Studies on Lungs and Kidneys pathology in stillbirth mice from infected mothers with *Schistosoma haematobium*

Ayad Qasim Mahdi AL-Makki
MS.C. MEDICAL PARASITOLOGY

Department of Pharmacology &Clinical laboratory sciences, College of Pharmacy, University of Basrah- Iraq

Abstract

In the present work, 50 pregnant female Balb/c mice (20 control and, 30 infected by ***Schistosoma haematobium***).are included in the experiment . exposure to cercaria occurs on 10^{th} day of pregnancy(midperiod of pregnancy)with continuous low concentration of cercaria for 5 days. Abortions occur after 7-8days after first exposure (17^{th}-18^{th} day of pregnancy) . Histopahtological studies of the stillbirths revealed very marked changes including Lymphocytic infiltrations within the parenchyma of the alveoli,Congestion, haemorrhage and necrosis in the lung. The main pathological changes in kidney were atrophic glomeruli , rupture of parietal layer of Bowman's capsule, necrosis and tubular atrophy .

Key Word/ abortion; stillbirths; *Schistosoma haematobium*

Introduction

Schistosomiasis is one of several parasitic diseases in which the pathology associated with infection is caused by the immunological and inflammatory responses of the host rather than by the parasite directly (Taylor, 1987). Brito *et al.* (1970) Observed advanced renal disease in humans with the hepato-splenic form of schistosomiasis mansoni, using light and electron microscopy of kidney biopsy specimens. they found a marked proliferation of mesangial cells with matrix deposition, and focal thickening of the basement membrane . The focal electro-dense deposits seen by electron microscopy

appeared to correspond gamma globulin and complement seen by immunofluorescence.

Several lines of evidence suggest that maternal infection or prenatal exposure to soluble Ags in humans leads to immunologic sensitization of the developing fetus. The offspring of woman with mumps or toxoplasmosis during pregnancy exhibited Ag- specific Ab and memory T cell responses to viral and toxoplasma Ags (Aase *et al*., 1972; Hara *et al*., 1996).

The Japanese findings are supported by Chinese studies (Wang, 1959) in which adult schistosomes have been recovered from aborted calf fetuses, and newborn calves and water buffaloes have been found to pass *S. japonicum* eggs in their feces .they hereby report that the pig, an important natural host of *S. japonicum*, can become infected in utero with the parasite.

Modification of the immune response to schistosomal antigen in children born to mothers infected with *Schistosoma mansoni* has been demonstrated in human (Camus *et al.,* 1976 and Tachon and Borojevic 1978) and in experimental schistosomiasis. This modification may be related either to congenital transmission of immunological information (Gill *et al.,* 1971), or to postnatal sensitization by contact with circulating antigen and /or immune complexes transmitted by milk (Santoro *et al.,* 1977).

The aim of the current study is to investigate the effect of parasitism on the pregnant mice & the resultant abortion .

Materials and Methods

Source of infection

The infective cercariae have been isolated from snail (Bulinus truncates) which used as Intermediate host.(Meier-Brook, 1978)

Infection of pregnancy

Gestation periods lasted the normal (21) days in the Balb/c mice (Dantzer and Bjorkman, 1993). Mixing between male and female mice allowed for 5 days,then female isolated from male . However, where weigh female before mix, any weight gain female after this mixture consider primary indicator to Pregnancy (Al-maki, 2001).

The 30 pregnant mice were infected percutaneously by the Leg immersion technique (VanWyk *et al*., 1975).using (100) cercariae per pregnant mice per day for 5 days starting from 10^{th} day of pregnancy,the other 20 pregnant mice left unexposed to ***Schistosoma haematobium*** as a control group.

Histopathological study

specimens (Lung and Kidney) were obtained from 8 Stillbirths from experimental infected pregnant mothers .They were fixed in buffered formalin (10%), dehydration, clearing, embedded in paraffin wax,(5-6μ)thick section were cut and tissue sections were stained by Hematoxylin & Eosin (Luna,1960) and examined under Light microscope.

Results

The control fetus did not show any pathological changes. Control fetus lung **(Fig 1)** showing a group or cluster of alveoli opening into an alveolar duct which is opened into an alveolar sac. Regarding the aborted mice lung specimen of mice aborted in 7 days after exposure show very marked changes including infiltration of inflammatory cells; mainly of lymphocytes within the parenchyma of the alveoli, haemorrhage and there is also extensive necrosis **(Fig 2).** (8) days after exposure section in the lung showed a Congestion **(Fig 3).**In **(Fig 4)** control fetus kidney consisting of a glomerulus (a mass of branching Capillaries,) glomerular capsule (Bowman's capsule)and tubules, lie adjacent to the glomerulus . In the kidney of aborted fetus : specimen of abortion after 7 days show atrophic glomeruli, rupture of parietal layer of Bowman's capsule and extensive necrosis **(Fig 5).** (**Fig 6**) after (8) days of exposure to cercariae , show in some instance neutrophil inflammation of the tubules. and shrinkage and atrophied glomeruli and necrosis **(Fig 7)** . There was atrophy of some tubules (**Fig 8) .** in the kidney obtain from aborted mice after (8) days of exposure , Acute inflammation and hemorrhage (**Fig 9**).

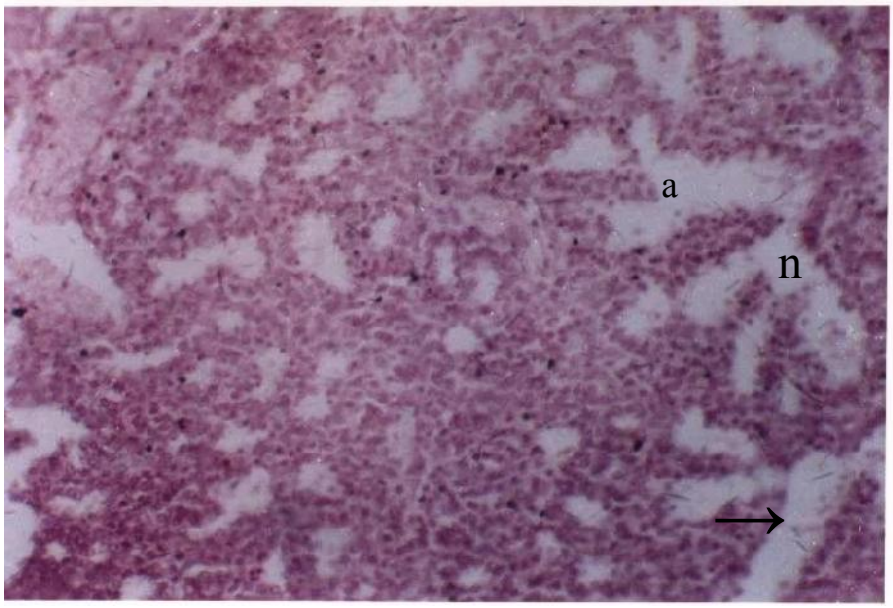

Fig (1) Normal fetus lung tissue showing Alveolar sac (n), Alveolus (a) and Alveolar duct (→) (H&E, magnification 175X)

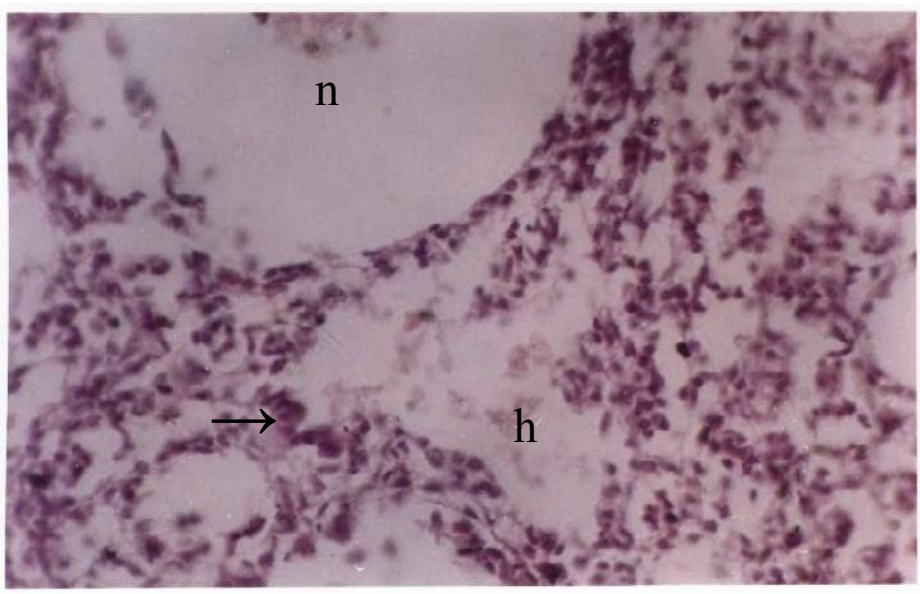

Fig (2) Section of lung after (7) days of exposure shows infiltration of lymphocytes (→), haemorrhage (**h**) and necrosis (**n**)
(H&E, magnification 370X)

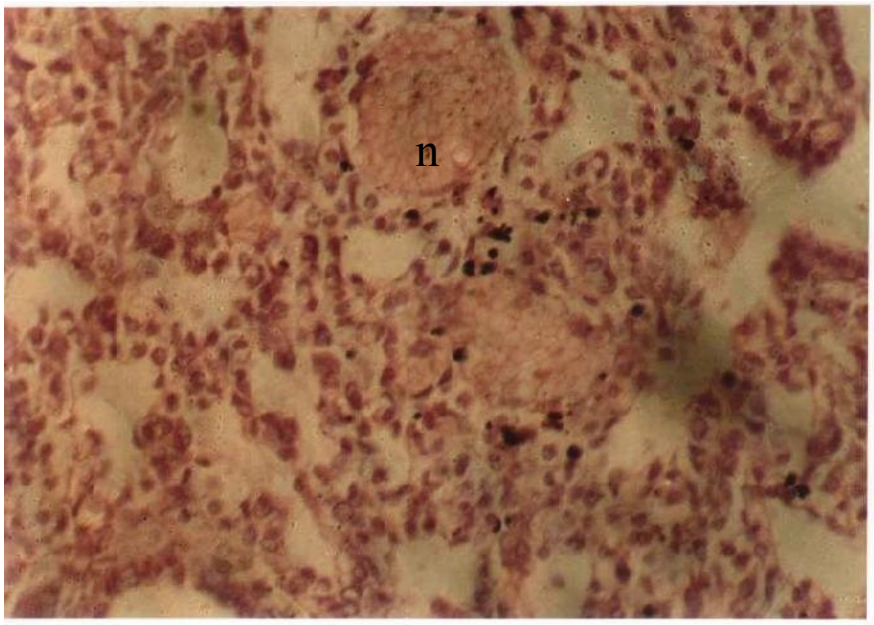

Fig (3) Section of lung showing a Congestion (**n**) after (8) days of exposure
(H&E, magnification 160X)

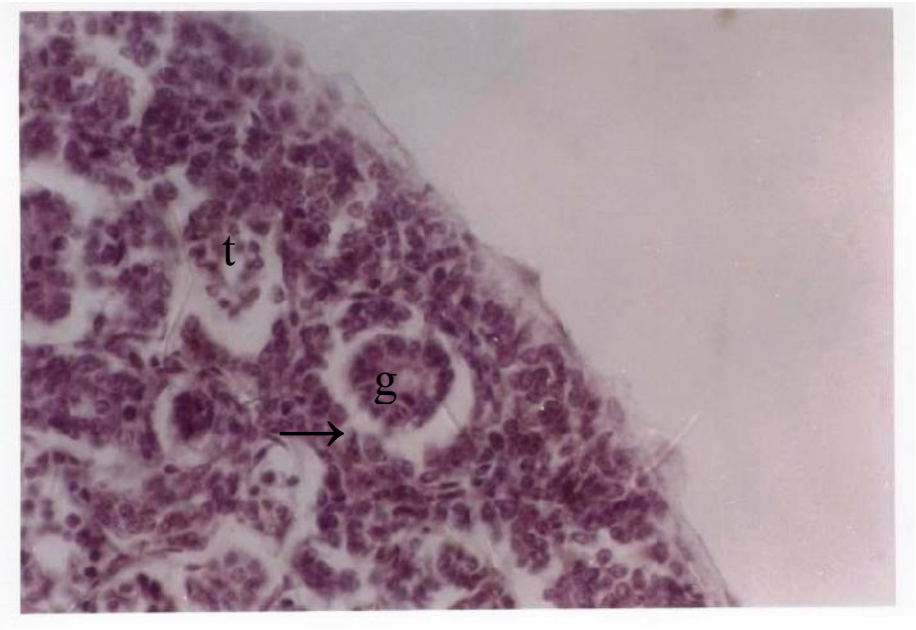

Fig (4) Normal fetus kidney tissue showing a glomerlus (g) , Bowman's capsule (→) and tubules (t). (H&E, magnification 400X)

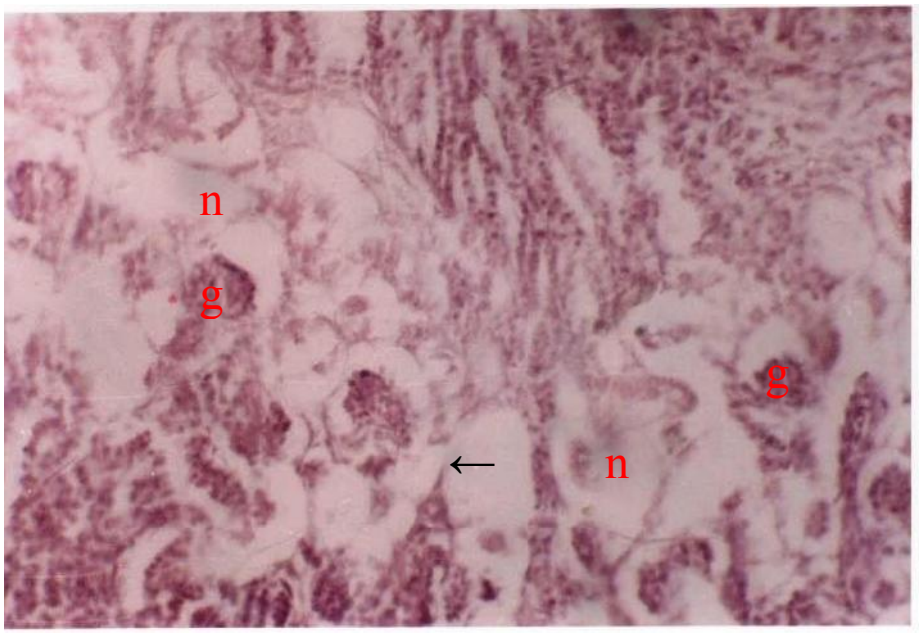

Fig (5) Kidney section from aborted mice after (7) days shows atrophic glomeruli (g), rupture of parietal layer of Bowman's capsule (←) and extensive necrosis (n). (H&E, magnification 250X)

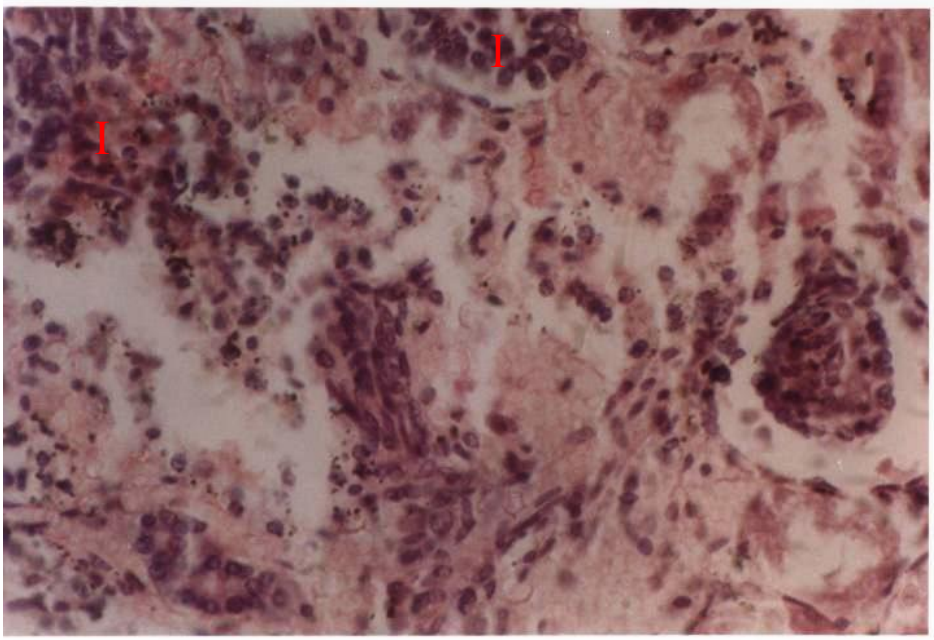

Fig (6) Section of kidney tissue of stillbirth after (8) days shows diffuse inflammation (I) within the tubules. (H&E, magnification 360X)

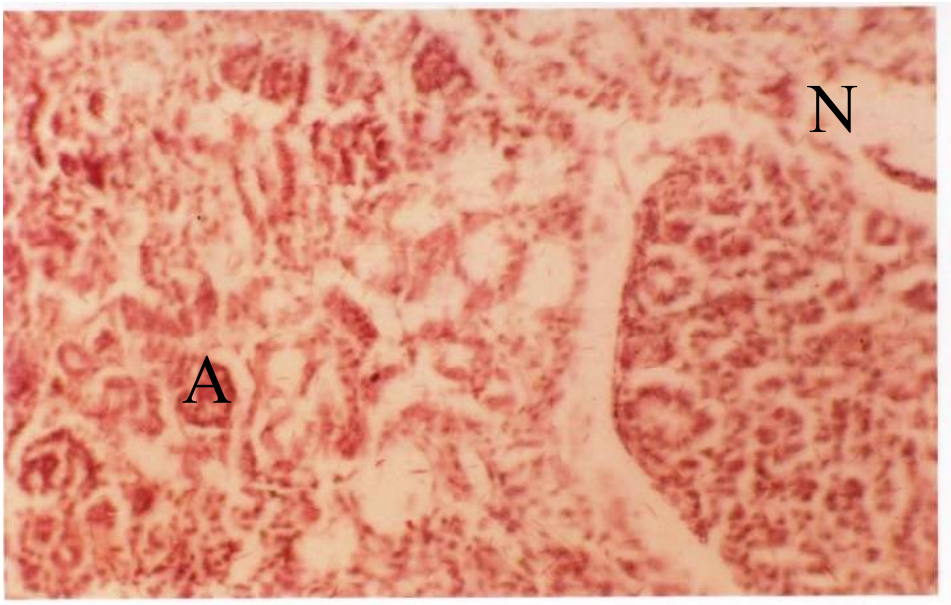

Fig (7) Section of kidney tissue of stillbirth after (8) days shows atrophic glomeruli (A) and extensive necrosis (N) (H&E, magnification 340X)

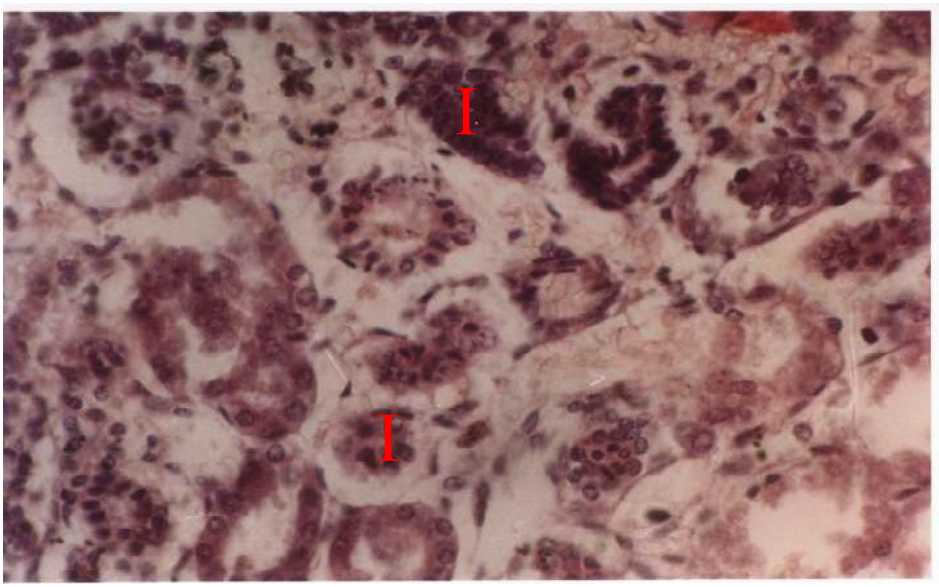

Fig (8) Section of kidney after (8) days showing some tubular Atrophy (I) in renal corpuscle. (H&E, magnification 360X)

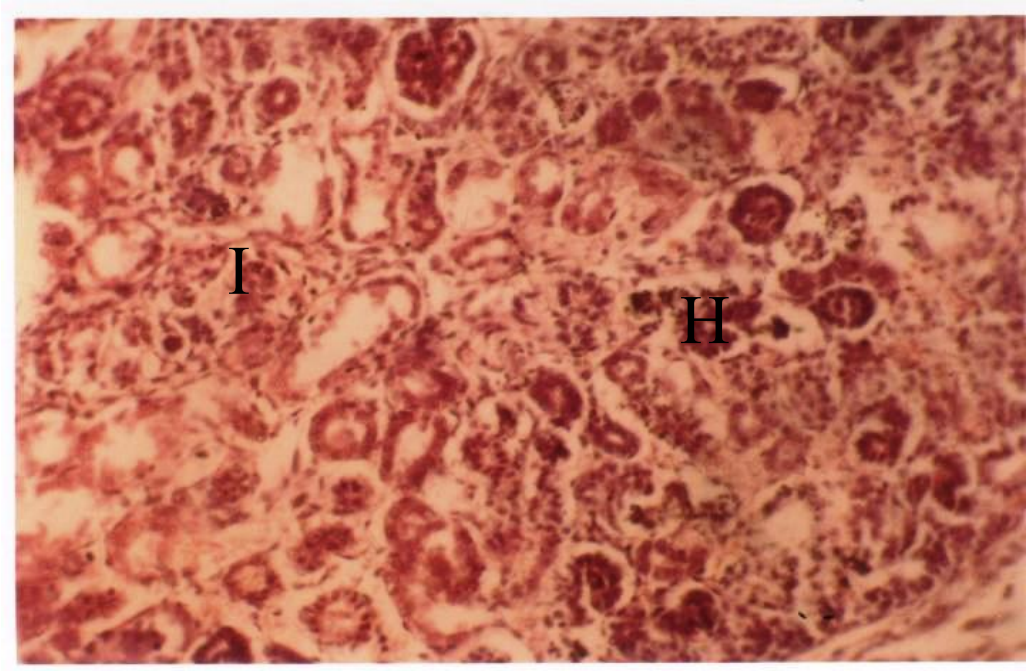

Fig (9) Section of kidney after (8) days exposure showing Acute inflammation (H) and hemorrhage (I) (H&E, magnification 180X)

Discussion

Abortion occur usually late in the pregnancy period of mice . the pregnant mice exposed to cercaria in accumulated concentration.. the percentage of aborted mice is 26.6 % It was found that a reduction in the amount of haemoglobin in the blood,causing cardiac output to increases but not enough to compensate for the reduced oxgen carrying capacity of the blood and the tissues suffer from anamic hypoxia (Macsween and whaley, 1992).

The current study findings in the lung tissue showed lymphocytic infiltrations within the parenchyma of the alveoli, haemorrhage and necrosis may result from antigen that released in the circulation and subsequently reacts with its specific antibody, when coupled to complement it could lodge in other organs such as the lung (Wang , 1959) , A chemotactic response to this complex could ensue and cause damage to the organ & causing further hypoxia was also suspected by Carpenter (1970) and Muller-Eberhard (1969). However, this inflammation in Lung due to presence of persistent irritants/antigens, of infectious or non-infectious nature, serving as a chronic inflammatory stimulus (Weinstock and Bors, 1983).

In a recent study of different newborns in an area of Kenya where found that schistosomiasis, and filariasis during pregnancy can stimulate Ag-specific B cell immunity as well as T cell memory in utero and produce polyclonal IgE and helminth Ag-specific IgG Abs (Christopher et al.,1998). Therefore, in utero development of B cells with the capacity to make IgE may also predispose an infant to the development of allergic responses to environmental and Ags (Actor et al., 1994). On the other hand, the kidney selected for investigation due to their important role in the different metabolic activities, besides their role in excretion of dangerous substances.

In the present study histological changes in kidney were directly related to the immunological renal injury could be produced by two means: the first, by antibodies capable of reacting with antigens fixed in the kidney as in the case of anti-kidney sera or, second, by circulating antigen-antibody complexes which are themselves immunologically unrelated to the kidney but will accumulate in the glomeruli was also proved by Unanue and Dixon (1967).

This in line with histopathological studies by Al-maki (2006) of the tissues of stillborns mice from experimental infected pregnant mothers by *S. haematobium* revealed variable degrees of damage including inflammatory response, Congestion, haemorrhage and necrosis in the liver. whereas, The main pathological changes in spleen were the red pulps are dilated, proliferation of macrophages and fibroblasts in the splenic cords and haemorrhage resultant of a specific circulating antigen (soluble parasite Ags) pass form the maternal to the fetal circulation

.alternatively, transplacental transfer of maternal helminth-specific anti-iodiotypic Abs(Eloi-santos *et al*.,1989)) and/or maternally derived cytokines may influence Neonatal sensitization to parasite Ags(Christopher et al.,1998).on the other hand, regarding antigen-antibody complexes, they found that the size of the complex was of major importance in their localization within the glomerular wall. Thus immune complexes formed in antigen excess were the ones which tended to localize in the glomeruli whereas complexes formed in antibody excess or near equivalence were rapidly eliminated from the circulation and deposited in the liver, lung, and spleen and cause damage to these organs (Gabriel *et al.,* 2004).

Conclusion

The histopathological effect of schistosomiasis on fetuses of infected mothers is attributed to immunological response of antigen-antibody complex reaction and deposition in sensitive organs as kidney causing renal failure, or in lung leading to hypoxia,both finally causing fetal death and abortion.

As these changes may occur in human infection so there is a possibility of similar effect of schistosomiasis in human.

References

- **Aase, J.M.,G.R.Noren, D.V. Reddy, JrJ.W.St. Geme (1972).**Mumps-virus infection in pregnant woman and the immunologic response of their offspring. N. Engl. J. Med. 286:1379.
- **Al-maki,K.M.(2001).** Congenital transmission of *S.haematobium* in mice Embryo and its histological effect on first and second delivery infants born from experimental infected mothers. athesis, college of science, University of Basrah .109 pages.
- **Al-maki,K.M.(2006).** A study on the histopathological effect of *Schistosoma haematobium* on stillborns mice.J.Basrah .Res. Vol:32,part 2 :88-96.
- **Actor,J.;Shirai Kullberg,M.; Buller,R.; Sher, A.&Berzofsky,J.(1994).** Helminth infection results in decreased virus-specific $CD8^+$ cytotoxic T-Cell and Th1 cytokine response as well as delayed vurus clearance.Proc. Natl.Acad.Sci.USA 90:948.
- **Brito,T.,Gunji,j.,Camargo,M.E.,Penna, D.O.,and Silva,L.C.,(1970)**.Advanced kidney disease in patients with hepatosplenic schistosomiasis Mansoni. Rev.Inst.Med.Trop.s.paulo,12:225-235.
- **Camus,D.;Carlier,Y.;Bina,J.C.;Borojevic,R.;Prata,A.and capron,A.(1976).** Sensitization to *Schistosoma mansoni* antigen in uninfected children born to infected

mothers. Journal of Infectious Diseases, (in press).

- **Christopher,L.K.;InduM.;Peter,M.;AlexW.;John,K.;John,H.O.;&James,W.K. (1998)**.B cell sensitization to helminthic infection develops in utero in Humans. J.Immuno.,160:3578-3584.
- **Carpenter,C.B.(1970)**.Immunologic aspects of renal disease.Ann.Rev.Med. 21:1-16.
- **Dantzer,V.and Bjorkman,N.(1993).** Placentation.Dellman HD.(ed) textbook of veterinary histology.philadelphia: Lea&Febiger.255-269.
- **Eloi-santos,S.M.;Novata-silva,E.;Maselli,V.M.;Gazzinelli,G.;Colly,D.G.&Correa- Oliveira, R.(1989)**. I diotypic sensitization in utero of children born to mothers with cshistosomiasis or changes disease.J.Clin.Invest.84:1028
- **Gabriel,S.;Phiri,I.K.;VanDam,G.J.;Deelder,A.M.;Duchateau,L.G.&Vercruysse,J.(2004)**.Variations in immune response to natural *Schistosoma mattheei* infections in Calves born to infected mothers. Veter. Parasitol.119:177-185.
- **Gill, T.J.,III,Kunz,H.W.,and Bernard, C.F. (1971)**. Maternal-fetal interaction and immunological memory. Science, 172:1346.
- **Hara,T.,S.Ohashi,Y.Yamashita,T.Abe, H.Hisaeda,K.Himeno,R.A.Good,K.Takeshita (1996)**.human $V\delta2^{+}\gamma\delta$T-cell tolerance to foreign antigens of *Toxoplasma gondii*. Proc.Natl. Acad.Sci.USA 93:5136.
- **Luna,L.G.(1960).**Manual of histologic staining methods of the armed forced institute of pathology.3rd ed .McGraw-Hill Book Co.London
- **Macsween,R.M.and Whaley,K.(1992).** Muir's, Textbook of pathology.13th ed.Edward Arnold,London.
- **Meier-Brook,C.(1978).**Calcium uptake by Marisa cornuarietis(Gastropoda: Ampullariidae),apredator of schistosome-bearing snails.Avchiv fur hydrobiology 82:449-464.
- **Muller-Eberhard, H.J.(1969).** Complement. Ann.Rev.Biochem.,38:389-414.
- **Santoro,F.,Borojevic ,R.;Bout, D. ; Tachon, P.;Bina,J.C.and Capron, A.(1977).** Mother-child relationship in human schistosomiasis Mansoni. I-Parasitic antigens and antibodies in milk.Am.J.Trop. Med. Hyg. Baltimore, 26:664-668.
- **Tachon,p.,and Borojevic,R,(1978).** Mother-child relationship in human schistosomiasis Mansoni .II.skin test and cord blood reactivity to parasitic antigen .
- **Taylor,M.G.(1987).**Schistosomes of domestic animals:*Schistosoma bovis* and other animal forms. In immune Responses in parasitic infections, Vol II:Trematodes and Cestodes (ed. Soulsby,E.J.L.),pp. 49-90,CRC press, Boca Raton, USA.

- **Unanue, E.R.,and Dixon,F.J.,(1967**). Experimental glomerulonephritis: Immunological events and pathogenic mechanisms .Adv. Immunol. 6:1-90
- **VanWyk,J.A.;Heitmann,L.P.and VanRensburg,L.J.(1975).**Studies on Schistosomiasis: 7, A Comparison of Various methods for the infestation of Sheep with ***schistosma mettheei***.Onder.J..Veter.Res, 42, 71-74
- **Wang,X.Y.(1959).**Abortion in cattle (in japanese).Ministry of Health peoples Republic of china, ed. Control of Domestic Animal schistosomiasis .shanghai: Shanghai science and Technology press.141-151.
- **Weinstock,J.V. and Boros,D.L.(1983).** Organ-dependent differences in composition and function observed in hepatic and intestinal granulomas isolated From mice with ***Schistosoma mansoni*** .J.Immunol.130:418-422.

دراسة التأثيرات النسيجية المرضية لطفيلي Schistosoma haematobium على الرئات والكلى للأجنة المجهضة من أمهات مصابة مختبريًا

أياد قاسم مهدي

جامعة البصرة – كلية الصيدلة –فرع الادوية والعلوم المختبرية السريرية

الخلاصة

الدراسة الحالية شملت(50)من الفئران الحوامل وزعت إلى(20)حامل سيطرة و(30)حامل عرضت للإصابة بطفيلي ***Schistosoma haematobium***، تم تعريض الحوامل للاصابة بالطفيلي في اليوم العاشر من الحمل (نصف فترة الحمل) وبجرعة قليلة ولكن مستمرة لمدة 5 ايام ، وحدثت الاجهاضات بعد 7-8 ايام من اليوم الاول للتعرض (اليوم السابع عشر- اليوم الثامن عشر من الحمل). تبين من الدراسة النسيجية المرضية للمقاطع المأخوذة من الاجنه المجهضة للولادة الأولى تغيرات في نسيج الرئة شملت ارتشاح للخلايا المفاوية ضمن الحويصلات الهوائيحتقان ونزف ونخر.في حين إن أهم التغيرات المرضية في الكلية شملت ضمور الكبيبات وتمزق في جدار محفظة بومان وتنخرات وضمور في النبيبات البولية واستجابة التهابية حادة ونزف.