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2	An Over View of Dermatophytosis in Rabbits
3	Abstract:
4	Dermatophytosis is a fungal infection of the skin caused by dermatophytes-filamentous fungi
5	which have ability to invade the epidermis and keratinized structure derived from it such as hair
6	or nails. Rabbits are one of dermatophytes host; young rabbit below 12 months of age were more
7	frequently affected with the disease. <i>T. mentagrophyte\s</i> is the most common dermatophytes
8	isolated species. The disease can be diagnosed by direct examination, fungal culture, skin biopsy
9	sero and molecular diagnosis methods. This overview will forecast more light of the different
10	aspects of this disease.
11	Key words:
12	Dermatophytosis, Rabbit, Clinical feature, Diagnosis. Treatment
13	Introduction:
14	Rabbits are calm by nature. They are prone to many bacterial, fungal or parasitic skin diseases if
15	proper care is not taken. Among them dermatophytosis is one of the most common diseases [1].
16	Dermatophytosis is a superficial cutaneous infection with one or more of the fungal species in
17	the keratinophilic genera Microsporum, Trichophyton, or Epidermophyton [2, 3]. Young or
18	immune compromised rabbits are most susceptible to the disease [4]. Dermatophytosis is a
19	zoonotic disease so it has important implications in public health [5]. Infection with
20	dermatophytosis can be occurred in receptive hosts via arthrospores present on the hair coats of
21	infected animals or in the environment. (Reference)
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23 24 25	Epidemiology:
26	The possibility of infection of dermatophytosis depends on fungal species, host age,
27	immunocompetence, condition of exposed skin surfaces, host grooming behavior, and nutritional
28	status [6,7]
29	Young below 12 months of age or immune compromised rabbits are thought to be most
30	susceptible [8]. The susceptibility of very young rabbit to dermatophytes is due to not fully

developed immune system, causing a delay in adequate host immunity [9]. However, differences 31 in skin secretions, especially lower levels of fungistatic fatty acids in sebum and lower levels of 32 33 fungal inhibitory sphingosine, and the fast growth and replacement of hair may also play a role in facilitating infection [9]. The presence of ecto-parasites, especially fleas and Cheyletiella 34 mites, can also lead to spread of dermatophytosis [9]. 35 36 37 **Risk factors:** 1- Young animal 38 2- Overcrowding 39 3- high humidity 40 4- poor sanitation 41 5- malnutrition 42 6- Immunosuppression (including immunosuppressive treatment) 43 7- Injury by ectoparasites or scratches due to pruritus 44 Reported by [10] 45 **Transmission** 46 47 Dermatophytosis can be transmitted by direct or indirect contact with infected hair, scales or 48 materials. Infectious microconidia in the environment or on fomites can persist for many months. 49 The pathogenesis of dermatophytosis includes several stages; adhesion, germination, invasion, 50 51 penetration. Natural defences against dermatophytes depend on both immunological and nonimmunological mechanisms so infectious microconidia must first overcome a couple of local 52 53 defenses to be able to adhere the keratinized tissue, the stratum corneum [11,12]. 54 55 [11].Clinical features: 56 57 58 Clinically, dermatophytes infect the epidermis and adhering structures, including hair follicles 59 and shafts [13, 14]. In rabbits dermatophytic infections may cause alopecia, redness scaly and 60 scurf localized mainly on the face, head, auricles, and dorsal area of the neck [15-17]. This 61

disease can also result in rabbit malnutrition, growth retardation, feed remuneration reduction and even death.



Fig.1: Alopecia in mouth. (17)



Fig.2: Localized skin lesion of dermatophytes on leg (21)



Fig.3: Numerous canary crusts and large scales were present on the head of rabbits with hair loss.

Etiology:

T. mentagrophyte\s is the most common dermatophytes isolated from rabbits and some researchers consider rabbits as asymptomatic carriers of this organism [18-22]. *M.gypseum* was also isolated from rabbits [23]. *M.canis* was reported by [24]. *T.verrucosum*. Arthroderma benhamiae were also recorded [25]. Rabbits are reported to be carrier for dermatophytes [26] so isolated *T. mentagrophyte\s*, *M.gypseum*, *M.nanum* and *M.canis* from healthy rabbits [27]

Diagnosis:

Skin scraping samples from the rabbit that were suspected to be infected with dermatophytes will be collected on the basis of gross lesion on their body. Hair and scrapings samples were collected with forceps or scalpel just behind the extending margin in the infected area. Samples can be

kept in polyethylene bags. [28]



Fig.4: Skin scraping

Direct examination:

Hairs and scales? can be mounted in potassium hydroxide (KOH) of varying concentrations [29-31]. Infected hairs appear pale, wide and filamentous compared with normal hairs when microscopically examined at x4 or x10 magnification. Arthrospores can be visible on high magnification (x40). Positive result of KOH direct test can lead to positive cultures, which are considered as the gold standard. Calcofluor white (a textile brightener) as an alternative to KOH can be used because it binds specifically to the fungal cell wall and fluorescess strongly when viewed under a fluorescence microscope [27].

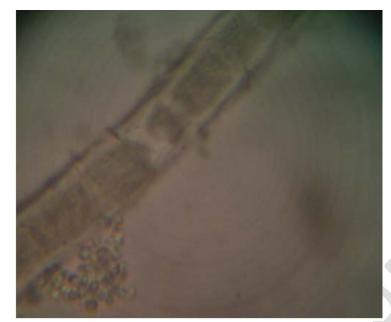


Fig. 5: Ectothrix arthrospores infection in hair

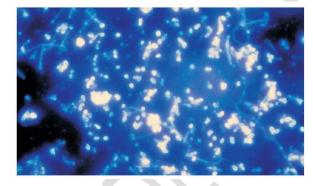


Fig.6: Fluorescent microscopy (calcofluor white stain) of *Trichophyton mentagrophytes* complex hyphae and conidia isolated from healthy rabbits

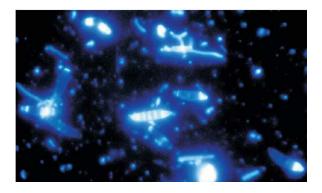


Fig. 7: Fluorescent microscopy (calcofluor white stain) of *Microsporum gypseum* hyphae and macroconidia isolated from healthy rabbits

Fungal culture:

Fungal culture is considered the 'gold standard' for diagnosis [32]. Sabouraud's dextrose agar (SDA) containing cycloheximide, penicillin and streptomycin were used in most diagnostic laboratories. Plates should be incubated at 25°C for 5 weeks. Dermatophytes test media (DTM) is recommended as the best media for isolation of dermatophytes because the presence of the red color indicated positive result, this can help in early identification of highly suspected cultures [33]. The isolates should be examined macroscopically and microscopically after staining with lactophenol cotton blue using wet mount technique [34].

In addition to technique steps mentioned above, pigment production on corn meal agar, urease activity on urea agar base, growth at 37°C on SDA.



Fig.8: Culture of *T. mentagrophytes*: surface of colony show powder-like shape, white, loose irregular mycelium on the edge.

Fig.9: Back side of Trichophyton mentagrophytes: pale yellow color



Fig.10: Microsporum canis culture, macroscopic colony



Fig.11: Microsporum gypseum culture, macroscopic colony

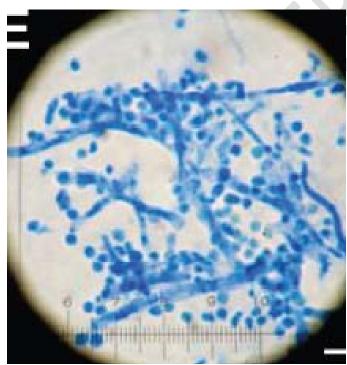


Fig.12: Small conidia (size: 2-3×2-4 μm) and mycelium of *T. mentagrophytes*



Fig.13:Spiral hyphae of *T.mentogrophytes var mentogrophytes* Slide stained with LPCB stain.



Fig. 14: Microsporum canis microscopic observation in lactophenol cotton blue



Fig.15: Microsporum gypseum microscopic observation in lactophenol cotton blue

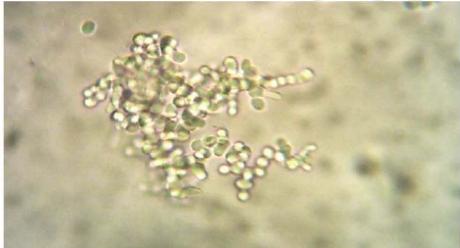


Fig.16: Lactophenol cotton blue mount shows chains of chlamydospore of *Trichophyton verrucosum* culture incubated at 37°C.



Fig.17: Growth of *T.mentogrophytes* on urea agar after 4 days showing hydrolysis of the urea.

Molecular diagnosis:

Diagnosis with conventional methods is time-consuming because it might take up to 4 weeks or longer to give the final results [35]. Furthermore, morphological identification may be confusing due to polymorphism of dermatophytes [36]. During the last decade, a wide variety of molecular techniques has become available as possible alternatives for routine identification of fungi in clinical microbiology laboratories [37, 38]. *T. mentagrophytes* isolated from nine rabbits and three farm staff were identified by using amplification of CHS-1 gene and ITS+ sequence. The results of sequences of CHS-1 and ITS from different DNA samples revealed that they were identical [21].

Serodiagnosis:

Indirect ELISA tests were developed to detect specific IgG in rabbits infected with *T. mentagrophytes*, found that (ELISA-rabbits test) is highly sensitive (96.0 %) and highly specific (94.1 %) [39].

Skin biopsy:

Skin biopsy from rabbit infected with *T. mentagrophytes* showed pathological changes with adherence of fungus to keratinocytes, through the stratum granulosum of the epidermis. In this period of infection there was a hyperkeratosis, thickening of epidermis with hair follicle plugging in addition to keratinized squamous epithelial lining with underlying moderate periappendageal tissue and perivascular chronic inflammatory cells infiltration (lymphocytes)

In 8-10 days of induced infection there is keratinized squamous epithelial lining with focal area of surface erosion and underlying moderate periappendageal tissue chronic inflammatory cells infiltration (lymphocytes)

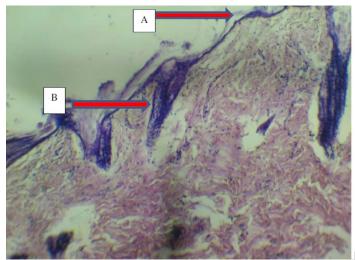


Fig.18: The bland looking (A) Hyperkeratosis, thickening of epidermis with (B) hair follicle plugging in 4-5 days (stained with H&E,10 X)

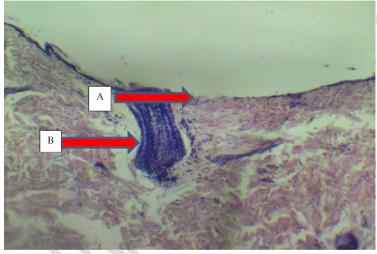


Fig.19: The bland looking with A- surface erosion and B- lymphocytes infiltration in 8-10 days (stained with H&E,10~X)

haematoxylin and eosin staining (H&E) may or may not identify dermatophytes and special stains such as periodic acid Schiff (PAS) and Grocott methenamine silver (GMS) are needed The epidermis infiltrated with variable fungal septate hyphae in size in the surface of the squamous epithelium [40].

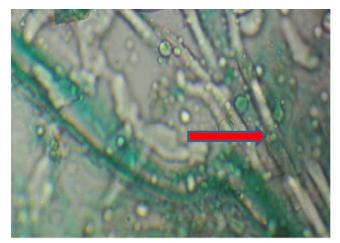


Fig.20: Proliferation of septate hyphae of *T. mentagrophytes* in epidermis in 8-10 days (stained with PAS,40X).

Treatment:

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- Optimal therapy of dermatophytosis requires a combination of topical antifungal therapy,
- 225 concurrent systemic antifungal therapy and environmental decontamination. The treatment
- should be continued until two consecutive negative cultures (at weekly or bi-weekly intervals)
- are obtained [41]. Topical treatments speed resolution of clinical lesions and may help prevent
- 228 zoonotic contagion. Systemic therapies that have prolonged residual activity in the skin and hair
- provide the most effective treatments.

230 Topical Therapy:

- 1. nystatin ointment for treatment of rabbit experimentally infected with *T. mentagrophytes* for 3
- 232 weeks [42].

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- 2. Clotrimazole is well-documented antifungal agent for treatment of rabbits [43].
- 3. 0.12g of terbinaphine 1% cream, for 28 days [44].

Systemic Therapy:

- 1. Griseofulvin 25–30 mg/kg during 5–6 weeks. Avoid its use in pregnant animals [45,46].
- 2. Itraconazole 5-10 mg/kg daily, for 1 month [47].

239 Environmental decontamination:

- 241 Enilconazole emulsifiable concentrate will be sprayed onto the walls and ceiling of rabbit house
- 242 (50 mg per m²) twice weekly for 23 weeks. Treated farm showed reduction of number of
- clinically infected rabbits [48].

- 244 Vaccination:
- 245 It is a dried culture of an attenuated strain of *T.mentagrophytes*. It has a high immunogenic
- 246 activity for dermatophytosis in rabbits. The vaccine is non-reactogenic and is injected
- intramuscularly. The vaccine has been recommended for practical use in USSR [49].

- 249 Conclusion:
- Dermatophytoses are the most common fungal infections in rabbits. Many studies were done
- 251 considering different aspects of the disease (eg. epidemiology, clinical presentation and
- diagnosis, treatment, prevention, and control). As many rabbits share the environment with
- owners as companion animal so they become a source of infection to human this can lead to
- public health problem.

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