Ischemia of tissue in animals in FD oriented research

There are presented studies dealing with testing of FD in animals.

FD has been tested in healthy pigs (12) in a special breed of hereditary malanoma bearing pigs called MeLiM and in sarcoma rat model in the Institute of Animal Physiology and Genetics, Laboratory of Tumour Biology, Academy of Science of the Czech Republic, in Libechov. (16)
FD was tested in various organs in healthy pigs including: rectum and sigmoideum (12), stomach (11), kidney (13; 14), large and small intestine (5). There were reported no serious adverse effects in connection with FD in healthy organs (5, 11, 12, 13, 14).
An interesting finding was made when E coli type 0,1, 0,4, Citrobacter and Enterococci at concentration of 10 up 5 to 10 up 9 per ml where injected into the lumen of FD treated intestine at the dose of 4 – 10 ml. There were reported no serious adverse effects (12).
Degradation of healthy kidney was tested by devascularisation of kidney in 16 pigs and 20 rats. FD was performed by double ligature of blood vessels and embarrassing of all the above structures.
Macro- and microscopic changes were examined by laparotomies in 1, 2, 8 and 12 weeks afterwards. The devascularised kidney or kidney segment in the case of segmental devascularisation at first increased the total size of about one third of its original size. The capsule stretch tight and on dissection the parenchyma was dry, fragile, yellowish grey. Then fibrous tissue appeared in the vicinity of devascularised tissue which eventually replaced the shrinking original tissue. Thus just a small amount of fibrous tissue was found in the place of the original organ. Necrosis followed by inflammatory fibroid replacement was observed on microscopical level as well (13).
A special MeLiM breed of mini pigs which are afflicted by hereditary melanoma were used as a primary cancer animal model for testing FD. The melanomas appear at the birth or up two months after birth. They are usually nodular, multiple and distributed in various body parts. Melanomas metastase mainly into spleen, lymph nodes, lungs. 34% of affected mini pigs die during the first two months after birth. Tumour cells were detected in 27% of visually unaffected animals (17).
Melanoma removal start off by disintegration of melanoma cells inside the tumour two weeks after performing FD, continuing by degradation of MB for the next 6 to 8 weeks after devitalisation when there were only rarely found tumour cells. Destroyed MB cells were accompanied by a dense infiltration with macrophages and lymphocytes. A fibrous replacement of tumour tissue was completed in 4 to 6 months after devitalisation. Surprisingly, the same development was observed at the same time in untreated tumours and metastasis (17).
An investigation of the impact of FD on immunity of MeLiM pigs revealed that 1 day after devitalisation of melanoma there was evidence of a higher expression of heat shock proteins HSP70 and gp96 which persisted for the next two weeks and then returned to normal levels. A continuing destruction of MB was reflected in decreasing levels of IL8 in blood serum. Flow cytometry showed an increase in TIL phenotypically cytotoxic T lymphocytes (CTL-CD3+CD4-CD8+) and helper/memory T lymphocytes (DPL – CD3+CD4+CD8+) in treated, untreated tumours, untreated skin and blood for 1-3 weeks after devitalisation in melanoma pigs. (16).
A comparative cancer model was prepared by inoculating sarcoma cells subcutaneously into two places in rats. Growth of sarcomas was followed by an increase in myeloid cell (CD3-CD8-CD11bCD45+) in peripheral blood and in subcutaneous tumours. After FD therapy of one of the tumours, there was only a 3 days' increase in heat shock proteins which was not followed by a significant increase in TILs. The untreated tumour rarely disappeared. Protective immunity was demonstrated in rats showing regression of untreated sarcoma. These rats did not develop new tumours after repeated inoculation of sarcoma. The overall

success rate was about 20%. The increase in HSP for not sufficient time is supposed to be the reason for the low success rate in the rat model in comparison to melanoma pig model (16). The reported success rate is about 80% in MeLiM pigs and about 20% in inoculated sarcoma rats. No reccurence of the disease in MeLiM pigs was found (16). Vitiligo which was observed regularly in melanoma FD treated MeLiM pigs was the most serious adverse effect reported (17).

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