of incipient pulmonary tuberculosis in 63.4% and considered the phlycten as an initial stage of pulmonary tuberculosis.

Rosenhauck (1910) observed pulmonary tuberculosis in 20 out of his 50 cases localization being: Chest, 13; bone, 6; and pleura 1.

Kird (1916) found tuberculosis in 23 out of 30 cases lesions including lungs, 12 (including active and healed).

Gold beck (1917) series of 39 cases found pulmonary tuberculosis 7 times, of wrist 1; & hip 1.

Nawak (1922) reported more than half of his group of 260 adults with phlyctenular ophthalma had active lung tuberculosis.

Stalder (1926) observed 47 cases of active pulmonary tuberculosis in his series of 100 examined radiologically.

Wittenton (1926) noted 25 cases of phlyctenulosis of which 22 had active tuberculosis, 14 being bone tuberculosis and 6 gland tuberculosis.

Carvill (1929) recorded 175 cases of tuberculosis in a series of 350 cases of phlyctenular ophthalma. Of these lungs-29; meninges-2; spine-5; hip-1; heel-1; Shin-1; cervical glands-25; and paribronchial glands-79; (Radiologically).
Fuscarino and Lasaressen (1935) in 468 patients under age of 20 years found glandular tuberculosis in 220 cases, pulmonary-13, bone-7, 4 cases each of skin and joints tuberculosis.

Siwe's (1935) in group of 140 children including 8 cases of pleurisy 6 of skin tuberculosis, and 3 of brain and meninges.

Heinemann (1936) observed 7.3% cases of tuberculosis of various part in a series of 301 case. In 11000 school children, 2.6% cases of phlyctenulosis noted, of which 23.5% were sufferer of cervical lymphedineopathy against 10.1% of control group.

Sorsby's (1942) series of 592 cases with phlyctenulosis 38 had clinical tuberculosis of these 26 cases of active pulmonary including cervical gland, bones and meninges tuberculosis.

Thygren (1951) observed a low incidence of tuberculosis, in his series of active and inactive cases of phlyctenulosis 33% school children, and 43% children from orthopaedic hospital of these 33.3% were suffering from tuberculosis.

Instead of giving high incidence of active tuberculosis in phlyctenular cases. Some observers have
stressed the absence of tuberculosis in patients with phlyctenulosis (Goldenberg, 1917; 1930; Golden, 1936; Davis and Vaughan (1912) found none in the series of 40 cases, Savin and Preston (1935) one in 50 and Norman (1925) 8 in 242 cases.

A number of observers have reported the association of phlyctenulosis in erythema nodosum (Neumann, 1933; Nohocourt and Duans, 1934; Jacquet et al, 1938; and Garcia Montes and Silva, 1938).

Grenet and Langlois (1934) described the occurrence of phlyctenulosis in a child suffering from tuberculosis of skin and mucosa of the nose and pharynx.

Rossett (1936) observed phlyctenulosis in a case of tuberculous conjunctivitis.

**Family history of tuberculosis:**

It is not directly concerned to the problem but definitely has relation indirectly. This has been considered by very limited observers who found family history of tuberculosis.

Davis and Vaughan (1912) found family history of tuberculosis in 17% members of the family of 40 cases.

Weekers (1910) reported a positive family history 60 times in 156 cases and Blair (1924) 20% of 305 cases. Stephenson and Jameson (1910) reported 75% and Cohen (1909) 63% in 133 adults suffering from tuberculosis.
Savin and Preston (1925) took history of tuberculosis in the family members of his 50 cases of phlyctenuleosis and found 24 deaths from tuberculosis and 9 of illness, did not consider that this represented an undue incidence as compared with the general population of a corresponding social status.

Carvill (1929) found that 77 (22%) of his 350 cases had contact with tuberculosis patients, through 32 out of 77 showed no evidence of personal tuberculosis. In 33 instances one parent had died from tuberculosis, in 2 cases both parents, and in 7 cases, a sibling; active tubercolulosis was present in 17 parents and 14 sibs. In 10 cases in which more than one of a family member was affected with phlyctenuleosis. The tuberculosis in the home was found in six instances. Burgen noted positive family history of tuberculosis in 22% of his 502 cases. Friedenwald and Robertson (quoted by Wood, 1932) found 20 instances of open tuberculosis in the social environment of 21 cases of phlyctenuleosis.

Sorsby (1942) in a series of 363 cases of phlycten reported the positive family history of tuberculosis in 76 (20.9%), while 187 (71.1%) negative. Agreement to the high incidence of positive family history of tuberculosis in phlycten cases, true to all groups whether white, Negro, Indian or Eskimo.
Subsequent Tuberculosis:

Regarding this aspect literature is scanty. Because this requires follow up of the patient, somewhat longer period.

Irgarshheimer and Prins, in 1922 reported on 92 cases follow up a period of 10-30 years. 12 cases (13%) were found to be tuberculous.

Kassau and Zweig (1923) found 9 cases (16.3%) of tuberculosis among 63 patients followed up for 1 to 16 years. Carvill (1929) reported 3 (0.6%) death from tuberculosis in a series of 380 cases.

Weringer (1931) reported 2 deaths, 1 from pulmonary tuberculosis and the other from tuberculous meningitis among 29 cases, remaining cases were doing well.

Patients with hilar lymphnode infection examined after 2 years, showed with remarkable regularity well healed lesions.

An alterative study of follow up of cases by Ajo (1930) done during (1912-1927). Age ranging 1-33 years. In formation on 367 could be obtained. 33 (13%) had died at average period of 7.4 years after onset of phlyctenula-losis death being due to tuberculosis in 25 (9.5%) and possibly in 39 (10.6%) patients. Clinical examination became possible in 89 patients who had been traced. and
in 11 abscess. In this group of 100 cases, 39 showed evidence of tuberculosis, the distribution being chest, 7; Cervical adenitis, 9; including 6 in whom the condition was quiescent bone, 1; lupus, 1; calcified hilar lymphnode, 10; pleurisy, 2; visible enter lobular streaks, 1.

Sorsby (1943) reported on after history of 794 cases of phlyctenulosis as compared to with 526 cases of blepharitis and 498 cases of conjunctivitis. He found an incidence of 5.3% in phlyctenulosis group as compared with 0.95% in blepharitis group and 0.6% in conjunctivitis group. Seven times higher in phlyctenulosis group than control group.

LABORATORY FINDING:

Tubercle bacilli:

(a) In blood:

Presence of tubercular bacilli has been reported by very limited number of observers. Richm (1931) reported tubercular bacilli in a blood of 5 patient out of 9 cases of phlycten and Urbansk (1939) reported in 5 cases out of 54. He also submitted 19 cases to another investigator (Marosh), who found bacilli in 1 case out of 19.

(b) In Phlycten (lesion):

Tubercular bacilli has not been reported from lesion by any observer. Stavgardt (1916) described the occurrence of such granules in phlycten, his observation
being checked by much. This finding of doubtful significance appears to be an isolated instance. Bruckner (1929) observation may have some bearing on this matter.

Tubercular bacilli implanted into conjunctives of rabbit and guinea pig undergo degenerative changes after initial alteration in staining reaction.

2. E.S.R.:

Sedimentation rate report in phlyctenular case is contradictory. Franceschetti Guggenthein (1929) found a definitely raised rate in only 6 out of 50 cases of "scrofulous eye condition", in these cases the rate was moderately raised. Schmelzer (1930) in 50 cases of "scroephulous disease of the eye" found a definite raised rate in 9 and slightly raised rate in another 9 patients and noted that with clinical healing of eye condition raised sedimentation rate comes to normal.

Parkovits Bugarsky (1930), who in 50 cases of phlyctenulosis found only 6 cases with normal E.S.R., in 22 cases slightly raised and 22, it was definitely raised. Raised rate was not explained by any associated general condition but affected actively was associated with eye condition and returned normal after subsided ailments of eye.
Fontana (1933) attaches importance to the underlying tubercular infection as the responsible factor for a raised E.S.R., with evidence of tuberculosis in 14 of his 30 cases, while in remaining 16, the rate was normal and no sign of tuberculosis.

Sorsby (1942) in 124 cases of active phlyctenula
tosis 99 (79.8%) showed a rate of over 10 mm. in 1st hour.

Worm infestation:

Bakly (1929) attributed a high incidence of phlyctenular eye disease in Port-Said, Egypt, to asciasis. Jaffery (1955) found that Ascaris lumbricoides, Ankylostoma duodenale, Enterobesus vermicularis and E. hystolytica are responsible for a number of diseases of eye, phlyctenulosis being the most common.

All Hussaini and Saoudi (1968) found that 20% cases of phlyctenulosis occurring in acute form in children age group does not seem to be tuberculoprotein as a factor, but worm infestation. In (1977) showed an association of phlyctenulosis with Hymenolepis nana (the dwarf tape worm). A careful examination of the stool of 135 cases of phlyctenular eye diseases showed that 57.4% of them had Hymenolepis nana in their stool. In cases of multiple or recurrent phlyctenae the eggs were found in 73.4% of cases. In(1979) he studied a series of 471 patients suffering from phlyctenular eye disease were examined stool and found 62.6% of them had Hymenolepis nana. One in their stool as
compared to control group 10.8%. All patients had
Hyponeoplastic nona immune sera.

**Nutritional:**

In the old literature dietary faults have been
incriminated as a cause of phlyctenular ophthalmia. An
excess of starch in food by Romsey (1933) and various
vitamins deficiency by Lowenstein, 1925; Papagne, 1935;
Foster, 1936, being particularly stressed.

No valid evidence is available except for the
suggestive finding by Praniaspolous (1940) that the
vitamin 'A' concentration in the blood of phlycten patients
is often not always distinctly subnormal. This observer
regards vitamin 'A' as a precipitating factor in some cases.
Such evidences has been brought forward for intestinal
intoxication (Calumba, 1935; Papagne, 1935; and others)
based on the fallacious test of indicarios.

A deficiency of calcium has been suggested on the
strength of therapeutic results from the administration
of this metal (Cremar, 1929; Lazarev and Dzian, 1936).

**Focal Lesions:**

Enlarged and septic tonsils are regarded by some
observers as causative factor (Nelson, 1923; Roche-Duval,
1934; Gaulden, 1936; Nagitel et al., 1936; Sorgnun, 1939).
Pediculosis Capitis

An extensive but rather uncritical literature incriminates pediculosis capitis (Thierry, 1937), whilst not altogether dismissing this hypothesis. Heinonen, (1936) could not find any conclusive support for it in his own statistical material.

McLean (1963) during ophthalmic survey 28% of 780 Canadian Eskimos were found to have stigmata of phlyctenular keratoconjunctivitis. Attention was drawn to the high incidence of pediculosis capitis in the Eskimos and a relationship between this infestation and phlyctenulosis is suggested.

Experimental Studies:

On account of failure to isolate any organism from the lesion in patient of phlyctenulosis has made unspecific type of condition. Besides the hypothetical etiological factor many observers have tried to produce similar lesion by experimental trial using different material being either from lesion or other living organism or chemical substances.

In beginning of century Lever and Muller (1901) introduced phlycten material in anterior chamber of rabbit eye, but failed to obtain tubercles on iris through one of the Muller’s 20 experimental animals did develop a transient nodule on the iris and this particular animal died later of
miliary tuberculosis. Wassely (1919) failed to obtain any tuberculous changes in conjunctiva of eyes into which he had repeatedly implanted phlycten material, and this in spite of great susceptibility of monkeys to minimal quantity of tuberculous material. All this evidence suggests that phlycten is not only histopathologically but also biologically sterile.

Successful experiments with the tubercle bacillus has been observed. Phlycten is not produced by the virulent or living tubercle bacillus. Lever (1909) attempted to obtain phlyctenulosis by implanting into the cornea, tubercle bacilli sterilized by heat. Resulting corneal reaction was essentially tuberculous; giant cells were present and, after 8 weeks bacilli that stained could be recovered from the lesion.

Burns (1904) had rather similar results by using an emulsion of tubercle bacilli. He did obtained lesion clinically suggestive of phlyctenulosis but histologically different by the injection of emulsion into the jugular vein of rabbit.

Schieck's observation quoted by Stargardt (1916) that phlyctenulosis can be produced by injection of living tubercular bacilli into the carotid artery, does not appear to have been substantiated.
Weebers and Rosenhaush (1910) obtained phlyctenulae of histological structure seen in men by the use of two different methods both involving the previous tuberculous sensation of rabbits by infection with bovine tuberculous. Following on tuberculous sensitisation, the first observer instilled tuberculin into the conjunctival sac and second implanted staphylococcus auricus using either the living or dead organism. Weebers procedure is of course an experimental counterpart of the calanette and has been confirmed repeatedly (Robbort, 1912; Stargardt, 1916; Gibson, 1918; Kuboki, 1924; Kuniya, 1935). It is generally agreed that Rosenhaush's procedure though valid, is less certain in effect (Rubert, Fanairhi, 1923; Foleu and Savalsky Fisson, 1915; Muniya, 1938).

Tuberculous sensitisation was not an essential condition shown by a series of observers. Tuberculin is still used as the local exciting agent. It was seen that animals could be sensitized by different agents. Guillory (1921) found proteolytic factors (Ferments of B. Predigioso and B Subtilis. Trypsin etc.) effective, whilst Loddenk (1930) obtained results with sensitisation by horse serum and Kuniya by sensitisation with staphylococcus.

In further work, instead of using tuberculous sensitisation or tuberculin as local exciting factor, sensitisation was induced by organism like staphylococcus.
(Funaishi, 1923), biological product like - horse serum (Richm, 1928), chemicals like - Tyramine, Cocaine (Funaishi, 1923) or calcium caseinate or milk ferment, Moya Bulgarica (Morelli, 1924); since the animal was sensitised phlyctenulas could be excited by the instillation of the specific sensitising agent into the conjunctival sac. The specificity of these phlycten-inducing reactions does not appear to be absolute, for staphylococci, with induce phlyctenulas in the tubercular sensitised rabbit (Assen bauch's procedure). Tuberculin will act like wise in animal sensitised to variety of substances, and staphylococci act effectively in the rabbit sensitised to horse serum (Richm, 1928).

An elaborative series of experiments by Richm (1928-32) suggest that the phlycten is a non-specific local anaphylactic reaction that can be induced by a variety of agents, in various ways. Phlyctenulae can be induced in a specific manner by the use of horse serum for sensitisation and as the local exciting agent; in a non-specific manner by sensitisation with horse serum and staphylococci as the local agent; in an anaphylactic manner as when phlyctenulas are induced specifically by horse serum and made to recur after subsidence by injecting the serum into the blood stream; in the manner of selective sensitisation of the conjunctiva as by inducing phlyctenulas in both eyes on the
intravenous injection of horse serum into the rabbit
first sensitized locally by instillation of horse serum
in one eye. The mechanism underlying this anaphylactic
reaction has been discussed by Massote (1929); Iga (1930),
and Szily (1930). A toxic effect on the capillaries is
suggested.

Carbohydrates may play a part in the production of
phlyctenulacae is suggested by the recent work of Ketnalsom,
Kazhan and Yufa (1939), who obtained phlyctenulacae in
tuberculous sensitized rabbits on the introduction of sodium
lactate into the stomach. Furthermore, they observed
transient conjunctive reaction on the instillation of
tuberculin into the conjunctival sac of healthy non-sensitized
animals in whom a hyper lactacimia had been induced.

Visual acuity and phlyctenulosis:

Phlyctenulosis is not a common cause of blindness,
but definitely effecting the vision if involves the cornea.
Corneal scar or opacity as a result of phlyctenulosis may
effect the vision from minimal to complete blindness
depending upon the site and extend of involvement of cornea.

There is no more literature available about this
but the study of Thysen (1951) and his co-workers in
the native of Alaska. In (1946) careful clinical study of
400 natives of Alaska was done. They found corneal opacity
in 127 patients clearly attributed to phlyctenulosis. 38 had a vision of less than 6/18 and in 19 patients vision was less than 6/18 (20/70) in better eye.

In the series of 346 children corneal scars were observed in 149 cases. Among these 143 scar due to previous phlyctenulosis. Bilateral scar were in 112 cases and unilateral in 31. Scar involving the pupillary area were noted in 164 cases of possible 285 eyes with scarring.

All these above cases were refracted to determine corrected vision. In 143 cases (388 eyes), there were 27 eyes with vision of 20/40 (6/12) or less in 22 eyes with a vision of 20/70 (6/18) or less and nine eyes with a vision of 20/200 (6/60) or less.

In the eyes with clear pupillary area with peripheral scarring the corrected vision was 20/40 (6/12) or less in only one eye of 27 cases. This was due to amblyopia or anopia second to convergent squint; this had vision 12/400.
CLINICAL TYPES:

1. Phlyctenular Conjunctivitis:

Typical phlycten appears as a pinkish-white elevation surrounded by a hyperaemic area. A tiny grey crater develops at apex by a progressive destruction, sinks down to conjunctival level, thereupon lesion clears up without leaving a scar phlycten does not spread like an infected ulcer but two neighbouring lesions coalesce to form an larger lesion. Apart from hyperaemic area of conjunctive rest of the conjunctive is clear and unaltered in absence of secondary infection, when one or more discreet nodules of this type present, called SIMPLE PHLYCTENULAR CONJUNCTIVITIS.

The site of election is at limbus they are commonly found in bulbar conjunctive. On the palpebral conjunctive, they may occurs, much rare, as whitish flecks frequently close to lid margin (Thygeon, 1981) some times even on lid margin (Stargardt, 1921). In Tropics (India) the palpebral form is more common.

Instead of resolution, some times very large phlycten results into PUSTULAR CONJUNCTIVITIS, and subsequent necrosis may extensive and may penetrate to the sclera underneath such necrotising phlyctenules persists for longer time and involve some permanent scar formation.
One more type of phlyctenular conjunctivitis
known as MILITARY PHLYCTENULAR CONJUNCTIVITIS in which
a larger number of phlycten particularly around the limbus,
in more sever form whole of this area is covered with tiny
moulds as if it had been strewn with sand (Leisillier -
Toulant, 1955) many of them resolve without breaking down.
On other hand they may become confluent, producing a sever
form of clinical picture Ring ulcer. This hampers the
nutrition to cornea may lead extensive perforation.

2. Phlyctenular keratitis:

This may develop in cornea de novo or may spread
to this tissue from conjunctiva. The epithelium of cornea
is both anatomically and embryologically the direct
continuation of conjunctiva so disease has tendency to spread
from one to other more frequently in phlyctenulosis. Cornea
may be involved in two ways, by localised infiltration and
ulceration or by diffuse infiltration and vascularisation
to form a characteristic type of pannus.

The ulcerative type may assume three forms - marginal,
saccular and miliary. It appears as a small grey nodule
in the superficial layer of cornea mark the site of phlycten.
later it breaks in centre involves little loss of tissue
results in shallow ulcer, which may clear up without leaving
a scar, phlyctenular or serofloous ulcer.
Grey infiltration at limbus frequently appear as marginal ulcer which can be differentiated from the catarhal ulcer due to not leaving a clear space between limbus and ulcer and long axis of ulcer is perpendicular rather parallel to circumference. This ulcer remain stationary but when it acquires a serpigenous route and vanders towards the centre of cornea. The peripheral area of the ulcer heals while central margin constantly remains active and eats cornea preceded by a grey infiltration. Following it out from the periphery a band of vessels runs straight without branching to in the furrow dug by ulcer. As ulcer travels axially towards the centre of cornea, the picture is presented of a grey infiltrated area preceded by the tiny half moon progressive border and followed by a sharp band of vessels running from the limbus, infiltration and subsequent break down at the advancing edge keeping pace with the reparative process in the peripheral edge (Fascicular ulcer). FASCICULAR KERATITIS ulcer remains superficial and never perforates. Vessels gradually diminish after the condition quietens, but band shaped opacity persist densest at the print where, ulcer stops.

Miliary ulcer results when minute minute ulcer scattered over a portion of cornea.
A diffuse central infiltrate in the cornea either superficial or deep is also a manifestations characterised by rich vascularization from periphery and when it appears from all around the limbus form phlyctenular pannus. In milder cases vessels remain superficial and not much vascular pannus. Cornea appears cloudy due to loss of epithelium and uneven surface but soon after becomes clear.

It does not show predilection for the upper segment like trabeculous pannus but is uniformly distributed.

In severe form of (Deep seroflesus infiltration) a grey clouding with indistinct margin appears under Bowman’s membrane over which epithelium becomes stippled. It gradually clears up but some times to remarkable extent, leaves opacity. At other time, however area becomes more yellow supuration develops and extensive neurosis occurs 'result and is dense permanent scar with vascularisation'. When secondary infection is super added a malignant pustular form of infiltration may supervene, acute supuration occurs and occasionally perforate.

Differential diagnosis:

The diagnosis of phlyctenulesis is not difficult in children but great difficulty in adults. Some resemblance can be found with the condition like.
Acne rosacea keratitis, trachome, staphylococcus marginal ulcer with pannus. Episcleritis, inflamed pinguicule.

Simple phlyctenular conjunctivitis simulates the episcleritis but can be differentiated because of its typical features and episcleritis may associated with other collagenous disorders, found in adults.

Acne rosacea keratitis differentiated from phlyctenular keratitis from the points, that it occurs in adults, typical lesion on face, fascicular ulcer is not found in rosacea keratitis and dilated conjunctival vessels is diagnostic aid in rosacea.

Recurrent staphylococcus marginal ulcer with pannus differentiates due to not showing fascicular ulcer leaves: the scar extending to limbus. Scar in central papillary area, which is very common in phlyctenulosis, presence of hypopyon iritis are features of infective corneal ulcer.

Trachome has typical extension of pannus from upper quadrant of cornea, scarring of palpebral conjunctiva and thickening/resolution of tarsal plate as sequelae.

Sulbar type spring catarrh differential due to less photophobia and inflammation itching rather than pain ulceration and massive eosinophilia.
THERAPY:

On account of lack of knowledge about the exact etiology, there is no specific treatment. Because it has been accepted as an allergic manifestation. Antiallergic therapy (corticosteroid) is present method of therapy though there has been given various type of therapy by various observer previously.

In (1905) W. Bishop Norman described the treatment of phlyctenulosis in book "The conjunctive in health and disease" as follows.

The care of the general body health and removal of all possible source of irritation, stomatitis decayed tooth sore of the face, lips and nose, nasal discharge pediculosis are the first care. Cod liver oil, plenty of fat food bacon butter etc, invariably reduce the further attack. Application of atropine ointment. An ointment of finely precipitated and reprecipitated yellow oxide of mercury in lanoline and vaseline of 1% and later 2% strength is good. A phlycten in early stage, unbroken the attack may be quickly absorbed by touching the tip simply with a fine brush deeped in a 1% solution of silver nitrate.

Until the recent introduction of cortisone therapy seemed hardly to have progressed. Since 1905 and certainly no specific treatment can yet to exist. If one excepts theory that phlyctenulosis is in most instances a bacterial allergy
to products of tubercle bacilli. It would seem logical to attack the disease by attaching the tubercle bacilli by means of chemotherapy.

Upto present time no series of phlyctenulosis cases have been reported in which antitubercular agent have been employed. The underlying tuberculosis, however, has been treated indirectly by desensitization with tuberculin and dietory measure.

**Tuberculin Therapy:**

Tuberculin desensitization ought to be valuable in phlycten of hyper allergic phase of tuberculosis. Favourable results have been reported by a number of observers but control group has notoriously unpredictable effect.

Sulizberger in his Demato logical allergy states that administration of tuberculin can either increase or decrease the level of skin tuberculin sensitivity. Lower degree of skin sensitivity can some times be raised rapidly by one or two intracutaneous injections of tuberculin. Further he stated that degree tuberculin sensitivity can often be specifically decreased, one or a few intracutaneous injections some times sufficing to achieve a general, marked hypo sensitization of the skin that in many other cases the level of the skin tuberculin sensitivity can not be demarked by specific injections.
The relationship between conjunctival and skin sensitivity to tuberculin has not been thoroughly explored but it is generally believed that they run parallel.

In spite of the theoretical reasons which would favour the use of tuberculin therapy, this method has not come into general use.

**Dietary therapy.**

Some observers have claimed that phlyctenulosis is due to faulty diet specially those who eat diet rich in carbohydrates and vitamins deficiency, so they have proposed dietary therapy but no agreement as to its mode of action.

Sorsby (1942) has denied the direct role of diet but Thygeson (1952) observed on many occasion in New York phlyctenulosis cases when the child hospitalized and given proper adequate nutrition and rear when child returned to his home environment. He found dramatic response of diet during the course of study at school run for trachoma.

He was struck by high incidence of active phlyctenulosis in children coincidentally with trachoma in these children. They advised for adequate diet and in next year visit only rare cases were seen. Diet advised was new regime, adequate and rich in fresh fruit and vegetables.
Antiseptic therapy:

A third method of therapeutic method for phlyctenulosis tried is antiseptic agents topically. If secondary bacterial infection act as precipitating factor, their control would seem to be most important. Calomel treatment can only be explained on the basis of bactericidal effect of mercury liberated from the Calomel. Thryson found the control of secondary infective organism e.g. staphylococcus prevents recurrence.

Cortison therapy:

As it has been accepted by larger number of observers that phlyctenulosis is an allergic manifestation of cornea and conjunctiva due to protein of tubercle bacillus. So antiallergic inerm of cortison therapy has become present therapy and well responding. Cortison is used topically.

Favourable results have been noted by Von Sellmann, McLean and Garden and others.

Fritz reported a series of 10 cases in which topical instillation or sub-conjunctival injection results in rapid disappearance of lesion usually within 24 to 48 hours.
Although cortison can of course not be considered curative. Since it has no effect on systemic cause of disease. It can abort the acute attacks and thus to prevent corneal ulceration and cicatrization, is obviously great value.