

## DEMODICIDAE — STATUS AND PROGNOSTICS<sup>1</sup>

BY

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The most recent comprehensive review of mites of the family Demodicidae was published in 1919 by HIRST. He noted that he had assembled a list of over 230 publications, most of which dealt with *Demodex canis*, and that even this list was incomplete. In the ensuing forty-four years approximately 650 titles have been added ; of the current total some 250 are case reports, 85 are textual references, and 230 are reports of attempted control. These last three categories will be omitted for the most part from the following review which will, instead, concentrate upon available information on affinities, life cycles, distribution, transference, physiology, pathology and control of demodids with some indications of areas under study or in need of investigation.

### AFFINITIES.

Little has been added to the studied suggestion of HIRST (1918a) based in part on OUDEMANS (1897), that the genus *Demodex* is most closely related to the cheyletids. HIRST (1919) stated that in all probability a mite similar to *Myobia* or *Psorergates* which shares such features as identity of mouth-parts, capitular spines, and dorsal male genitalia gave rise to the demodids. Lack of an anus in *Harpyrhynchus* (HIRST, 1919) and marked similarity of larval and nymphal " legs " to those of demodids in *Psorergates* (HIRST, 1923) lend further credence to this view. DUBININ (1958) reviewing this situation decided that the demodids and psorergatids should be included in the Demodicoidea with close affinity to Cheyletoidea. WOOLLEY (1961) notes the sexually dimorphic nature of the Cheyletoidea wherein males are usually smaller than females. Of 18 species of *Demodex* in which both sexes have been measured, 16 are so dimorphic ; small numbers measured in the other 2 make even these suspect for the same situation. WOOLLEY also mentions

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the heavily sclerotized aedeagus of cheyletids ; examination of chitinase digestions and histological sections reveal that the aedeagus of *Demodex caprae*, is composed of chitin which represents two-thirds of the cross-section of the shaft (NUTTING, unpublished).

Both OUDEMANS (1897) and HIRST (1919) remark the close resemblance of demodicids to members of the Sarcoptidae. The discovery that *Demodex criceti* burrows pits in the epidermis (NUTTING and RAUCH, 1961) and that *Rhinodex* and *Stomatodex* are found in the nasal and oral mucosa (FAIN, 1959, 1960) coupled with the unsatisfactory resolution of the problem of tracheation in demodicids suggest that a careful restudy of the affinity problem should be undertaken. The internal anatomy (nearly completed in our laboratory) and embryology of *Demodex* should be compared with suspect groups. A careful examination of similar aspects of *Rhinodex*, *Stomatodex* and the demodicids of marsupials may well shed some light on this situation.

The family Demodicidae has been expanded recently to include 2 new genera, *Rhinodex* Fain (1959) and *Stomatodex* Fain (1959). The former is represented by a single species, *Rhinodex baeri* Fain, found in the nasal mucosa of *Galago senegalensis moholi*. Unfortunately only nymphs and females are known, and these have been described in a very limited way. FAIN's figures and account indicate a form which is relatively less specialized than other demodicids, although the palpi are reduced to two segments. The tortoise-shaped podosoma, the somewhat ventrally positioned gnathosoma, and the long heavily-clawed legs suggest a mite which wanders freely across the nasal mucosa rather than one which burrows as does *Demodex criceti*. From the reduced nymphal legs one would anticipate that immature stages are somewhat cryptic in habit.

FAIN (1959, 1960) has described three species and one subspecies of the genus *Stomatodex* from the buccal mucosa of a lemurian and several chiropterans : *S. galagoensis*, *S. rousetti*, *S. corneti*, and *S. c. myotis*. Characteristics of these drawn from FAIN's work show close correspondence in external features to *Demodex*. The long, heavily clawed legs indicate an adult which is very active in its habitat. Immature stages are unknown.

One would hope that studies of the long-known (HENLE, 1841) genus *Demodex* Owen (1843) would uncover relationships within the genus based upon host phylogeny. So far 38 species and subspecies in this genus have been described from 8 orders of mammals (Insectivora, Chiroptera, Carnivora, Rodentia, Lagomorpha, Primates, Artiodactyla, Perissodactyla) (Table I). The rather low incidences of recovery, such as obtained in our laboratory in a screening program of local mammals (4 % in *Tamias striatus* to 60 % in *Tamiasciurus hudsonicus*), has undoubtedly held back progress along these lines. Two undescribed species from marsupials in the writer's possession are disappointingly similar to demodicids of rodents. The issue is further obscured by the fact that remotely related mammals apparently harbor identical demodicids (NUTTING, 1961). Three chiropterans of two different genera possess the same species of *Demodex* (DIBENEDETTO, unpublished)

while one host species, *Mesocricetus auratus*, maintains two distinct species of *Demodex* in different niches (NUTTING, 1961). Although many reports (e.g. MAYNARD, 1922) suggest inter-species transfer, the evidence is far from convincing. In any event there is no assurance as yet of any phylogenetic pattern or of species specificity.

TABLE I. — Described species of the family Demodicidae with hosts and authority.

Mammalian Order	Genus	Host	Authority
Insectivora			
	<i>D. erinacei</i>	<i>Erinaceus europoeus</i>	Hirst, 1917
	<i>D. soricinus</i> (= <i>nanus</i> ?)	<i>Sorex araneus castaneus</i>	Hirst, 1918
	<i>D. talpae</i>	<i>Talpa europaea</i>	Hirst, 1921
Chiroptera			
	<i>D. phyllostomatis</i>	<i>Phyllostoma hastatum</i>	Leydig, 1859
	<i>D. chiropteralis</i>	<i>Plecotus auritus</i>	Hirst, 1921
	<i>D. soricinus</i> (= <i>nanus</i> ?)	<i>Plecotus auritus</i>	Hirst, 1918
	<i>D. aelleni</i>	<i>Myotis daubentoni</i>	Fain, 1960
	<i>D. myotidis</i>	<i>Myotis lucifugus lucifugus</i>	(Nutting, 1950)
		<i>M. keenii septentrionalis</i>	(Di Benedetto, 1961)
Carnivora			
	<i>Stomatodex corneti</i>	<i>Eptesicus fuscus</i>	(Di Benedetto, 1961)
	<i>Stomatodex corneti</i> subsp. <i>myotis</i>	<i>Barbastella barbastellus</i>	Fain, 1960
		<i>Myotis myotis</i>	Fain, 1960
		<i>Myotis dasycneme</i>	Fain, 1960
	<i>Stomatodex rousetti</i>	<i>Rousettus leachi</i>	Fain, 1960
Rodentia			
	<i>D. canis</i>	<i>Canis familiaris</i>	Leydig, 1859
	<i>D. cati</i>	<i>Felis domestica</i>	Megnin, 1877
	<i>D. ermineae</i>	<i>Mustela erminea</i>	Hirst, 1919
	<i>D. melesinus</i>	<i>Taxidia taxus</i>	Hirst, 1921
	<i>D. bonapartei</i>	<i>Mustela erminea cicognanii</i>	(Nutting, 1950)
	<i>D. caviae</i>	<i>Cavia cobaya</i>	Bacigalupo, 1954
	<i>D. arvicolae</i>	<i>Microtus (Arvicola) agrestis</i>	Zschokke, 1888
	<i>D. musculi</i>	<i>Mus musculus</i>	Oudemans, 1898
	<i>D. ratti</i>	<i>Rattus norvegicus</i>	Hahn
	<i>D. nanus</i> (= <i>soricinus</i> ?)	<i>Rattus rattus</i>	Hirst, 1918
		<i>Rattus norvegicus</i>	Hirst, 1919
	<i>D. muscardini</i>	<i>Muscardinus avellanarius</i>	Hirst, 1917
	<i>D. apodemi</i>	<i>Apodemus sylvaticus</i>	Hirst, 1918
	<i>D. longior</i>	<i>Apodemus sylvaticus</i>	Hirst, 1918
	<i>D. glareoli</i>	<i>Evotomys glareolus britan- nicus</i>	Hirst, 1919
	<i>D. glivicolens</i>	<i>Arvicola amphibius</i>	Hirst, 1921
	<i>D. sciurinus</i>	<i>Sciurus vulgaris</i>	Hirst, 1923
	<i>D. criceti</i>	<i>Mesocricetus auratus</i>	Nutting & Rauch, 1958
	<i>D. aurati</i>	<i>Mesocricetus auratus</i>	Nutting, 1961

TABLE I (continued).

Mammalian Order	Genus	Host	Authority
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Lagomorpha	<i>D. cuniculi</i>	<i>Oryctolagus cuniculus</i>	Pfeiffer, 1903
	<i>D. transitionalis</i>	<i>Sylvilagus transitionalis</i>	(Maravelas, 1962)
	<i>D. sylvilagi</i>	<i>Sylvilagus transitionalis</i>	(Maravelas, 1962)
Primates	<i>Stomatodex galagoensis</i>	<i>Galago senegalensis moholi</i>	Fain, 1959
	<i>Rhinodex baeri</i>	<i>Galago senegalensis moholi</i>	Fain, 1959
	<i>D. araneae</i>	<i>Ateles</i> sp.	(Nutting, 1950)
	<i>D. folliculorum</i>	<i>Homo sapiens</i>	Simon, 1843
Artiodactyla	<i>D. phylloides</i>	<i>Sus scrofa</i>	Csokor, 1879
	<i>D. cervi</i>	<i>Cervus</i> sp.	Prietsch, 1885
	<i>D. bovis</i>	<i>Bos taurus</i>	Stiles, 1892
	<i>D. ovis</i>	<i>Ovis aries</i>	Railliet, 1895
	<i>D. caprae</i>	<i>Capra hircus</i>	Railliet, 1895
	<i>D. pseudaxisi</i>	<i>Cervus hortulorum</i>	Shpringol'ts-Shmidt, 1937
Perissodactyla	<i>D. equi</i>	<i>Equus caballus</i>	Railliet, 1895
	<i>D. folliculorum</i> var. <i>equi</i>	<i>Equus caballus</i>	Bennison, 1943
( ) unpublished			

Validation of species distinctions is still based upon the criteria used by HIRST (1919), e.g. differences in capitular spines, genitalia, and measurements or ratios of major body divisions. LOMBARDINI (1942) used the additional characters of shape of opisthosoma, shape of coxa, podosomal striations and morphology of the tarsal claws in his key to the species of *Demodex*. NUTTING and RAUCH (1958) were the first to include means and standard deviations of statistically valid numbers of measurements of selected body areas for each stage in the life cycle. Unfortunately of the 43 demodicids known only 2 have been reported in this fashion and in only 14 did more than 1 to "several" specimens serve as the basis for description. With one relatively weak exception (NUTTING, 1961), no attempt has been made to assess the effect of the environment on the morphology despite several situations of suspect polymorphism (as FUSS, 1935). Further studies are obviously called for to reinforce subspecies distinction and lend assurance to certain species designations.

It seems evident that both new and described members of the genus *Demodex* need intensive study and assessment with descriptions grounded upon measurements of a statistically significant series of each stage of the life cycle, accurate drawings of (1) male and female genitalia, (2) capitular spines, (3) larval appendages, and (4) podosomal striations, before valid in-genus affinities can be established. Reports

of new species, except for unusual forms, as for example *Stomatodex*, if based on less than these criteria will only serve to delay our resolution of the problem of demodicid affinities.

#### LIFE CYCLES.

All four stages in the life cycles of 10 demodicids are known but in only one is there any determination of the number of moults or the time of development of each stage. SPICKETT (1961b), on the basis of cultures of *Demodex folliculorum* using sebum as a food supply, statistical analysis of stages obtained in histological preparations, and the assumption that equal numbers of males and females are produced, has calculated the approximate life cycle as 14 1/2 days : ovum 60 hrs, larva 36 hrs, protonymph 72 hrs, deutonymph 60 hrs and adult 120 hrs. The following reservations should be held with regard to the preciseness of this estimate : (1) Several demodicids, e.g. *D. criceti* and *D. myotidis*, are now known that live in tissue not associated with the sebaceous glands, indicating therefore that sebum is apparently not always necessary for mite survival. (2) Sebum is a very poor source of nitrogen (ROTHMAN, 1954) which would make it an unlikely diet for mite development. (3) Circumstantial evidence indicates that most demodicids feed on the contents of cells. (4) The 1 : 1 ratio of male to female is not apparent in our studies of *Demodex caprae*. (5) Histological preparations show 8-13 cells in the ovary of *D. caprae* and if each is functional and maintained as a developed egg up to 3 days in the female (as observed in our laboratory) the life cycle would be markedly longer than 14 1/2 days.

Work is underway in our laboratory using a modification of the subplant technique suggested in NUTTING, 1961. A micropore filter tube (porosity of c. 7  $\mu$ ) is loaded with embryonic skin and mites, sealed, and introduced beneath the skin or in the cheek pouches of hamsters. Live mites have been recovered after 100 days with this procedure. This technique shows some indication of maintaining developing demodicids without the ills of *in vitro* sebum culture.

#### DISTRIBUTION.

Thus far members of the family Demodicidae have been found only in mammals. Published accounts and our screening program in which 17 of the 18 species of mammals examined have been found positive for *Demodex* suggest that all mammals harbor demodicids. The absence of *Demodex* in the one species, *Blarina brevicauda*, may simply indicate that our procedure bypasses the niche of this parasite. In *Tamiasciurus hudsonicus* thorough examination of 126 specimens has shown that *Demodex* sp. ? is located only in the eyelids, while in *Mesocricetus auratus* maximal populations are found on the dorsum with reduced numbers in the skin of the ventrum, genitalia, mammae, muzzle, ear, eyelids, perianal area and axillae. A study

of eyelids from 84 specimens of rodents from Trinidad were all negative which may again indicate missed niches.

MARAVELAS (unpublished) working in our laboratory found preferential sites for a demodicid of *Sylvilagus transitionalis* in the eyelids and perianal glands. The post-abdominal region was cited by DIBENEDETTO (unpublished) as most heavily parasitized in *Myotis lucifugus*.

*Rhinodex* apparently prefers the nasal mucosa although one specimen was found in the buccal area (FAIN, 1959). The same author found all species of *Stomatodex* in the buccal mucosa.

A differential with respect to the sex of the host has been found for demodicids of *Mesocricetus auratus*, *Sylvilagus transitionalis* (MARAVELAS) and *Myotis lucifugus* (DIBENEDETTO). In the first, heavy infestations occur in the males with reduced numbers in females whereas in the last two the roles are reversed. Castration of male hamsters did not reduce mite numbers (NUTTING, unpublished). A study has been started to see what effect, if any, certain endocrine products have on the mite populations.

BENNISON (1943) gave the only precise account of a demodicid population fluctuating with season. He found in assembling records for 20 years that *Demodex equi* was markedly more common in late summer than at any other time of the year. A possible gradient of increase of *D. bovis* toward the equator was found in Australia (NUTTING, unpublished) which could correlate with skin temperatures (McDOWELL, 1958), although temperature variate runs in our environment chambers have so far revealed no correlation between temperature and mite abundance.

SPICKETT (1961b) provided the first report of the distribution of a demodicid in all stages of its life cycle in the pilo-sebaceous system. He found, in *D. folliculorum*, that adult males and females, protonymphs and deutonymphs, were usually situated at the mouth of the follicle, whereas ova, larvae and some adult females were in the pilo-sebaceous canal or sebaceous gland. The distribution of *D. aurati* is remarkably different (NUTTING and RAUCH, 1963) since here ova and adults are at or above the sebaceous canal whereas larvae and nymphs are below, penetrating even to the level of the hair bulb in the telogen phase of the hair cycle. Such investigations as these on other demodicids would be helpful for studies on transference and methods of control.

#### TRANSFERENCE.

Closely allied to distribution, but economically more important, is the problem of transference among individuals of the same host species. Many papers (e.g. ALMOND, 1909) report successful transference of *Demodex* from host mother to young and between host adults. In no case is the evidence presented convincing. Trials with vital stain marking (NUTTING, 1950) have been fruitless because the acari do not stain sufficiently for re-identification. Attempts at providing mite-free hamsters using r-radiation (NUTTING, unpublished) have failed since the mites (*D. aurati*),



survived 1500 r ( $LD_{50}$  for the host is 800 r, RILEY and EVANS, 1956). Mites also survive extreme biotin deficiency (NUTTING and RAUCH, 1961) although populations are significantly reduced in numbers. All drugs reported as "controls" fail to provide, because of the lack of rigor of the procedures used for testing, evidence of absolute extirpation of the mites. Extended attempts at rearing mite-free hamsters obtained by Caesarean section have been so far, unsuccessful.

Since the discovery by CANEPA and DA GRANA (1941) that *D. canis* is found in the lymph nodes many (e.g. UNSWORTH, 1946) have noted the possibility of *in utero* transfer in *Demodex*. Well over 20 embryos of the Golden Hamster obtained by careful Caesarean section from mothers held 1 — 3 days beyond the usual 16 day gestation period with progesterone have been digested in KOH and found negative for *Demodex*. Maternal uteri, blood samples, lymph nodes, livers, etc. have also been found negative. *D. criceti* has been recovered from suckling young at 5 days of age and commonly from those isolated from the mother at 15 days. Since transference is virtually completely effective in hamsters (NUTTING and RAUCH, 1958) it is presumed that this occurs between 1 — 15 days post-partum by direct contact during suckling. ENIGK (1949) failed to find mites in the skin or internal tissues of 18 still-born pups. Adult mites (*D. aurati*) have been discovered leaving the hair follicle to ascend hairs, suggesting a likely behavioral pattern for transfer (NUTTING and RAUCH, 1963). SPICKETT (1961b) suggests that the nymphal stage of *D. folliculorum* which does have well-developed legs is the stage of transference.

As NUTTING and RAUCH (1963) have pointed out the marked difference in larval and nymphal morphology, locus of various stages (i.e. lymph nodes in dogs or pre-adult stages deep in the hair follicle of *Mesocricetus auratus*) of different demodicids and differing behavioural patterns of the host indicate that mode of transfer may differ within the genus.

A truly mite free colony of animals or an assured method of marking demodicids would contribute much to the resolution of this problem.

#### PHYSIOLOGY.

Only scattered reports are available on the physiology of demodicids. LEYDIG (1859) in studies on *D. canis* reported finding no anus, respiratory system (but see HIRST, 1919) or circulatory system. Reproductive and digestive structures were correctly described by HIRST, 1919. A brief account of the musculature and its function is provided by LOMBARDINI (1942).

Survival experiments such as those of FETSCHER (1921) who kept *D. canis* alive for 25 days in distilled water, DANIEL *et al* (1959) who found *D. folliculorum* alive in ear wax after 4 months, and NUTTING (1950) who maintained *D. aurati* 4 days in machine oil, show that they are very hardy organisms. Survival in machine oil suggests that *Demodex* is a facultative anaerobe, possibly using diffusion or host oxidative metabolic ingredients *in vivo*.

Knife-like chelicera and obvious damage to host cells indicate that demodids puncture and suck in cell contents. The large salivary glands could serve to liquify the cell protoplasm and/or provide digestive enzymes. The first would seem necessary in view of the minute lumen (c.  $2\ \mu$ ) of the esophagus leading to the bilobed terminal gut (WILSON, 1844). Although probably an ovary, a "kidney" was also reported by LEYDIG as associated with the jack-stone-like pigment bodies of the opisthosoma. These bodies may be waste products (guanine?) and if so, are of interest since they are in part incorporated in the ova prior to deposition.

HIRST (1919) mentions that the penis is eversible and yet no reports give evidence of copulation. Thin membranes divide the opisthosoma into three sinuses: two dorso-lateral and one ventral. The dorso-lateral sinuses embrace the large longitudinal muscles. Except for two latero-ventral muscles found in the female running to the chitinous lips of the vulva only longitudinal muscles are located in the opisthosoma. In view of the lack of other musculature associated with the gonads we feel that this muscle-sinus system is associated with sperm emission and egg-laying. Spermatophores (?) are found in a 6-chambered seminal receptacle in *D. caprae*. They are apparently incorporated in the egg just prior to deposition since sections of eggs high in the oviduct contain large germinal vesicles and no sperm nuclei.

SPICKETT (1961b) using small numbers of mites, *D. folliculorum*, for each experiment has shown: (1) negative phototaxy for all stages; (2) positive stereotaxy for larvae, protonymphs, and females with shifting stereotaxy for deutonymphs and males; (3) no reaction to gravity; (4) that larvae feed continuously, females intermittently, males rarely, and deutonymphs not at all. NUTTING (1950) reported no appreciable reaction to light or gravity and positive stereotaxy for adult mites of *D. aurati*. Some increase in activity was found with increase in temperature for both *D. aurati* and *D. caprae*. SHEAD and HARDENBERGH (1927) reported peak activity of *D. folliculorum* v. *canis* at  $45^{\circ}\text{C}$  with  $54^{\circ} \pm 1^{\circ}\text{C}$  as lethal temperature.

Experiments recently conducted in our laboratory show that, contrary to expectation, cholesterol is not a limiting factor in mite reproduction.

Whereas the marked population difference in *D. aurati* between sexes of the host may suggest that these are sensitive to levels of host hormones it is more likely that this effect is indirect, possibly by way of the well documented (HAMILTON and MONTAGNA, 1950) sex differential response of the sebaceous components of the skin, ingredients of which may well stimulate egg production in *Demodex*.

Histochemical studies of *Demodex caprae* are in progress at our laboratory in an attempt to clarify several points of *Demodex* physiology.

#### PATHOLOGY.

FAIN could discover no evidence of pathology occasioned by either *Rhinodex baeri* or *Stomatodex* spp. In the genus *Demodex*, however, very definite lesions (papules) are caused by *D. caprae*, *D. bovis*, and *D. canis*. In these, marked hyper-



plasia of the follicular epithelium is found with at least occasional invasion of leucocytes. This last seems to be the rule in *D. bovis* but may well be due to secondary infection by bacteria which is not the case in *D. caprae* (NUTTING, 1950). Bacterial infection is apparently also associated with demodectic mange in pigs (LEGRAIN and REGULATO, 1903), sheep (MURRAY, 1959), cats (MÉGNIN, 1877), horses (BEN-NISON, 1943) and foxes (WATKINS and HARVEY, 1942). MURRAY implies that demodectic papules are present in sheep in the absence of bacterial invasion.

MAJOCCHI (1896) reported blepharitis in man occasioned by *D. folliculorum* and AGOSTINI (1939) reported pigmentation of the face due to this species. Moderate pigmentation and complete penetration of the follicular epithelium has been found in *Mesocricetus auratus* caused by heavy infestation of *D. aurati* (NUTTING and RAUCH, 1963). Hyperplasia of sebaceous glands are said to accompany infestation of *D. folliculorum* (NICHOLAS, 1943) and *D. canis* (FAURE, 1923). Specimens of *D. canis* have been found in the dermis and subcutaneous tissues (KRULIKOVSKII, 1878), lymph nodes (CANEPA and DA GRANA, 1941), and all body tissues (KOUTZ, 1957a) of dogs but pathology of these structures is not indicated.

In 36 species of feral mammals gross evidence of pathology is wanting (published accounts, and our screening program). Sections of skin from 12 of these show destruction of the follicular epithelium and/or Meibomian or sebaceous glands. The entire epithelial lining of an eccrine gland of *Myotis lucifugus* was destroyed by demodids (NUTTING, 1950). DIBENEDETTO (unpublished) discovered hair follicles with heavily hypertrophied epithelia due to *Demodex* in this same host. The perianal glands of *Sylvilagus transitionalis* were markedly depleted of cells according to MARAVELAS (unpublished).

It has long been assumed that *Demodex canis* may be a mechanical vector of *Staphylococcus* spp. incriminated in Staphlo-demodicosis or demodectic mange (GMEINER, 1909). Recent work of SPICKETT (1961a) shows that *D. folliculorum* does in fact ingest minute bits of plastic and that bacteria are found in the gut. He has reopened the contention of BORRELL (1909) that this species of mite may be the vector of choice in leprosy and also a possible vector of other bacterial or viridial agents of disease.

BEERMAN and STOKES (1934) have provided us with an excellent review of the still unresolved pathology controversy re *D. folliculorum* of man. As they point out GMEINER (1908) after examining 12 common skin complaints came to the conclusion that the presence of the mites in these was fortuitous. On the other hand LAWRENCE (1916) and later AYERS and ANDERSON (1932) are quite convinced that *D. folliculorum* is causative organism for the clinical entity "Pityriasis folliculorum". In a recent paper AYERS and AYERS (1961) summarize 30 years of observation on demodicidosis of man and renew their contention that this mite is causative for pityriasis and one type of rosacea. It would seem certain to the writer that *D. folliculorum* : (1) destroys epithelial cells of the skin component in which it lives ; (2) causes distension of hair follicles and sebaceous glands with hyperplasia and possible plugging of the outlets of these structures ; (3) occasions pigment aggre-

gation. Beyond this we need further controlled experiments to document human demodicid damage !

AUDRY and SUFFRAN (1908) were the first to report *D. folliculorum* in epitheliomae. Experimental work along this line was performed by CRANE (unpublished) in our laboratory. Application of 9, 10-dimethyl-1, 2-benzanthracene (DMBA) to mite-infested hamsters produced epitheliomae in which *D. aurati* were found in numbers nearly identical to that of untreated areas of the same animal. It would seem, therefore, that their presence in other cancers may be without causal significance.

#### CONTROL.

As previously indicated and despite a plethora of affirmative reports no certain measure of control for demodicids has been found (see the review of KOUTZ, 1957b). Topical drugs must not only contact each hair follicle but must also penetrate to well below the sebaceous glands to be effective. Even the burrowing *D. criceti* seems remarkably resistant to acaricides (below). Systemic drugs have to be non-toxic to the host and yet sufficiently concentrated to kill the mites in an area buffered from the vascular system by constantly reproducing cells of the follicular epithelium. To date no carefully controlled experiments with either of these routes of application have been published for *Demodex* spp.

BUXTON (1911) reported eradication of *D. canis* with a one-minute spray of ethyl chloride, but we failed to kill *D. aurati* with spray schedules of over three minutes, to a point at which cells of the epidermis were badly damaged.

Ultra-violet radiation suggested by SHEARD and HARDENBERG (1927) for *D. caprae* had no effect on *D. aurati* or *D. criceti* (NUTTING, unpublished).

Systematic screening of mites, *D. aurati* and *D. criceti*, using 17 topical drugs both by direct application to the mite and to heavily infested hosts have shown that none of these will effectively eradicate *Demodex* (report in MS). Eleven of these are drugs sold as remedies for demodectic mange.

The sole indication of biological control lies in the report of KUSCHER (1940). He found *Cheyletiella parasitivorax* eating the demodicids of dogs and suggested that this may account for reports of spontaneous cures.

Of all host animals so far reported the Golden Hamster would seem ideal for experimental work on control. Occasional males (c. 1 in 25 in our strain) harbor populations of *Demodex* as dense as 1 — 3 mites per hair follicle. Pure strain colonies are available so that we may rule out genetic variation. The animals are also prolific, hardy under surgery, and easily maintained.

One of the most promising avenues of attack for control would seem to be an attempt to break the life cycle at the transference point of mother to young, that is if adult to adult transfer could be firmly disproved. In an attempt to do this, groups of 15 hamsters, lightly to moderately parasitized as ascertained by scrape-survey technique (a procedure which does not identify very low infestations), have

been maintained in single cages until reduced by natural death to 3 — 4 per cage. Even though animals were rather constantly in close contact and carcasses were allowed to remain in the cage for a day no appreciable increase in the mite populations of the survivors was noted. Final readings for the survivors :

Cage A 2 ♀♀ negative, 1 ♂ positive

Cage B 2 ♀♀ negative, 1 ♀ positive, 1 ♂ positive

— all by scrape-survey technique.

This rough experiment suggests little if any adult-adult transfer, since even the positive carried only small populations.

#### IN CONCLUSION.

Although we have made substantial gains along all fronts in our studies of the family Demodicidae we are still superficially situated in the overall problem of their biology and evolutionary relationships. Carefully documented investigations along the lines of attack herein suggested are most urgently needed.

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