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EVALUATION OF THE EFFECTS OF INTRA-ARTICULAR INJECTION OF DIMETHYLSULFOXIDE ON CHEMICALLY INDUCED ARTHRITIS IN EQUINES.

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SUMMARY

Experimintally chemically induced arthritis was performed using single intraarticular injection of 10 mg amphotricine B in left radiocarpal joint of 10 horses and 5 don keys. These animals were divided into 5 groups to discuss the therapeutic value of different concentrations of Dimethylsulfoxide and the effect of 40% dimethylsulfoxide on different stages of chemically induced arthritis. It is found the the use of Dimethylsulfoxide 40% weekly for three successive weeks after one week of induction was the best concentration for treatment of that condition. Dimethylsulfoxide 40% weekly was mainly effective in the treatment of mild degenerative stage.

INTRODUCTION

Aseptic arthropathies are a major cause of equine lameness (McIlwraith, 1981 A). Infammation within the joint induces increased metabolic activity and vascular permeability of the synovial membrane resulting in effusion and changes in synovial fluid composition (McIlwraith, 1981 A and Clyne, 1987). The development of intaarticular inflammation is associated with an accumulation of lyosomal enzymes, free radical oxides and hydroxide anions (McIlwraith, 1981 A & B and 1982 and Clyne, 1987).

Dimethylsulfoxide (DMSO) has been demonstrated to be an effective antiinflammatory analgesic and enzyme activato/inhibitor (Alsup, 1984 and Brayton, 1986). It is a very simple compound that has stimulated much controversy in the scientific and popular literature. It is a clear, colourless to yellow liquid that freezes at 18.5°C. It is a dipolar, aprotic, highly hygroscopic solvent (MacGregor, 1967; David, 1972; Kharasch et al. 1983 and Windholz, 1983). The dipolar nucleophilic character of the molecule is due to the available free electron pairs at the sulfur and oxygen terminals (Rammler et al., 1967; MacGregor, 1967; David, 1972 and kharasch et al., 1983). Many biological barries (lipoprotein membranes) are readily permeable to DMSO and not appreciably altered or demaged by dimethylsulfoxid's passage (MacGregor, 1967; David, 1972; Jacob et al., 1983 and Kharasch et al., 1983). The cellular toxicity is relatively low (Lovelock et al., 1959). A 90% dimethylsulfoxid is available in gel or liquid form; it is indicated for use in acute swelling due to trauma in horses, it should be applied only topical (Diamond Laboratories). A 50% dimethylsulfoxid solution may be administered by direct intravesicular instillation only in the treatment of interstitial cystis (A.M.A. Department of Drugs, 1980). As a result of its soothing effect and the promotion of rapid healing of mnor burns as well as relieving of pain and swelling of other injuries, research on DMSO for other biological and medical applications was stimulated. Robert hereschler of the crown Zellerbach Paper company, and Stanly Jacob of the University of Oregon medicial

School were strong proponents of the early studies of DMSO as a therapeutic agent (Leake, 1967, Leake, 1975; Bertfeld et al., 1975 and Doughlass et al., 1983). Some researchs revealed that DMSO inhibits or stimulates enzymes in vitro and in vivo (Mallach, 1967; Monder, 1967; Ralmmler et al., 1967; Sams, 1967; Perlman et al., 1968 and Sawada et al., 1975). In vitro, at different concentrations and at different hydrogen ion concentrations, DMSO may have opposite effects on enzyme activity (Mallach, 1967; Monder, 1967 and Rammler, 1967).

DMSO probably exerts its primary effect by reversibly altering protein configuration (Diamond Laboratories). It may (Tiegland et al., 1967 and Ward et al., 1967) or may not (Ashly, 1967) reduce inflammation and oedema in ecperimental models. In clinical situation, an antiinflammatory benefit from DMSO therapy is reported with acute musculoskeletal injuries (Rosenbaum et al., 1965 A & B; Brown, 1967; Demos et al., 1967; Goldman, 1967; John et al., 1967; Knowles, 1967; Steinberg, 1967; Averkin et al., 1975 Dubinsky et al., 1975; Brown, 1982; Grant, 1982 and Reed, 1983 A & B). In chronic inflammatory conditions, results are less consistently achieved, some successes are reported with rheumatic diseases (Matsumoto, 1967; Zuckner et al., 1967; Gorog et al., 1975; Jimenez et al., 1982; Scott et al., 1983 and Scheinberg et al., 1984) and in chronic arthritis (Blumenthal et al., 1967; Demos et al., 1967; John et al., 1967; Paul, 1967; Gorog et al., 1975 and Brown, 1982). Application of DMSO over acute sprains, strains, bursitis and their associated soft tissue swellings and haematomas relieves pain and swelling and improves function fo the affected part of the body more rapidly than do conventional mode of therapy, according to clinical investigations on humans (Rosenbaum et al., 1965 Blumenthal et al., 1967; Brown, 1967; Demos et al., 1967; Goldman, 1967; John et al., 1967; Steinberg, 1967; Dubinsky et al., 1975 and Brown 1982) dogs (Knowles, 1967; Averkin et al., 1975 and Jacob et al., 1982) and horses (Diamond laboratories, Levesque, 1967; Tiegland et al., 1967 and Grant, 1982). The primary mechanism of DMSO's acute antinflamatory effect is probably radical scavenging (Szmant, 1967; Torre, 1983 Kharach et al., 1983; Repine et al., 1983 and Rosenblum, 1983). This may contribute to the maintenace of microcirculation which reduces tissue damage in inflammation (Ward et al., 1967, Gorog et al., 1975; Torre, 1983 and Rosenblum, 1983). DMSO-mediated effects on the immune response may also contribute to its antiinflammatory effect. Investigators have reported inhibition of inflammatory cell migration (Antony et al., 1983), modulation of cell mediated immunoresponses (Bartfeld et al., 1975) inhibition of antiboey production (Pestronk et al., 1980) and inhibition of fibroblast proliferation which could be important in chronic conditions (Tiegland et al., 1967 and Berliner et al., 1967).

DMSO's therapeutic properities and intra-articular effect are understood only incompletley. Well designed experimental studies of DMSO's medical and therapeutic effects are desperately needed to provide the necessary information.

MATERIAL AND METHODS

This study was carried out on 20 horses and 5 donkeys. The animals were clasified into 5 gorups as follows:

Group No.	Number of animals	Induction (amphotricin B)	Treatment
1	5 horses	+	DMSO* 40% weekly for 3 successive weeks after one week of induction.
2	5 horses	+	DMSO* 40% daily for 3 successive days after one week of induction.
3	5 horses	+	DMSO* 20% daily for 7 successive days after one week of induction.
4	5 horses	+	DMSO* 40% weekly for 3 successive weeks after 3 weeks of induction.
5	5 horses	+	DMSO* 40% weekly for 3 successive weeks after 4 weeks of induction.

DMSO* = dimethylsulfoxide

Arthritis induced by injecting 10 mg amphotricin B (Bowman et al., 1983) into the left radiocarpal joint 5% dextrose solution was injected into the right carpal joint in order to serve as control.

The animals were subjected to daily clinical examination during the entire experimental period. Radiographs were made of each carpus at the begin of the experiment, weekly interval and immediately before euthanasia. Synovial analysis was performed weekly till the end of the experiment. Samples of synovial fluidwere obtained aseptically by arthrocenteis (Edwards et al., 1977 and Rose et al., 1982). The synovial fluid samples were transferred to plain and EDTA capped vials for examination. The laboratory and cytological values of the synovial fluid were evaluated at the time of arthrocentesis according to VanPelt and Connor (1963). Biochemical analysis of synovial fluid was carried throughout the experimental period. Total protein (Henry, 1964) akaline phosphatase (Sommer, 1954), glutamic oxalacetic transaminases and glutamic pyruvic transaminases (Reitman et al., 1975), lactic acid dehydrogenase (Anon, 1970), and lysozyme (Shuger, 1952) were measured. In addition, hyaluronic acid levels (Meyere et al., 1960 and Tolksdorf et al., 1979) was estimated. Synovial samples were cultured and examined (Haupt, 1964).

Morphological and histopathological examination of the articular cartilage, subchondral bone, joint capsule and synovial membrane were performed after euthanasia. Bone sampels were decalcified using formic acid/HCl 10%. All sections were stained with haematoxyline and eosin according to Carlton et al., 1967.

Treatment of experimentally induced arthritis was carried out by using DMSO 40% weekly for three successive weeks, 40% daily for three successive days, 20% daily for seven successive days (Mostafa, 1993) after one week of induction. Also using DMSO 40% for three successive weeks after threee and four weeks of induction.

A. Experimental treatment of induced arthritis using dimethylsulfoxide with different concentrations one week after induction:

A.1. Dimethylsulfoxide 40% weekly (group 1):

A.1.1. Clinicalfindings:

The clinical findings were characterised by marked decrease in pain and stiffness of the joint, the animal could move freely. The diameter of the joint was reduced with an average of about 0.25±0.03cm. The lameness was gradually improved after the first injection and completely disappeared after the 2nd and 3rd injections. The hotness of the joint was decreased and returned to its normal condition.

A.1.2. Radiological findings:

No evidence of radiographic changes were observed.

A.1.2. Synovial fluid analysis:

The changes in synovial fluid in experimentally induced arthritis after one week of induction as a result of weekly dimethylsulfoxide 40% treatment are shown in Figures (1&2). There were no significant changes in hyaluronic acid ($P > 0.05$), viscosity ($P > 0.05$) and lymphocytes ($P < 0.05$). On the other hand, there was a highly significant increase in mucinous precipitation ($P < 0.01$) and pH ($P < 0.01$); while there was a highly significant decrease in total protein ($P < 0.01$), GOT ($P < 0.01$), GPT ($P < 0.01$), alkaline phosphatase ($P < 0.01$), lactic acid dehydrogenease ($P < 0.01$), lysozymes ($P < 0.01$), WBCs. ($P < 0.01$) and RBCs. ($P < 0.01$). Significant increase in neutrophils ($P < 0.05$) was recorded.

A.1.4. Histopathological changes:

The macroscopical examination revealed no evidence of any changes in the synovial membranceand articular cartilage (Fig. 3).

The microscopical examination revealed that the synovial membrane was lined with one layer of cuboidal epithelial cell. No pathological changes could be detected (Fig. 4). While the cartilage examination revealed individual degenerated cells. The matrix was apparently normal (Fig. 5).

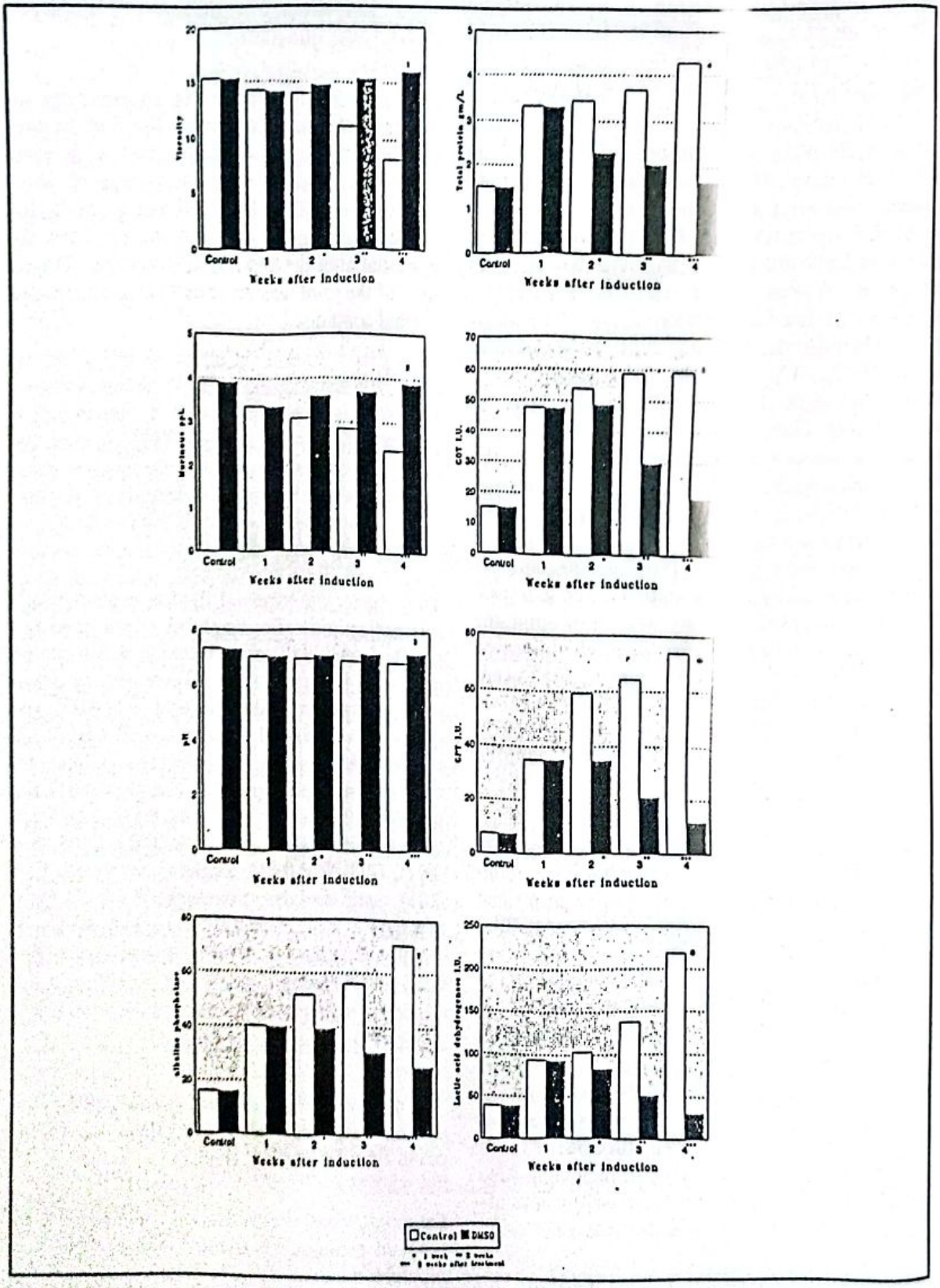

Fig. 1: The changes in synovial fluid of one week chemically induced arthritis after weekly treatment with Dimethylsulfoxide 40%.
1. Viscosity 2. Mucine ppt. 3. pH. 4. Total protein 5. GOT 6. GPT 7. Alkaline phosphatase 8. Lacic acid dehydrogenase.

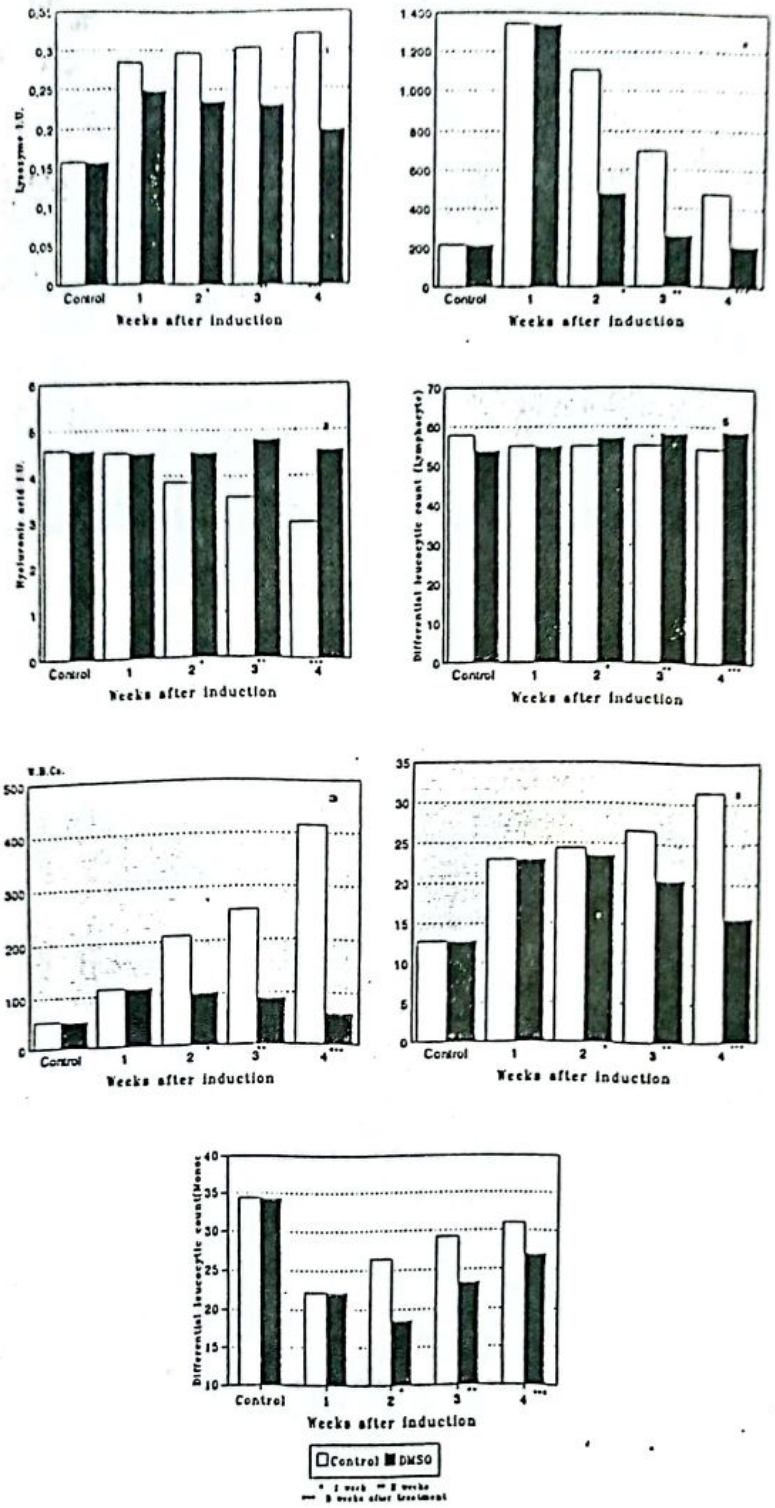

Fig. 2: The changes in synovial fluid of one week chemically induced arthritis after weekly treatment with Dimethylsulfoxide 40%.
1. Lysozyme 2. Hyaluronic acid. 3. WBCs. 4. RBCs. 5. Lymphocyte 6. Neutrophile 7. Monocyte.

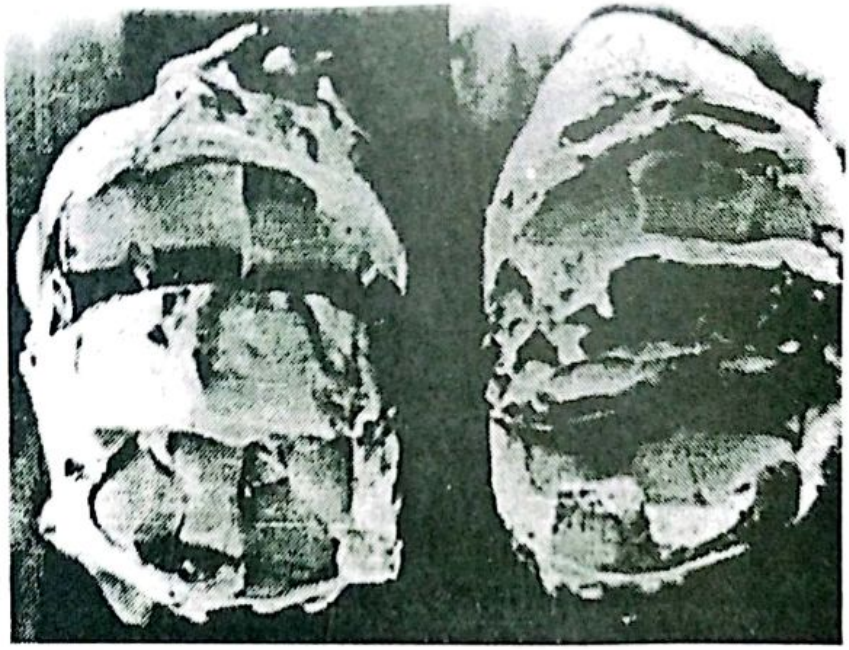

Fig. 3: Joint cavity of after weekly treatment 40% for three successive weeks. Note normal appearance of Joi cavity.

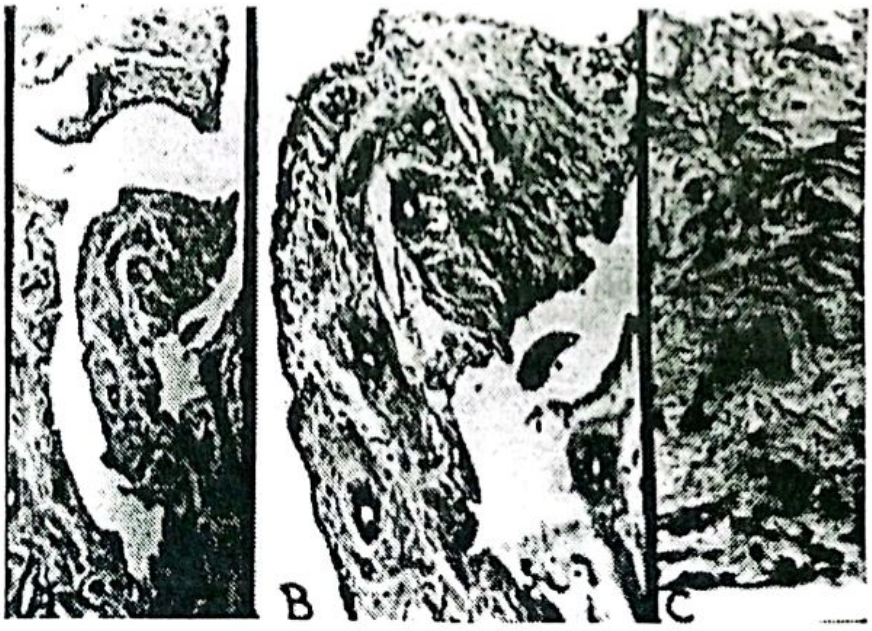

Fig. 4: Synovial membrane after weekly treatment with dimethylsulfoxide 40% for three successive weeks. No normal synovial membrane appearance. (H & E) A x 40, B x 100, C x 400.

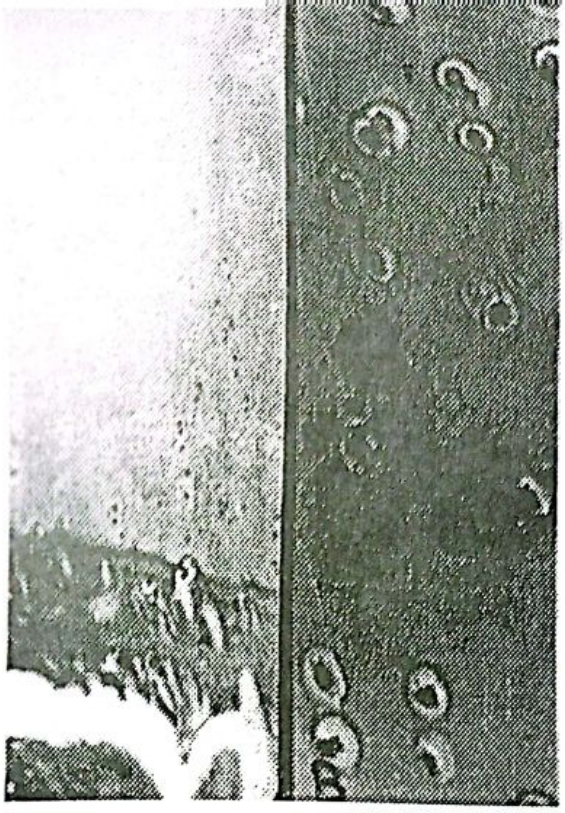

Fig. 5: Articular cartilage after weekly treatment with dimethylsulfoxide 40% for three succesive weeks Note normal appearance of articular cartilage. (H & E A x 40 B x 100).

A.2. Dimethylsulfoxide 40% daily for three successive days (group 2):

There was marked reduction in pain and stiffness of joint enabling the animal to move freely. The diameter of the joint was reduced with an average of 0.24cm ± 0.03. Synovial distension was decreased as well as lameness which declined after the first injection and compleltely disappeared after the third one. The hotness of the joint was decreased and returned to normal temperature.

A.2.2. Radiological findings:

No evidence of the radiological changes was observed.

A.2.3. Synovial fluid analysis:

The changes in synovial fluid in experimentally induced arthritis after one week of induction as a result of daily DMSO 40% treatment are shown in Figures (6 & 7). The recorded changes are relative to the first week value after chemical induction of arthritis. The profiles of total protein, GOT, GPT, Lysozymes, alkaline phosphatase, lactic acid dehydrogenase and RBCs. exhibited highly significant decrease ($P < 0.01$), while the changes in mucinous precipitation, pH and monocytes levels were highly significantly increased ($P < 0.01$). On the other hand, insignificant changes could be detected in viscosity, WBCs., lymphocytes, neutrophiles and hyaluronic acid ($P > 0.05$).

A.2.4. Histopathological changes:

No evidence of any macrosopical changes of the synovial membrane and articular cartilage could be observed (Fig. 8).

Microscopically, no evidence of inflammatory changes in synovial membrane could be detected

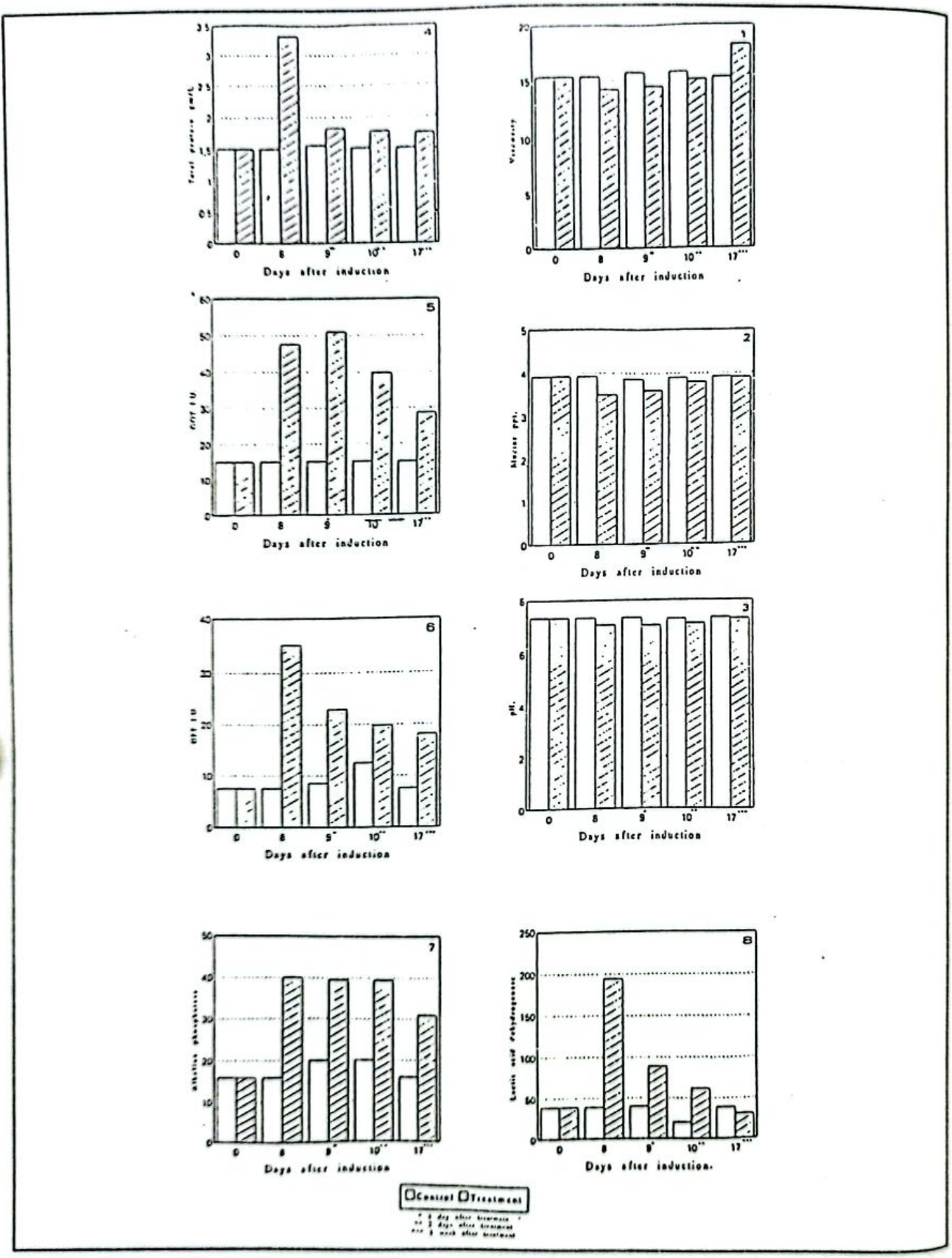

Fig. 6: The changes in synovial fluid of one week chemically induced arthritis after weekly treatment with Dimethylsulfoxide 40%.
I. Viscosity 2. Mucine ppt. 3. pH. 4. Total protein 5. GOT 6. GPT 7. Alkaline phosphatase 8. Lactic acid dehydrogenase.

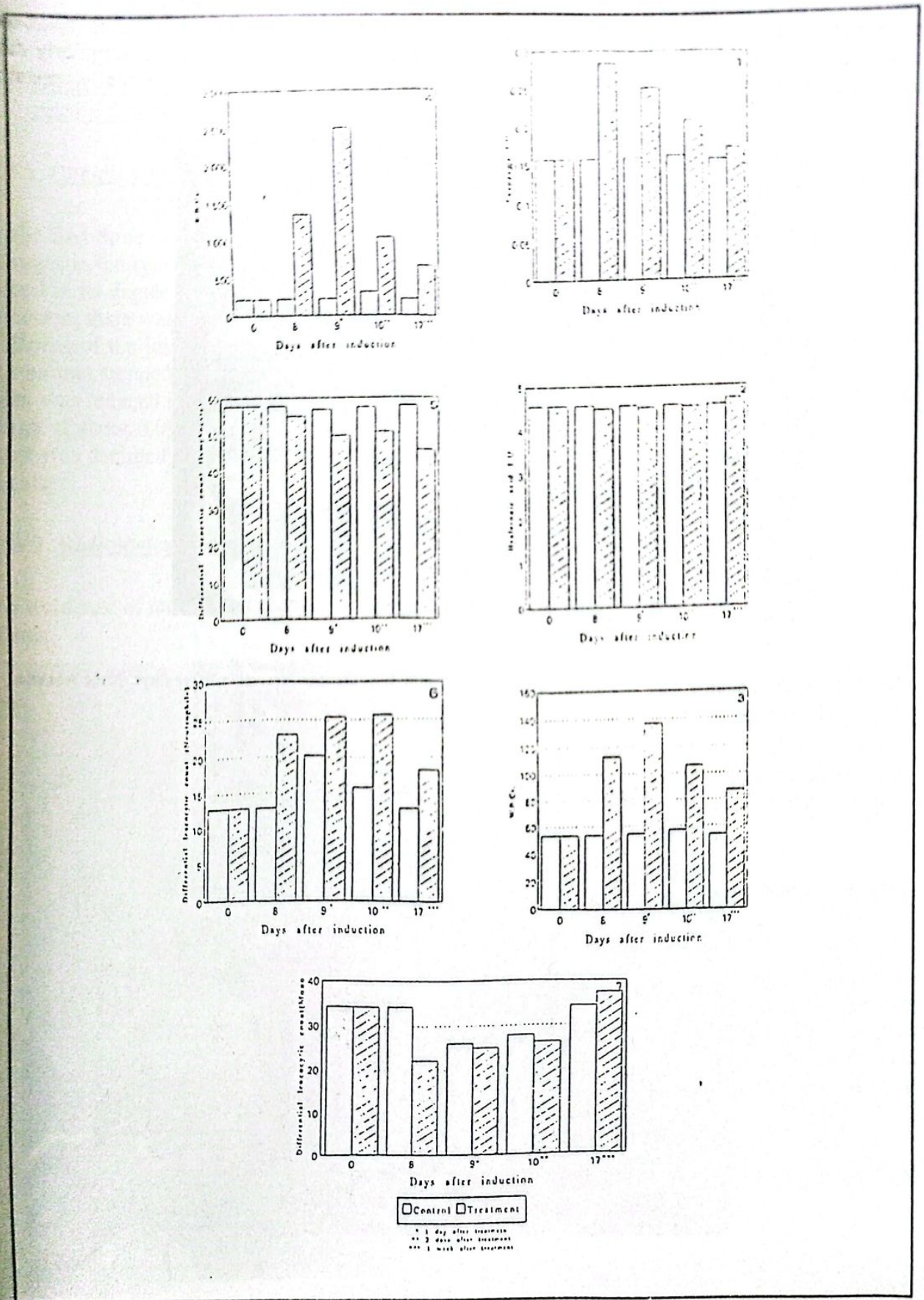

Fig. 7: The changes in synovial fluid of one week chemically induced arthritis after weekly treatment with Dimethylsulfoxide 40%.
I. Lysozyme 2. Hyaluronic acid. 3. WBCs. 4. RBCs. 5. Lymphocyte 6. Neutrophile 7. Monocyte.

and it regained its normal appearance (Fig. 9). The examination of the articular cartilage revealed individual degenerated chondrocytes. There was little chondrocytic degeneration or even necrosis. The chondrocytes appeared to be irregularly distributed. The matrix was apparently normal

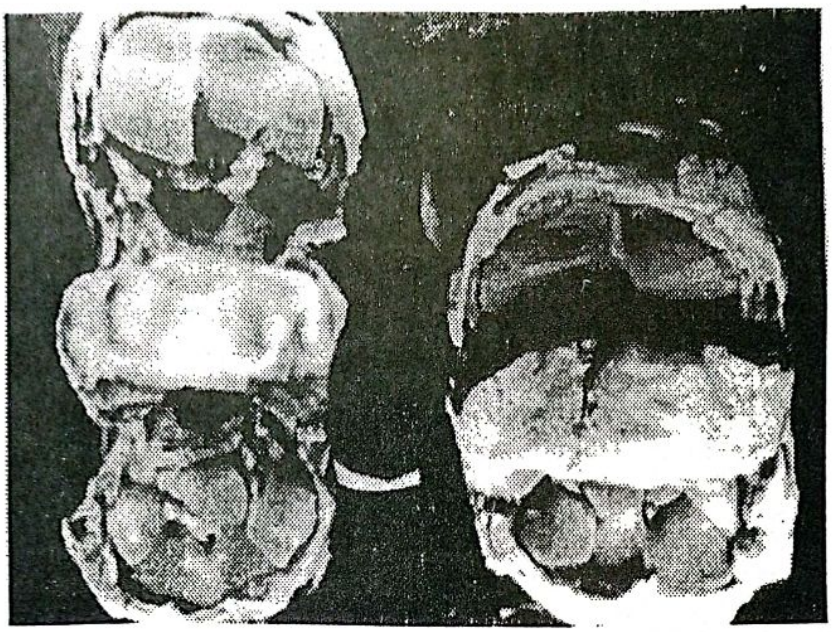

Fig. 8: Joint cavity of after daily treatment with dimethylsulfoxide 40% for three successive days. Note normal appearance of joint cavity.

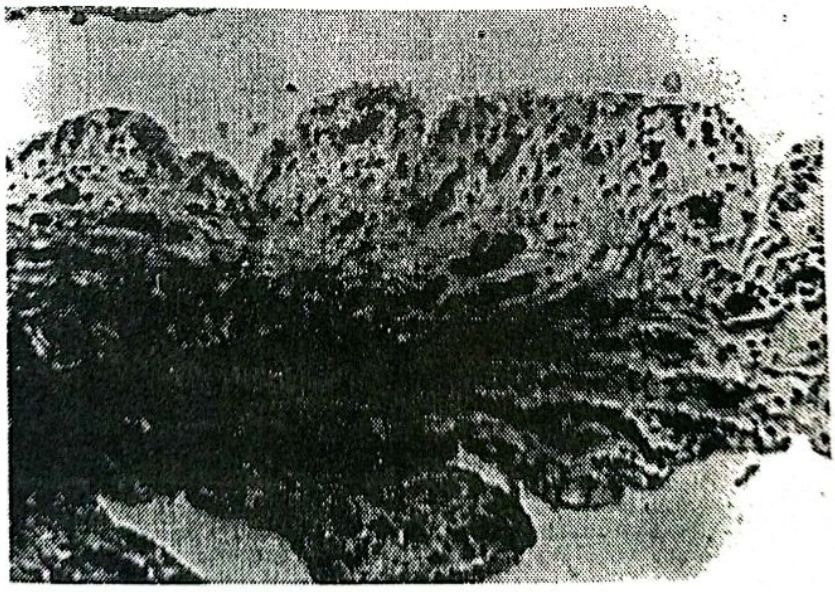

Fig. 9: Synovial membrane in joint after daily treatment with dimethylsulfoxide 40% for three successive days Note normal appearance of synovial membrance . (H & E x 100).

(Fig. 10).

A.3. Dimethylsulfoxide 20% daily for seven successive days (group 3):

A.3.1. Clinical findings:

In the first three injections, there were no marked changes in the synovial effusion. The pain was reduced in its degree. After that and till the seventh injection, there was a marked decrease in pain and stiffness of the joint completely disappeared and the animal stepped normally. The diameter of the joint was reduced in its circumference with an average of about 0.05 cm ± 0.03. The hotness of the joint was declined and returned to its normal temperature.

A.3.2. Radiological findings:

No evidence of radiological changes on the carpal bones.

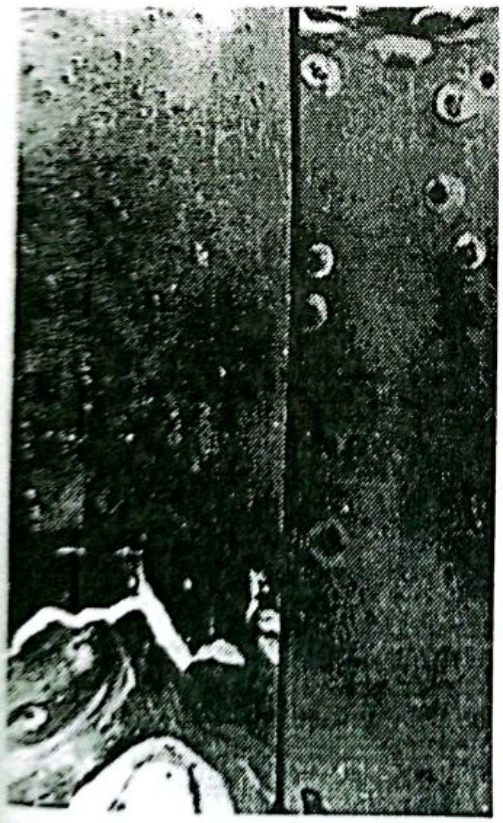

Fig. 10: Articular cartilage in joint after dayily treatment with dimethylsulfoxide 40% for three days, Note individual cell degeneration. (H & E x 100).

A.3.3. Synovial fluid analysis:

The changes in synovial fluid in experimentally induced arthritis after one week of induction using daily DMSO 20% treatment are shown in Figures (11 & 12). The following recorded changes are relative to the first week values after chemical induction of arthritis. Total protein, GOT, GPT, Lysozyme, alkaline phosphatase, lactic acid dehydrogenase and RBCs. were exhibited highly significant decrease ($P < 0.01$). While the changes in mucinous precipitation, pH and monocytes levels were highly significantly increased ($P < 0.01$). On the other hand insignificant changes in viscosity, WBCs, lymphocytes, neutrophils and hyaluronic acid ($P < 0.05$) were observed.

A.3.4. Histopathological changes:

No evidence of any macroscopical changes of the synovial membrance and articular cartilage (Fig. 13) were seen.

Microscopical examination of the synovial membrane revealed that it was lined with one layer of cuboidal epithelial cells. The connective tissue core showed increased vascularization and infiltrated with round cells (Fig. 14). There were scattered degenerated chondrocytes. Some of them had a ghost like appearance. The matrix was apparently normal (Fig. 15).

B. Experimental treatment of different arthritic phases:

According to the previously recorded data on the effect of different concentrations and application time of DMSO on chemically induced arthritic joint, we chose the best concentration and duration to evaluate their effect on the different stage of arthritis.

B.1. Experimental treatment after three weeks of induction (group 4):

B.1.1. Clinical findings:

The results were characterised by a marked decrease in lameness and stiffiness of the joint which

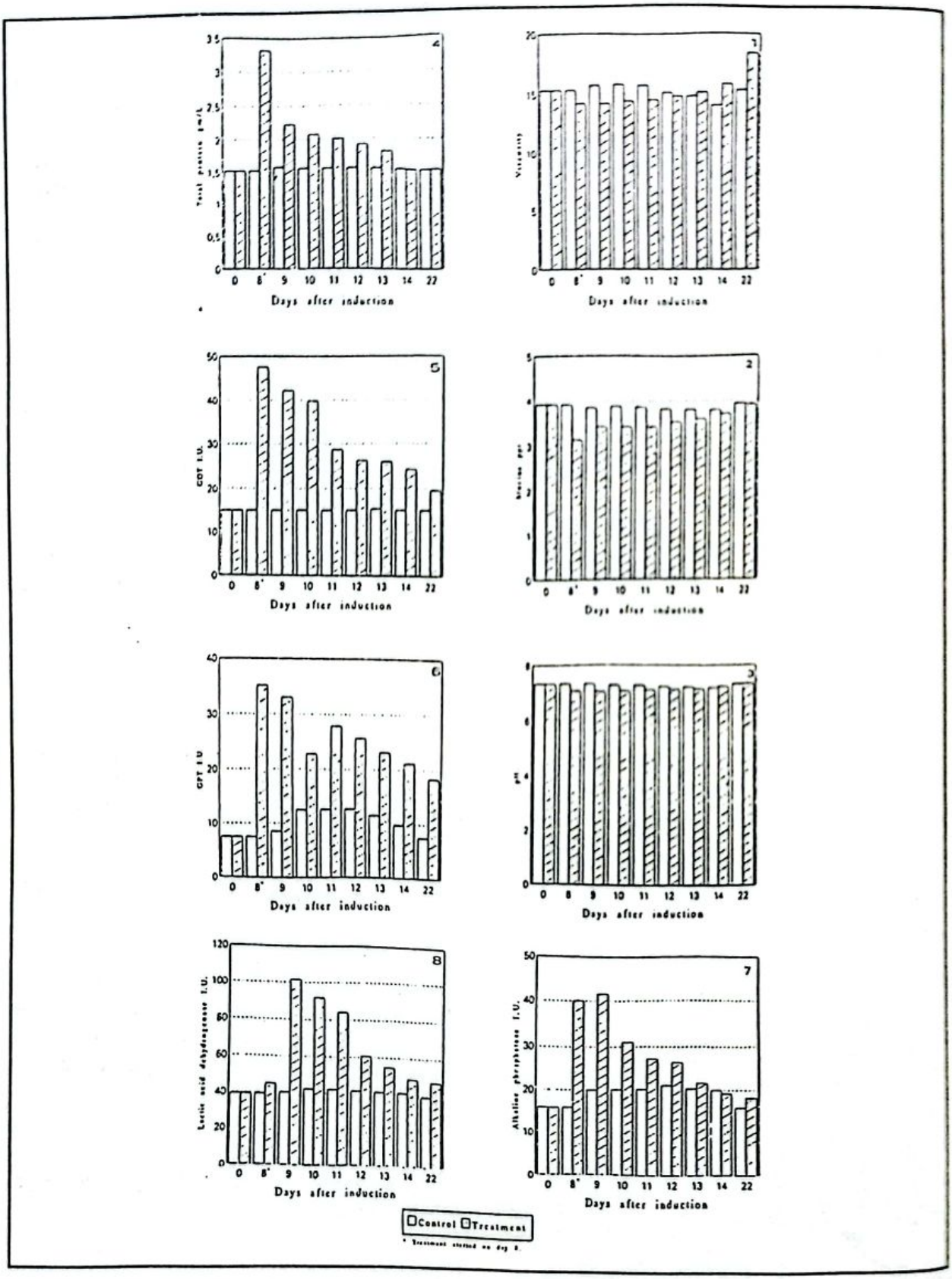

Fig. 11: The changes in synovial fluid of one week chemically induced arthritis after daily treatment with Dimethylsulfoxide 20%.
I. Viscosity 2. Mucine ppt. 3. pH. 4. Total protein 5. GOT 6. GPT 7. Alkaline phosphatase 8. Lactic acid dehydrogenase.

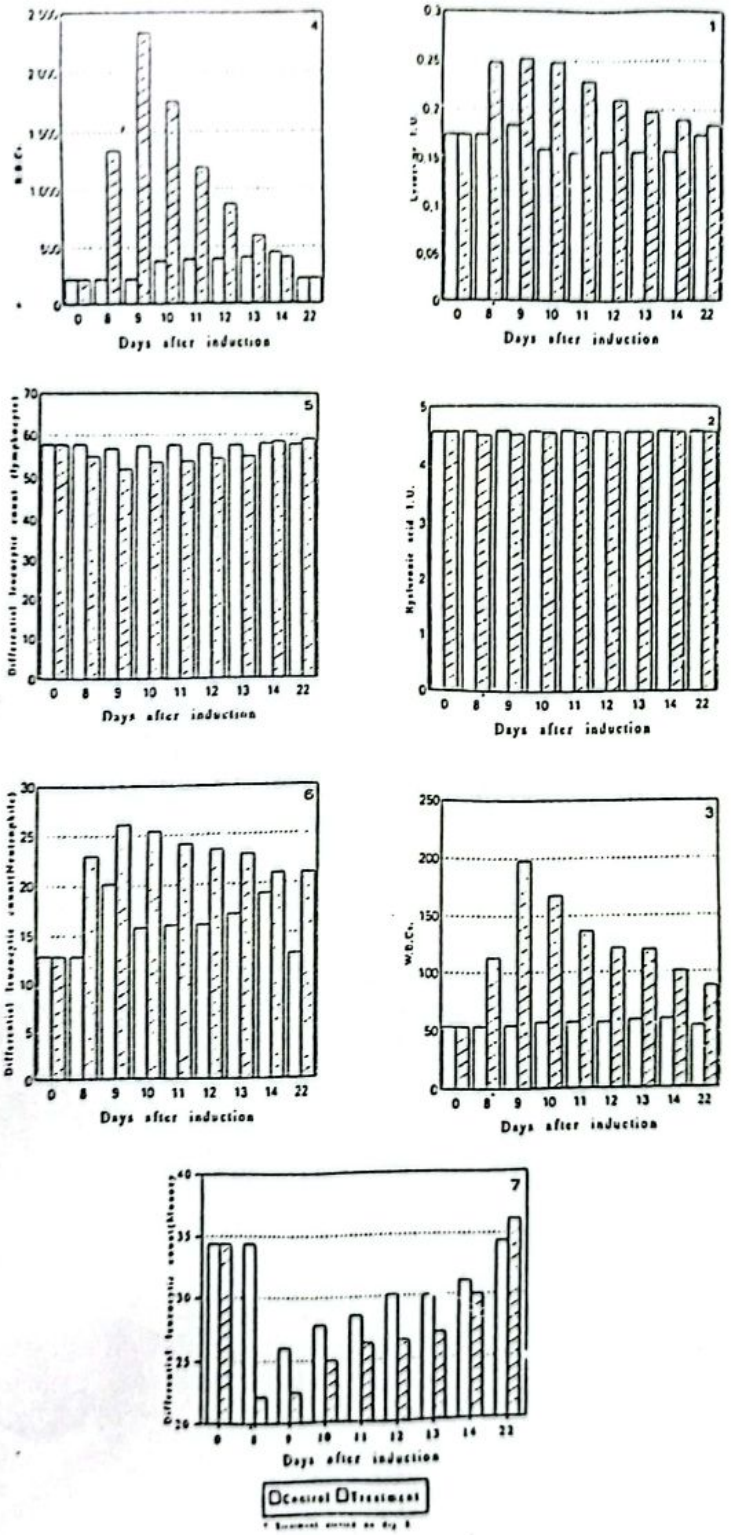

Fig. 12: The changes in synovial fluid of one week chemically induced arthritis after weekly treatment with Dimethylsulfoxide 20%.
1. Lysozyme 2. Hyaluronic acid. 3. WBCs. 4. RBCs. 5. Lymphocyte 6. Neutrophile 7. Monocyte.

Fig. 13: Joint cavity after daily treatment with dimethyl-sulfoxide 20% daily for seven days. Note normal appearance of the joint cavity.

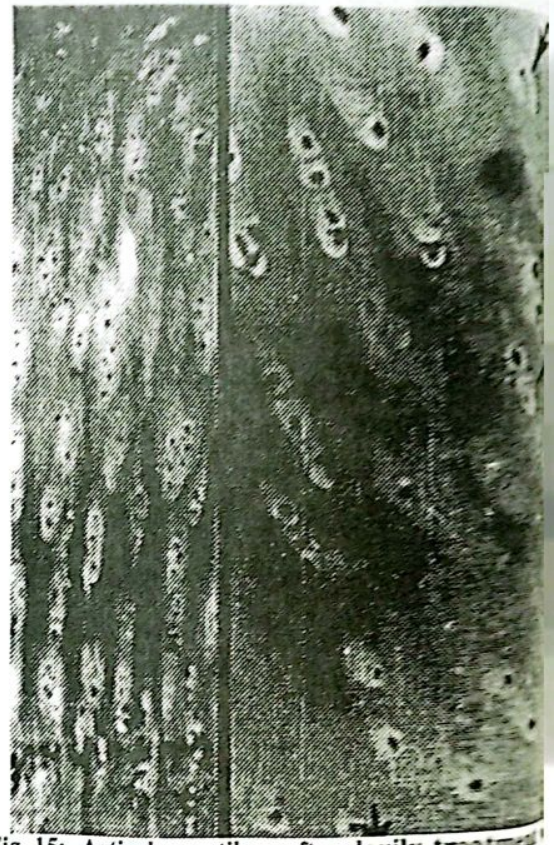

Fig. 15: Articular cartilage after dayily treatment dimethylsulfoxide 20% for seven days scattered indicidual degenerated chon (H & E x 100).

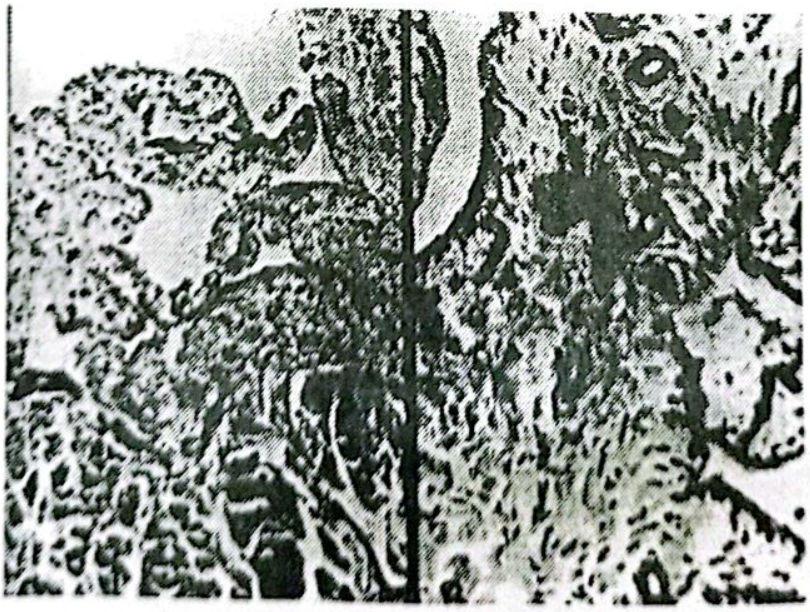

Fig. 14: Synovial membrane after daily treatment with dimethylsulfoxide 20% for seven days. Note normal appearance of synovial membrance . (H & E x 100).

enabled the animals to move freely. The synovial effusion of the joint became scantly as well as the joint circumference was decreased with an average of about 0.5 cm ± 0.03. The hotness of the joint was declined as returned to its normal temperature.

B.2.2. Radiological findings:

No changes could be detected.

B.2.3. Synovial fluid analysis:

The changes in the synovial fluid in chemically induced arthritis after three wekks of induction as a result of weekly DMSO 40% treatment are showin figs (16 & 17). The following recorded changes are relative to the first week values after chemical induction of arthritis. A highly significan increase in the levels of the hyaluronic acid, mucinous precipitation and pH ($P < 0.01$), a highly significant decrease in total protein, lysozyme, GOT, GPT, alkaline phosphatase, WBCs, RBCs and neutrophiles ($P < 0.01$) and significant decrease in monocytes ($P < 0.05$) were recorded. On the other hand, insignificant changes in viscosity and lymphocytes ($P > 0.05$) were detected.

B.2.4. Histopatholobical changes:

No evidence of any mactosopical changes of the synovial membrane and the articular cartilage were seen (Fig. 18).

Microscopical examination of the synovial membrane revealed that it was lined with cuboidal epithelial cells (Fig. 19). Individually degerated chondrocytes were detected. The matrix appeared mostly normal with slight fibrillation of the tangential zone (Fig. 20).

B.3. Expermiental treatment afte four weeks of induction (group 5):

B.3.1. Clinical findings:

The results were characterised by reduction of the pain and stiffness of the joint. The lameness as well as the hotness of the joint were declined. The diameter of the joint was reduced in its circumference with an average of about 0.6 cm ± 0.03 as a results of decreased synovial effusion.

B.2.2. Radiological findings:

The radiographic examination revealed no changes.

B.2.3. Synovial fluid analysis:

The changes in synovial fluid in chemically induced arthritis after 4 weeks of induction as a result of weekly DMSO 40% treatment are shown in Figures (16 & 17). The recorded changes changes are relaive to the first week values after chemical induction of arthritis. A high significant decrease in the levels of total protein, GOT, alkaline phosphatase, WBCs., RBCs. and monocytes ($P < 0.01$) were recorded. A high significant increase in mucinous precipitation and pH ($P < 0.01$); significant increase in viscosity ($P < 0.05$); significant decrase in lysozyme ($P < 0.05$) and no significant changes in hyaluronic acid ($P > 0.05$) could be detected.

B.2.4. Histopathological changes:

The macroscopical examination of the joint revealed blister formation of the articular cartilage of the articular cartilaged of the distal extremity of the radius with discoloraion of articualr surface (Fig. 21).

Microscopical exmaination of the synovial membrane revealed no signifcant pathological changes (Fig. 22), while examination of the articular cartilage revealed different degenerative changes of chondrocytes in the tangential zone and transitional zone. The matrix appeared sightly fibrillated (Fig.23).

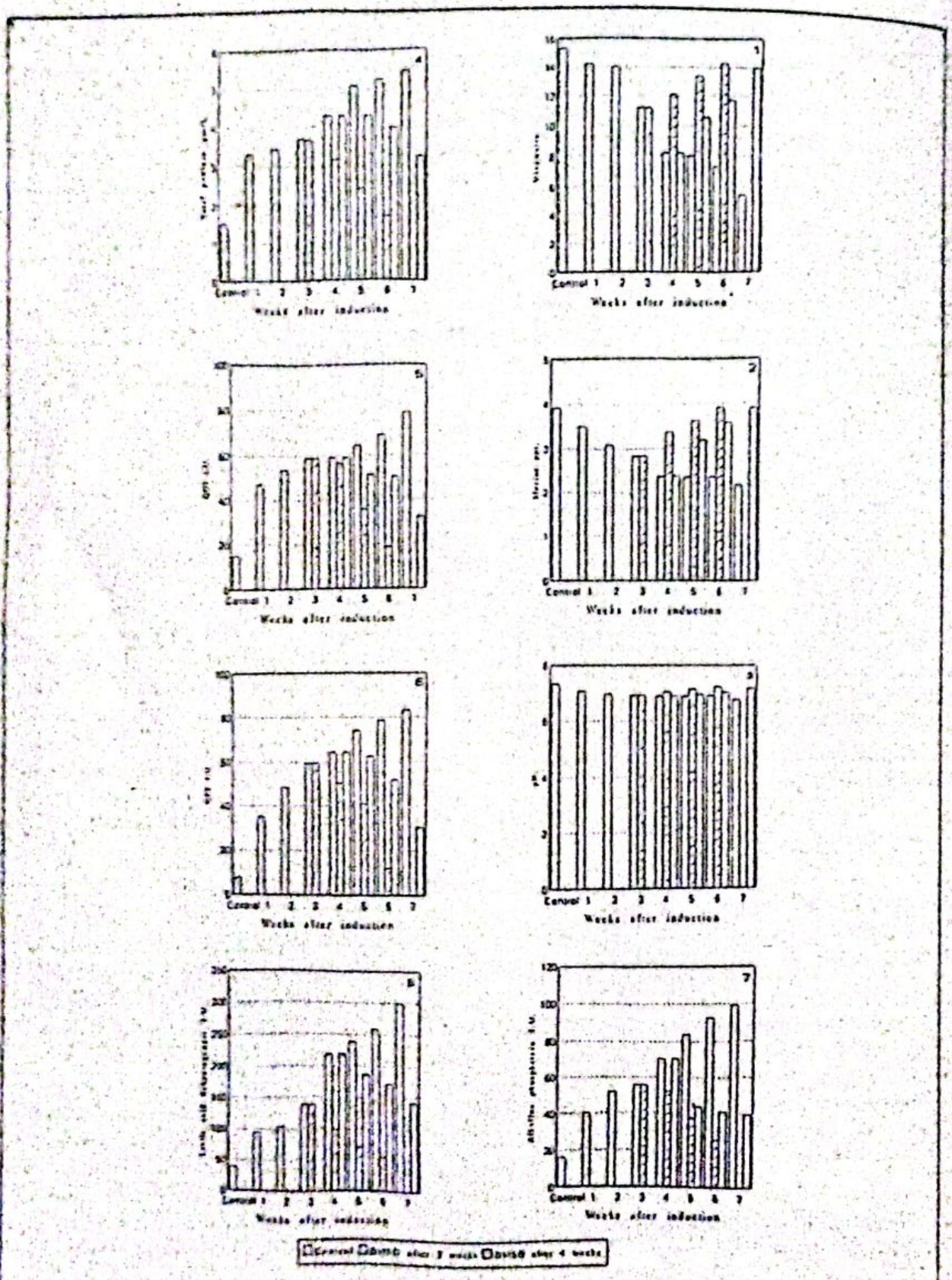

Fig. 16: The changes in synovial fluid of three & four weeks chemically induced arthritis after daily treatment with Dimethylsulfoxide 40%.
1. Viscosity 2. Mucine ppt. 3. pH. 4. Total protein 5. GOT 6. GPT 7. Alkaline phosphatase 8. Lactic acid dehydrogenase.

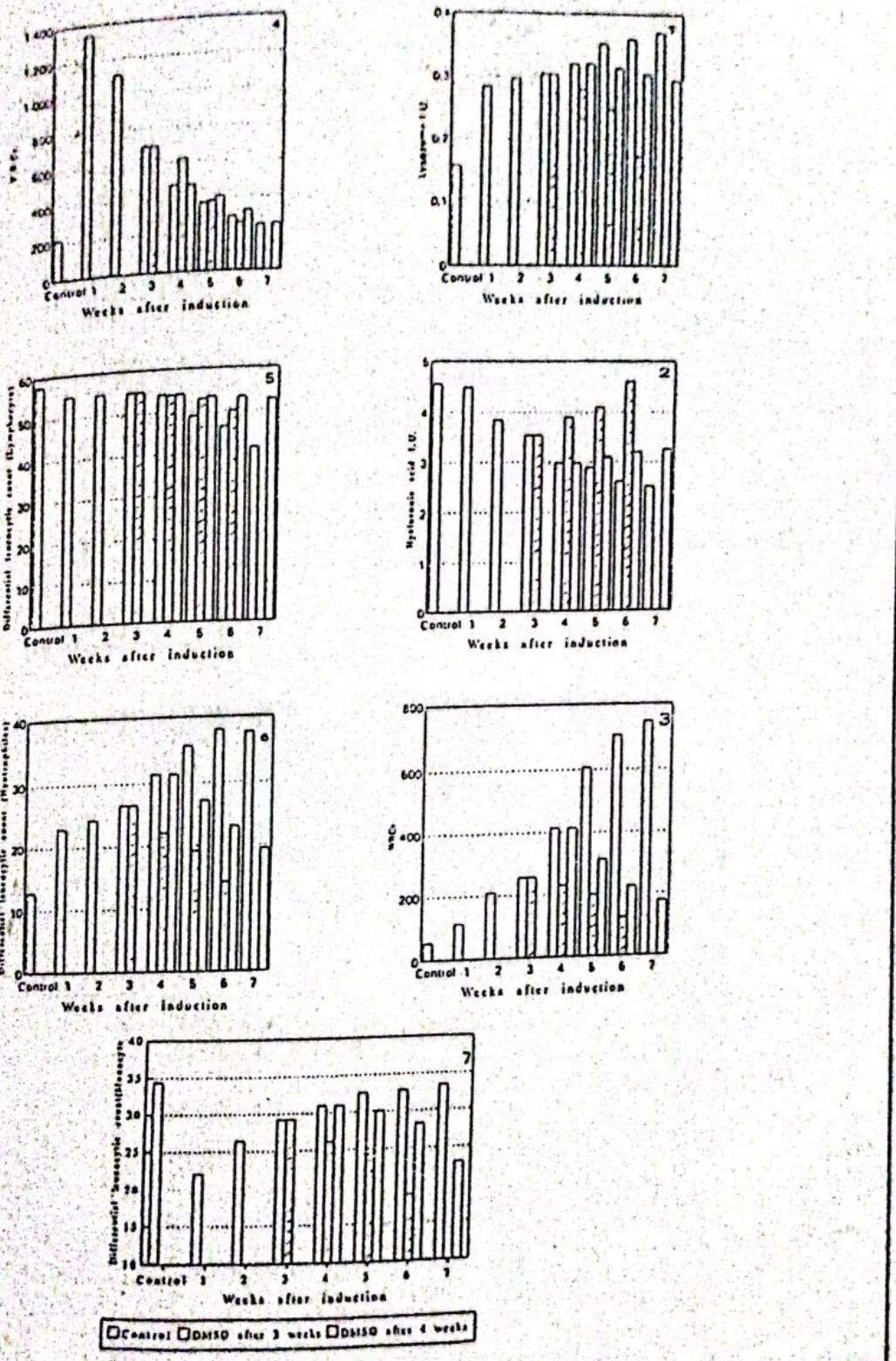

Fig. 17: The changes in synovial fluid of three & four weeks chemically induced arthritis after weekly treatment with Dimethylsulfoxide 40%.
1. Lysozyme 2. Hyaluronic acid. 3. WBCs. 4. RBCs. 5. Lymphocyte 6. Neutrophile 7. Monocyte.

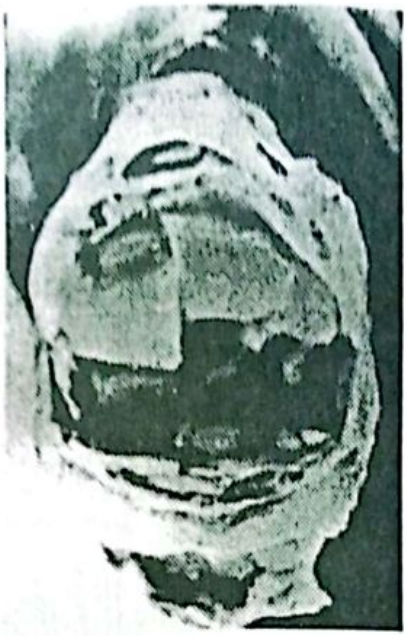

Fig. 18: Joint cavity in daily with three weeks chemically induced arthritis after weekly treatment with dimethylsulfoxide 40% daily for three weeks. Note normal appear-ance of cavity.

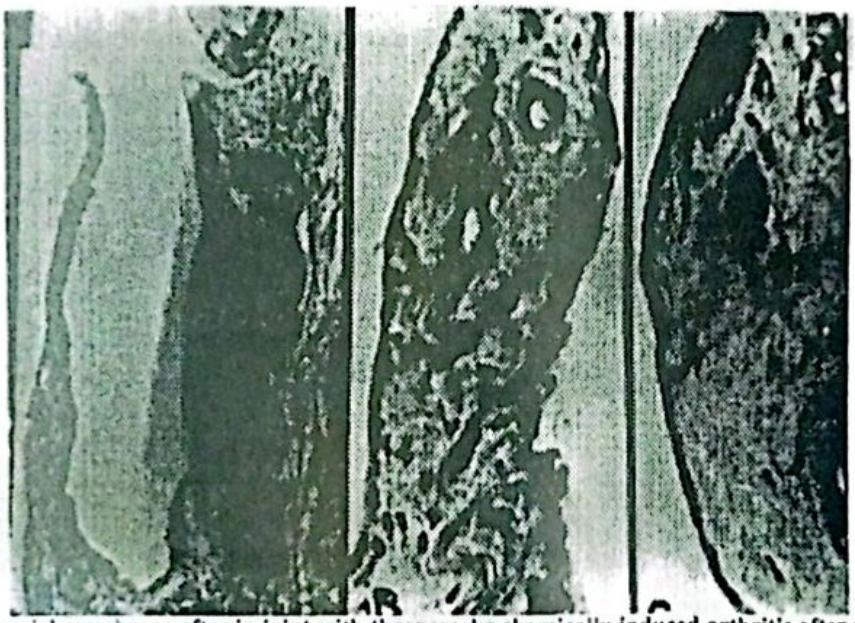

Fig. 19: Synovial membrane after in joint with three weeks chemically induced arthritis after weekly tr ment with dimethylsulfoxide 40% for three weeks. Note normal appearance of synovial membran (H & E A X 40 BX 100 C X 400).

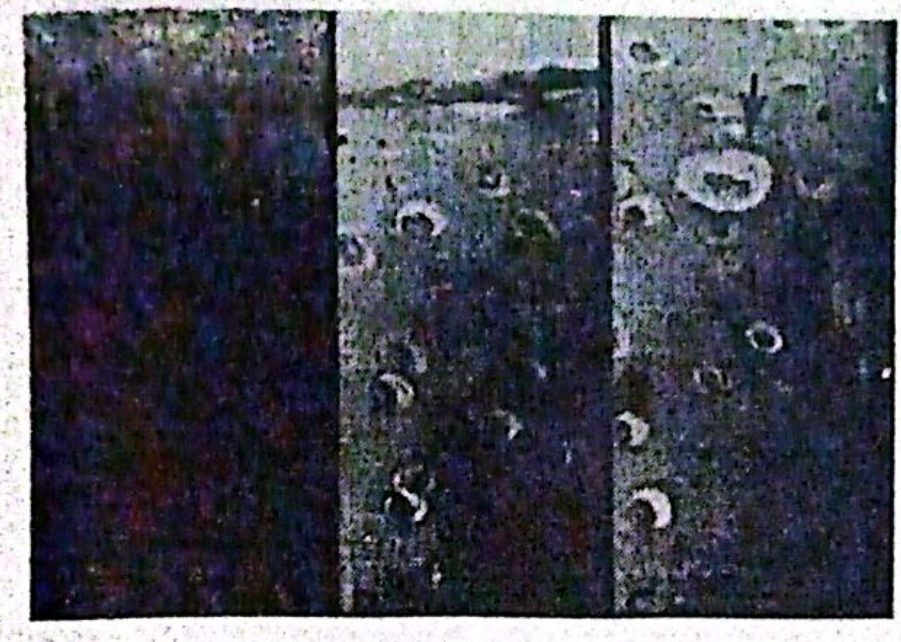

Fig. 20: Articular cartilage in joint with three weeks chemically induced arthritis after weekly treatment with dimethylsulfoxide 40% for three weeks Note individual chondrocyte degeneration . (H & E A X 40 BX 100 C X 400).

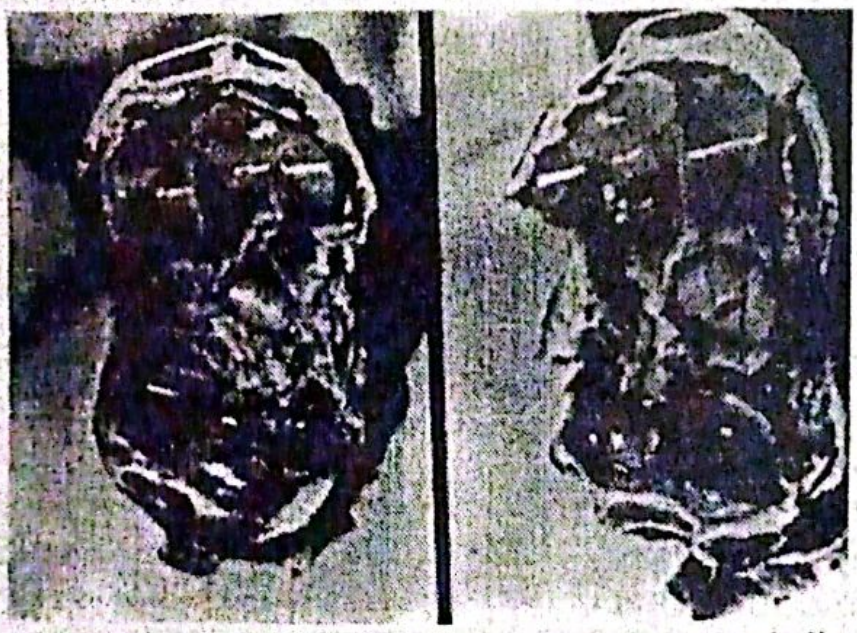

Fig. 21: Joint cavity after weekly treatment with dimethylsulfoxide 20% for three weeks. Note discolouration of the articular surface with blister formation.

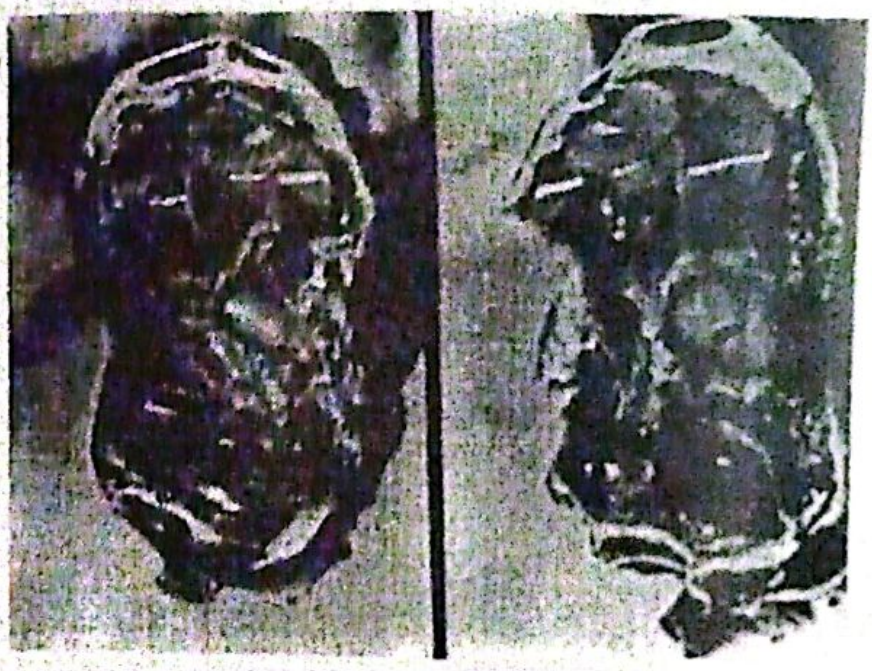

Fig. 22: Synovial membrane in joint with four weeks chemically induced arthritis after weekly treatment w dimethylsulfoxide 40% for three weeks Note normal appearance of the synovial membrane (H & E A X 40 BX 100).

Fig. 25: Articular cartilage in joint with three four weeks chemically induced arthritis after weekly treatme with dimethylsulfoxide 40% for three weeks Note fibrillation and necrobiotic changes of chondro (H & E A X 40 BX 100 C X 400).

DISCUSSION

The weekly treatment with dimethylsulfoxid 40% for three successive weeks (gorup 1) lead to marked decrease in lameness, joint stifness, diameter of joint and no evidence of peristeal reaction as well as the synovial analysis indicated that all parameters were returned back to normal values as compared to negative controls. This could be interpreted as a result of the antiinflammatory action of DHSO on synovial membrane and its effect in healing process as confirmed by histopathological findings where the cartilage restored its normal structure. Dimethylsulfoxide 40% seems to be the drug of choice for treatment of synovitis and acute inflammatory phase of degenerative arthritis. This was supported by the work on chronic musculoskeletal conditions such as chronic osteoarthritis and degenerative disc diseases in humans (Demos et al., 1967; John et al., 1967; Paul, 1967 and Steinberg, 1967) which have been treated with dimethylsulfoxide in chinical trials and with good results were seen in acute conditions.

The daily inection of DMSO 40% for 3 successive days (Froup 2) and DMSO 20%) for 7 successive days (Group 3) revealed that there was a minemum retrogressive changes of chondrocytes in the tranzitional zone in first concentration which extended to includ tandinetal zone in the second concentration. The variation in the picute may be related to the concenation of the compound and frequency of injection.

It seems to be used in weekly interval with concentration 40% to give the best results. DMSO which has been previously used as an analgesic drug (Alsup, 1984 and Brayton, 1986) seemed to has a great effect on prevention of cartilage degeneration. The parameter of synovial analysis which returned back to normal may be attributed to its antiinflammatory effect gbby suppresion of prostaglandine and prevention of depolymerization of hyaluronic acid by oxygen derive free radical (Greenwald et al., 1976; fox, 83 and Greenwald, 1984). In addition to reduce catabolism (Hill, 1983) and edema (Tiegland and saurino, 1967 and Sautino et al., 1967). The prevention of osteophyte formation may be attributed to its capacity in reduction of soft tissue mineralization (Demos et al., 1967; John et al., 1967; Parson et al., and Tiegland and Sautino 1967).

The results of gorup 4 & 5 were amied to find out the maximum effect of DMSO in treatment of arthritic joint in relation to the duration of degeneration. It was cleared that the intraarticular injection of DMSO 40% weekly for 3 successive weeks in joints suffered from chemically induced arthritis after 3 weeks of induction (first degenerative stage) revealed that the clincial, radiological, synovial analysis as well as histopathological examination were returned back to apparentally normal condition.

However the injection with the same concentration after 4 weeks of induction (second degenerative stage) was succeded in clinical symptom, improve synovial parameter which returned back to normal and prevention of osteophytic changes. However the histopathological examination revealed persistance of degenerative changes in milk from this experiment.

It seems that DMSO had a limited effect on improving the inflammed joint and preventing degenerative changes of cartilage up to 3 weeks of chemically induced arthritis (first degenerative phase). However, in the cases suffered from arthritis for a period exceeding 3 weeks (first stage), the capacity of DMSO to improve this joint to be decreased. There was no clear explanation for that except the the tissue in the first case was still to regeneral. However in the second stage, the capacity of tissue to regenerate was decreaed and exceed the power of DMSO for prevention of degenerative changes which was based on its antiinflammatory effect and prevention of hyaluronic acid deterioration.

Therefore we recommended the use of DMSO in the treatment of traumatic arthritis and degenerative joint disease during the acute inflammatory phase and mild degenerative stage, not however in the moderate or severe stages.

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