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REPORTING AND PREVENTING RADIOTHERAPY COMPLICATIONS IN CARCINOMA OF UTERINE CERVIX.

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1530 patients (pts) with cervical carcinoma were accrued from 1970 to 1983 in a multi-institutional cooperative study. They were treated with radiotherapy (RT) alone using external megavoltage RT, followed by brachytherapy (BT) applications in 87%, by external RT alone in 10%, and by BT alone in 3%. Complications (cns) are reported with French-Italian glossary to identify 5 grades (G0 to G4) per tissue or organ at risk with an accurate description of signs and symptoms per grade. No complication (G0) was reported in 922 pts (60%). 1384 cns of all grades were reported in 608 pts. 46% of these were G1, 39% were G2 and 13% were G3. 28 pts (1.8%) had G4 (death directly or indirectly induced by treatment cns). The incidence of lethal cns per tissue or organ shows that, although death from small bowel cns only represents 0.4% of pts, lethal cns account for 16% of small bowel cns. Most G1 rectal cns were G1b (minor rectorragia). G3 rectal cns are mostly represented by G3a (recto-vaginal fistulae 1.6% from a total of 2.5% G3 rectal cns). Death occurred because of rectal cns in 0.4% of pts. A similar beadkdown of cns data is available for each tissue and organ. Severe bladder cns are rare (0.6% G3, 0.6% G4). Statistical analysis also includes cumulative rates with time for each grade and organ at risk. Thanks to a better use of computer dosimetry, grades 3 & 4 cns fell from 14.5% before 1979 to 6% since 1980 while the pelvic failure rate remained unchanged (15% versus 13%).

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PHASE II STUDY OF A COMBINATION OF ACTINOMYCIN (A) AND ETOPOSIDE (E) IN GOOD RISK (GR) TROPHOBLASTIC DISEASE (TD).

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Between 5/87 and 4/92, we have treated prospectively 21 not pretreated pts with GRTD as previously defined at IGR (M. Azab, Cancer, 62, 1988) by a combination of A+E.

Pts: mean age = 31 years (range 25-54); histological pattern: hydatiform mole (HM):11; triploïd syndrom: 4; raising HCG levels only after curettage: 6; metastasis: lung (1 pt) vagina + cervix (1 pt). Treatment I (TI) from 5/87 to 6/89 (10 pts) consisted of: A: 0,500 mg/m²/d and E: 200 mg/m²/d d1 and TII from 10/89 to 4/92 (11 pts) of: A: 0,750 mg/m²/d and E: 150 mg/m²/d d1, both weekly and until 6 weeks after beta-HCG normalization.

Toxicity (Tox):195 cycles (cy) are evaluable. TI (86 cy) induced mucositis grade (gr) 1: 1 cy, gr 2: 1 cy, gr 4: 1 cy and neutropenia gr 3: 4 cy, gr 4: 1 cy (1 neutropenic fever) with 12 delayed cy and 19 dose reductions. TII did not induce major Tox. Alopecia was universal. There were neither neurological nor renal Tox.

Actually Delivered Dose Intensity of drugs (mg/m²/w): Etoposide, TI: 146, TII: 133; Actinomycin, TI: 454, TII: 659.

Results There were 21 CR, one of whom obtained by AE + Cisplatin (HCG plateau after 3 cy of AE). Twenty pts are continuousy NED after 6 to 66 months of follow-up. All patients are alive and disease free. One pt experienced a second HM at 54 m. There were 13 pregnancies: 1 HM, 3 abortions (1 spontaneous) and 9 normal deliveries.

We conclude that the combination of Actinomycin and Etoposide with the second schedule is active and safe.

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TREATMENT OF CARCINOMA OF THE UTERINE CERVIX BY COMBINATION OF BRACHYTHERAPY AND COLPO-HYSTERECTOMY WITH LYMPHADENECTOMY (CHL). RETROSPECTIVE ANALYSIS OF 186 CASES (dec.1975/sept.1983).

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We report an interim analysis about a retrospective study of long term results and therapeutic complications in radiosurgical treatment of cervical carcinoma, treated in our institute between dec. 1975 and sept. 1983. Since 1980, a computer program of optimization of brachytherapy has been used; so we distinguished two periods, A (before), and B (after) optimization has started. All patients who underwent full radiosurgical sequence, i.e. utero-vaginal brachytherapy with ^{137}Cs (1 or 2 insertions) and CHL (completed or not by external radiotherapy), and followed-up at least 6 months after treatment, are included in this study.

Group A (dec. 75 /dec. 79): n = 94; group B (jan. 80/sept. 83): n = 92. Median age: 54 yr +/- 12,1 (A: 50,8; B: 58,2). Stage distribution: Ia: 8 (4/4), Ib N-: 81 (41/40), Ib N+: 15 (8/7), IIa: 39 (17/22), IIb prox: 41 (22/19), IIb distal: 1 (1/0), IIIa : 1 (1/0).

Global survival (Kaplan-Meier's method), for the whole population: 87,9% at 2 yr, 74,1% at 5 yr, 63,3% at 10 yr. Survival by stage: Stage I (2 yr: 95%, 5 yr: 81%, 10 yr: 79%), Ib N- (96/87/84), Ib N+ (86/48/48). Stage II (2 yr: 82%, 5 yr: 68%, 10 yr: 52%), IIa (83/71/60), IIb prox (80/63/41).

Survival stages I > stages II ($p<0,01$); stage IbN- > stage IbN+ ($p<0,001$); stage IIa > stage IIbprox ($p<0,05$). Whatever the stage, the presence of invaded lymph nodes strongly affected survival. There are no statistical differences between group A and group B, both for global and stage survival ($p>0,05$).

Further results will extend to the whole period of interest (1973 -> 1986), and will determine whether optimization of brachytherapy succeeded in reducing rate of complications without effect on local control and survival (multivariate analysis).

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ADENOCARCINOMA OF ENDOMETRIUM: INTERRELATION BETWEEN ETIOCHOLANOLONE AND CHOLESTEROL

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The content of steroid excretion with urine of healthy women in reproductive and postmenopausal periods and of patients with adenocarcinoma of endometrium and various forms of hyperplasia of endometrium in the postmenopausal period was determined with the aid of the gas-liquid chromatography technique. An interrelation between cholesterol (Ch) and etiocholanolone (Et) which is an androgenic metabolyte, is established. During a comparative study a reliable reduction of the Et to Ch ratio dependent on the age and endometrium pathology growth was observed, which can be possibly ascribed to the increase of hormonal disbalance in the organism. The value of the Et to Ch ratio is worthwhile using for adenocarcinoma of endometrium screening diagnostics.

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COMBINED EXPERIENCE OF 3 CENTERS IN ISRAEL IN THE TREATMENT OF CARCINOMA OF THE UTERINE CERVIX.

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Carcinoma of the uterine cervix is relatively rare in Israel, with an annual incidence for Jewish females of 4.4/100.000. We have combined experience of 3 medical centers in the treatment of 259 pts with carcinoma of the uterine cervix, 202 pts had squamous cell carcinoma (SQC) treated by radiation therapy. We observed an age-ethnic related pattern in our pts population. The mean age of Ashkenazic pts (60 y) was significantly higher than the mean age of non-Ashkenazic pts (53 y) and Arabic pts (51 y). The mean XRT dose was 4850 cGy and brachytherapy was given using Fletcher-Suit applicators and Cs-137 with a mean of 4960 mgh. The mean follow up was 56 m, the 5-y actuarial survival for pts with SQC was 69%.

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Ten Years Experience with an HDR After-loading Technique in the Treatment of advanced Cervical Cancer

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In 1981 the HDR afterloading technique using iridium 192 protocol was introduced for the delivery of our radical radiotherapy for uterine cervical cancer. This replaced our previously used radium brachytherapy technique. From 1981 to 1991 a total of 2o4 patients with stage IIb and IIIb disease have been treated. We report in this paper on the 159 patients who now have a minimum follow-up period of three years.

Our results with radical combined radiotherapy for uterine cervical cancer stage IIb and IIIb show that the remission rates are comparable with those in the literature and of the era of radium therapy. The change from LDR therapy to HDR therapy has in gereral brought problems in determining doses and in optimisation. Radiobiological findings show that in HDR therapy the total dose must be reduced and higher fractionation prescribed.