Summary and Conclusion

720 inbred albino mice 6-8 weeks of age were used in this study. Cercariae of *S. mansoni* and *S. haematobiun* were liberated separately from relative snails after placing under electric lamp for two hours. After determining the count of each cercarial type, 100 cercariae, of each were added to dechlorinated water in funnel-shaped bottles for infecting mice. Schistosomal antigens: cercariae, egg and worm antigens of *S. mansoni* and *S. haematobiurn* were supplied by Theodor Bilharz Research Institute and reconstituted by PBS to a concentration of 1g/1000 ul for injection.

The animals were divided into three groups as follows:

Group (1): control group comprising 48 untreated mice.

Group (2): comprises animals infected and injected with cercariae and antigens of *S. mansoni.* The animals were divided into 7 subgroups according to treatment. Subgroup (I) infected with living cercariae only, subgroups (II), (V) and (VII) injected with cercariae, egg and worm antigens respectively. Sugroups (III), (IV) and (VI) all infected with living cercariae and injected with cercariae, egg and worm antigens respectively.

Group (3): comprises animals treated with living cercariae and antigens of *S. Imematobium* in a way similar to group (2).

After treatment, the animals of threee groups were sacrificed at 8, 22, 32 and 44 weeks intervals. Liver specimens were taken from animals of group (1) and (2), while urinary bladder specimens were taken from animals of group (1) and (3). All specimens were processed for histopathological and immunohistochemical studies. Haematoxylin and eosin staining was used for histopathological evaluation while the immunohistochemical staining includes AFP (for liver) and Cytokeratin (for Bladder) monoclonal antibodies.

** The histopathological changes in the hepatocytes were showed no pathological changes in 97.6% of animals sacrificed at 8 weeks. And hydropic degeneration and fatty changes in 2.4%, 88.1%, 61.9% and 19% in animals sacrificed at 8, 22, 32 and 44 weeks respectively. These pathological changes were restricted to subgroup IV in animals sacrificed at 8 weeks and subgroups injected with antigens only in animals sacrificed at 44 weeks.

-The second pathological changes in hepatocytes were degeneration and necrosis in 11.9%, 31.0% and 42.9% in animals sacrificed 22, 32 and 44 weeks and were present in subgroups with concomitant infection in animals sacrificed at 22

and 32 weeks and with high percentage in subgroups injected with antigens only in animals sacrificed at 44 weeks.

-And the third pathological changes in hepatocytes were degeneration and necrosis with regenerated hepatocytes in the 7.1% and 35.7% in animals sacrificed at 32 and 44 weeks respectively, the hepatocytes showed atypical hyperblastic hepatocytes in 2.4% of animals sacrificed at 44 weeks and restricted to subgroup IV.

*The histopathological changes in the portal tract showed mild dilation and fibrosis in 88.1%, 38.1%, 35.7% and 28.6% in animals sacrificed at 8, 22, 32 and 44 weeks and restricted in most subgroups in animals sacrificed at 8 weeks, while restricted in subgroups injected with antigens only in animals sacrificed at 22, 32 and 44 weeks.

-Second pathological changes were moderate dilation and fibrosis with percentage 11.9%, 57.2%, 45.2% and 40.5% in animals sacrificed at 8, 22, 32 and 44 weeks and restricted to the subgroups IV and VI in animals sacrificed at 8 weeks, while present in subgroups I, III, IV, V, VI and VII in animals sacrificed at 22 weeks and present in all subgroups except subgroup VII in animals sacrificed at 32 weeks and present in all subgroups in animals sacrificed at 44 weeks.

-The third pathological lesions is marked dilation and fibrosis (broad bands fibrosis pipe stem appearance) and bile duct proliferation and this present in subgroup IV in animals sacrificed at 22 weeks and restricted in subgroups III, IV and VI in animals sacrificed at 32 weeks. Finally restricted in subgroups I, III, IV and VI in animals sacrificed at 44 weeks.

*The pattern of inflammatory infiltrate in the portal tracts were diffuse inflammatory infiltrate these were present in subgroups injected with antigen only in animals sacrificed at 22, 32 and 44 weeks.

-The second pattern of inflammatory infiltrate in the portal tract was few and moderate bilharzial granuloma, present in subgroup infected with cercariae only in animals sacrificed at 22 and 32 weeks and few, moderate and prominent granuloma in subgroups infected with cercariae and injected with antigens in animals sacrificed at 22, 32 and 44 weeks.

* The immunohistochemistry study to AFP showed negative reaction in 100%, 96.4%, 52.4% and 7.1% in animals sacrificed at 8, 22, 32 and 44 weeks. But 3.6% showed mild positive reaction restricted to subgroup infected with cercariae and injected with egg antigen in animals sacrificed at 22 weeks,

35.7% in animals sacrificed at 32 weeks restricted to subgroups I, III, IV, VI and VII and 50% in animals sacrificed at 44 weeks represented in subgroups I, II, V, VI and VII.

-11.9% and 36,7% showed moderate positive reaction in animals sacrificed at 32 and 44 weeks respectively represented in subgroups I, III, V and VI. Finally 7.1% showed marked positive reaction in animals sacrificed at 44 weeks restricted in subgroups III and IV that infected with cercariae and injected with cercariae and egg antigens respectively.

** The histopathological changes in urinary bladder were showed no pathological changes in 57.1% of animals sacrificed at 8 weeks, but transitional cell hyperplasia only in mucosa with diffuse inflammatory infiltrate in submucosa represented in 42.9%, 61.9% 40.5% and 42.9% in animals sacrificed at 8, 22, 32 and 44 weeks respectively and these pathological changes restricted to subgroups with concomitant infection in animals sacrificed at 8 weeks and restricted to subgroups injected with antigens only in animals sacrificed at 22, 32 and 44 weeks.

-The second pathological changes were squamous metaplasia in mucosa and diffuse inflammatory infiltrate and granulomatous reaction in 38.1%, 19.0% and 11.9% in animals sacrificed at 22, 32 and 44 weeks and these pathological changes

restricted to subgroup infected with cercariae of *S. haematobium* and subgroups with concomitant infection in animals sacrificed at 22 and 32 weeks with high percentage in animals sacrificed at 22 weeks. While restricted to subgroup infected with *S. haematobium* only in animals sacrificed at 44 weeks.

-The third pathological changes were Brun's nest, Cystitis cystica, and cystitis glandularis in mucosa with the same pathological changes in submucosa in animals sacrificed at 32 and 44 weeks with percentage 40.5% and 23.8% respectively while the pathological changes restricted in subgroups I, III, IV and VI in animals sacrificed at 32 weeks and restricted in subgroups I, III, VI in animals sacrificed at 44 weeks with low percentage in subgroup I.

-The last pathological changes were displasia grad I and grad II in mucosa and diffuse inflammatory infiltrate with granulomatous reaction in submucosa in animals sacrificed at 44 weeks and restricted to subgroups with concomitant infections.

*The immunohistochemistry study to cytokeratin showed negative reaction in animals sacrificed at 8, 22 and 32 weeks with percentage 100%, 92.8% and 57.2% respectively, while 4.8%, 33.3% and 50% showed mild positive reaction in animals sacrificed 22, 32 and 44 weeks respectively and their reaction

were restricted to subgroups VI and VII in animals sacrificed at 22 weeks, subgroups I, III, IV, VI and VII in animals sacrificed at 32 weeks, with increase subgroup II in animals sacrificed at 44 weeks. But 2.4%, 9.5% and 42.9% showed moderate positive reaction in animals sacrificed at 22, 32 and 44 weeks and these reaction restricted to subgroup infected with cercariae haematobium and injected with egg haematobium antigen in animals sacrificed at 22 and 32 weeks. And in all subgroups except subgroup II in animals sacrificed at 44 weeks with high percentage in subgroups IV and VI.

-Finally 7.1% showed marked positive reaction in animals sacrificed at 44 weeks and restricted to subgroups IV and VI with high percentage in subgroup IV.

*** In view of these facts we may conclude that the concomitant infection promoted the occurrence of earlier changes in urothelial cells and hepatocytes that were absent from subgroups with living cercariae infection only and subgroups injected with antigens only. While with increase time of infection and injection premalignant changes in liver and bladder appeared in the animals with concomitant infection.