Chemosensitivity Testing of Advanced Lung Cancer by the Chick Embryo Assay

The usefulness of the chick embryo assay as an in vivo chemosensitivity test was studied in the prediction of the response to combination chemotherapy regimens in clinical use for lung cancer in Japan, such as cisplatin+vindesine (PV therapy), cisplatin+adriamycin+mitomycin C (PAM therapy), and mitomycin C+vindesine+cisplatin (MVP therapy). One hundred and seventeen surgical specimens of advanced lung cancer were examined by this method. All the tumor specimens tested could be grafted on the chorioallantoic membranes of chick embryos, so the evaluation rates was 100%. In this system, the efficacy rates of PV, PAM, and MVP therapy were 16.9, 13.8, and 19.0%, respectively. The efficacy of therapy was in the following order: epidermoid carcinoma>small cell carcinoma>large cell carcinoma>adenocarcinoma>adenosquamous carcinoma. Interestingly, the effect of MVP therapy on epidermoid carcinoma was significantly high.

Twenty-six patients received the same chemotherapy regimens as those tested in the chick embryo assay, and 24 of them could be evaluated for clinical response. In 4 patients, the assay correctly predicted a clinical partial response (true positive). There were no false positive results for this assay, as well as 5 false negative results and 15 true negative results. The overall predictive accuracy was 79.2%. Thus, the chick embryo assay was a good predictor of the clinical outcome. This in vivo chemosensitivity assay for lung cancer is also advantageous because of its convenience, rapidity, and low cost.

Despite the many clinical trials of combination chemotherapy for advanced lung cancer performed to date, the response rate of this tumor to chemotherapy remains fairly low. This is partly due to the limited efficacy of the currently available therapeutic agents for lung cancer and also partly due to the difficulty of selecting suitable drugs for individual patients. Individual tumors of the same histological type vary widely and unpredictably in their response to chemotherapy. Unlike most other carcinomas, lung cancer has manifold histologic characteristics and high level of heterogeneity. Improvement of the prognosis for patients with this cancer will require the development of methods for the rapid and accurate prediction of the response to specific regimens of combination chemotherapy. A number of in vivo or in vitro chemosensitivity tests have been tested for their ability to predict the efficacy of anticancer agents treatment is started\(^{11-13}\). However, these tests have various problems such as a low graft take ratio, a high cost, delayed results, and inaccuracy. Moreover, it is difficult to evaluate the response to combination chemotherapy, which is usually used for adjuvant therapy after surgery.

In 1912, Murphy tried to inoculate rat and mouse tumors onto the chorioallantoic membranes of chick embryos, which are naturally immunodeficient and can accept various tumors\(^{12}\). Dagg et al. subsequently applied this method to human tumors\(^{13,14}\). This chick embryo assay system has the advantages of rapidity, convenience, and low cost. In the present study, we investigated the usefulness of the chick embryo assay for the in vivo chemosensitivity testing of combination chemotherapy for lung cancer.

**Materials and methods**

**Patients and tissue samples**

One hundred and seventeen patients with primary lung cancer, who were treated at the Department of Surgery of Kanazawa University between 1987 and 1989, were studied. The patients included 91 men and 26 women ranging in age from 31 to 84 years (mean: 64.3 years). Their tumors included 51 adenocarcinomas, 46 epidermoid carcinomas, 8 adenosquamous carcinomas, 5 large cell carcinomas, and 7 small cell carcinomas. Twenty-six of these specimens, were used for evaluation of the relationship between the assay results and the clinical response.

**Inoculation of lung cancers onto chorioallantoic membranes**

Chicken eggs (Plymouth Rock × White Leghorn) that
were 1~2 days old were obtained from the Goto Chicken Farm (Gifu, Japan). They were kept in an incubator at 37°C in a humidified atmosphere (relative humidity: 70%). At 10 days after fertilization, the eggs were used as recipients of tumor cells. Each egg was candled and a Y-shaped blood vessel junction in the chorioallantoic membrane (CAM) was marked on the shell with a pencil. Then the eggshell was cleaned with 70% alcohol and a window about 1cm² was cut out of it. The CAM was depressed by applying gentle suction at the air sac, and the shell membrane was carefully stripped off to expose the CAM. Surgical specimens of lung cancer with as few necrotic areas as possible were minced with scissors and transplanted on the CAM in a sample volume of 50 µl. The window in the shell was then sealed with OpSite (TJ Smith and Nephew Ltd., Welwyn Garden City, England).

Administration of anticancer drugs
After tumor transplantation, eggs were incubated at 37°C in a humidified incubator. Three days later, by which time the mean body weight of the chick embryos was 6.5g, the growth of the transplanted tumors was confirmed and anticancer drugs were administered. The eggs were candled and a line was marked on the shell over a large vessel in the CAM. Then a groove was ground through the shell at this site and a rectangular piece of shell was removed. A drop of paraffin oil was placed onto the shell membrane to make the vessel more visible, and the anticancer drugs were injected with a 30G needle. The drugs tested in this study were cisplatin (CDDP), vindesine (VDS), Adriamycin (ADM), and mitomycin C (MMC).

Three regimens commonly used in Japan for the treatment of non-small lung cancer were assessed. These were PV therapy (CDDP+VDS), PAM therapy (CDDP+ADM+MMC), and MVP therapy (MMC+VDS+CDDP). Each drug was injected into the CAM vein together with 0.1ml of 0.9% NaCl. The doses used corresponded to the clinical dose adjusted for body weight (Table 1).

### Table 1

<table>
<thead>
<tr>
<th>Protocol</th>
<th>Combination*</th>
<th>Clinical dose (mg/m²)</th>
<th>Dose for the chick embryo assay (µg/egg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PV</td>
<td>CDDP</td>
<td>80</td>
<td>12.0</td>
</tr>
<tr>
<td>PAM</td>
<td>CDDP</td>
<td>50</td>
<td>7.5</td>
</tr>
<tr>
<td></td>
<td>ADM</td>
<td>30</td>
<td>4.5</td>
</tr>
<tr>
<td></td>
<td>MMC</td>
<td>8</td>
<td>1.2</td>
</tr>
<tr>
<td>MVP</td>
<td>MMC</td>
<td>8</td>
<td>1.2</td>
</tr>
<tr>
<td></td>
<td>VDS</td>
<td>3</td>
<td>0.45</td>
</tr>
<tr>
<td></td>
<td>CDDP</td>
<td>80</td>
<td>12.0</td>
</tr>
</tbody>
</table>

* CDDP: cisplatin, VDS: vindesine, ADM: Adriamycin, MMC: mitomycin C

weight of the control group and Wt is that of the treated group.

Clinical treatment and evaluation
The lung cancer patients were administered anticancer drugs without considering the results of this test, and depending on the choice of their own physicians. Postoperative staging was performed by the new international TNM staging system proposed in 1987. Stage I patients or those over 75 years of age were not given postoperative chemotherapy. In addition, patients who received any radiation therapy were excluded from this study. Twenty-six patients in stages II, III A, III B, and IV were treated with the same protocols as those used in the chick embryo assay (Table 1). Chemotherapy was first given at 3~4 week after the operation and was repeated at 4-week intervals for 2 or 3 courses.

The clinical response to chemotherapy was evaluated from the survival time of the patients after surgery. Operations were classified as curative (the tumor and metastatic lymph nodes were completely removed) and non-curative (the tumor, the metastatic lymph nodes, or both were not completely removed).

As described by Watanabe et al., postoperative chemotherapy was defined as effective when stage IV patients or non-curatively resected patients survived >12 months, when curatively resected stage III patients survived >24 months, or when curatively resected stage II patients survived >36 months. The chemosensitivity test results were classified on the basis of the clinical outcome as true positive (both the chemosensitivity test and the clinical response were positive), false positive (the chemosensitivity test was positive, but no clinical response was obtained), false negative (the chemosensitivity test was negative, but a clinical response was obtained), and true negative (both the chemosensitivity test and the clinical response were negative).
Fig. 1  Histological appearance of human lung cancer growing on the chorioallantoic membrane (CAM). Epidermoid carcinoma obtained surgically was implanted onto the CAM of an 11-day-old chick embryo and tumor growth was observed 7 days later. Hematoxylin-eosin stain. ×400.

Statistical analysis
Student's t-test was used to evaluate the significance of differences and p<0.05 was taken to indicate statistical significance.

Results

Tumor growth on the CAM
All of the human lung cancers tested grew sufficiently well on the CAM to be weighed (mean control tumor weight was 30–80mg) and evaluated at 7 days after transplantation. Epidermoid carcinoma grown on the CAM is shown in Fig.1.

Effect of combination chemotherapy on in vitro tumor growth
The evaluation rate was 100%. The efficacy rates of PV, PAM, and MVP therapy for transplanted tumors were 16.9%, 13.8%, and 19.0%, respectively, and these rates were dose-dependent. When doses corresponding to double the clinical dose were tested in this assay, the efficacy rates of PV, PAM, and MVP therapy increased to 22.2%, 28.6%, and 30.8%, respectively. The response of the different histologic types of cancer occurred in the following order: epidermoid carcinoma (35.7%)> small cell carcinoma (28.6%)> adenocarcinoma (27.3%)> large cell carcinoma (25%)> adenosquamous carcinoma (14.3%).

Interestingly, the effect of MVP therapy on epidermoid carcinoma was significantly greater being 42.1% for epidermoid carcinoma and 17.6% for adenocarcinoma (p<0.05). On the other hand, the effect of PV therapy was similar (for adenocarcinoma and epidermoid carcinoma 14.8% vs. 23.8%). Chemosensitivity was not affected by tumor differentiation and there was no difference between the tumor with or without prior chemotherapy.

Correlation between chemosensitivity data and the clinical response
Twenty-six patients with lung cancer received the same protocols as used in the chick embryo assay (Table 2). The other 93 patients were treated with different protocols from those used for the chick embryo assay, or else received no chemotherapy. The 26 patients had 16 adenocarcinomas, 6 epidermoid carcinomas, 3 adenosquamous carcinomas, and 1 large cell carcinoma. Three tumors were Stage II, 16 were Stage III, and 7 were Stage IV. Thirteen patients had curative resection and 13 had noncurative surgery. Twenty-four of these 26 patients were evaluated for the agreement between chemosensitivity test results and the clinical response. There were 4 true positive, 15 true negative, and 5 false negative results, and the overall predictive accuracy of the test was 79.2%.

Discussion

Although many clinical trials of treatment for lung cancer have been performed using combination chemotherapy, an effective general regimen has not yet been established. Unlike other carcinomas, lung cancer has varied histologic characteristics and shows marked heterogeneity. Therefore, an assay that could select suitable drugs for individual patients might improve the response rate and survival obtained using the currently available chemotherapy agents. Thus, a good predictive assay for drug sensitivity could have a considerable impact on the management of lung cancer. In fact, a recent trial in patients with extensive small cell lung cancer compared the empirical selection of chemotherapy to selection based on the results of chemosensitivity testing and suggested that response rates may be improved by this approach. To aid in making therapeutic decisions, such an assay should be simple, rapid, inexpensive, and available at most institutes. However, no test that can accurately predict the clinical response of individual patients to chemotherapy has yet been developed.

This study evaluated the chick embryo assay as an in vivo chemosensitivity test for human lung cancer and also assessed the effect of various combination chemotherapy regimens that are under clinical trial in Japan. The immune system of the chick embryo does not mature until about day 18 after laying, so tumors transplanted onto the CAM can grow without being influenced by host immune responses. The graft take
Table 2  Association between the chick embryo assay data and the clinical response of individual lung cancers to combination chemotherapy

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Tumor histology</th>
<th>Operative radicality</th>
<th>Assay (inhibition rate %)</th>
<th>Clinical Therapy</th>
<th>Prognosis (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A II A</td>
<td>N</td>
<td>-2.5</td>
<td>PV</td>
<td>7, Dead</td>
</tr>
<tr>
<td>2</td>
<td>A II A</td>
<td>N</td>
<td>-11.3</td>
<td>PV</td>
<td>9, Dead</td>
</tr>
<tr>
<td>3</td>
<td>E II A</td>
<td>N</td>
<td>41.5</td>
<td>PV</td>
<td>31, Alive</td>
</tr>
<tr>
<td>4</td>
<td>A-S II B</td>
<td>N</td>
<td>1.3, -85.3</td>
<td>PV</td>
<td>4, Dead</td>
</tr>
<tr>
<td>5</td>
<td>A II B</td>
<td>N</td>
<td>7.8</td>
<td>PV</td>
<td>4, Dead</td>
</tr>
<tr>
<td>6</td>
<td>A II B</td>
<td>N</td>
<td>-11.9</td>
<td>PV</td>
<td>22, Alive</td>
</tr>
<tr>
<td>7</td>
<td>A IV N</td>
<td>6.6, -9.0</td>
<td></td>
<td>PAM</td>
<td>4, Dead</td>
</tr>
<tr>
<td>8</td>
<td>A IV N</td>
<td>-38.0, 4.5</td>
<td></td>
<td>PAM</td>
<td>6, Dead</td>
</tr>
<tr>
<td>9</td>
<td>A-S IV N</td>
<td>-14.2, -8.2</td>
<td></td>
<td>PAM</td>
<td>6, Dead</td>
</tr>
<tr>
<td>10</td>
<td>A IV N</td>
<td>6.8, 11.2</td>
<td></td>
<td>PAM</td>
<td>11, Dead</td>
</tr>
<tr>
<td>11</td>
<td>A IV N</td>
<td>3.4, 11.9</td>
<td></td>
<td>PAM</td>
<td>12, Dead</td>
</tr>
<tr>
<td>12</td>
<td>A IV N</td>
<td>3.5</td>
<td></td>
<td>PAM</td>
<td>43, Alive</td>
</tr>
<tr>
<td>13</td>
<td>A IV N</td>
<td>-18.1</td>
<td></td>
<td>PAM</td>
<td>49, Alive</td>
</tr>
<tr>
<td>14</td>
<td>A II C</td>
<td>-28.3, 11.5</td>
<td></td>
<td>MVP</td>
<td>13, Dead</td>
</tr>
<tr>
<td>15</td>
<td>A II C</td>
<td>-31.9, -6.3, -40.4, -54.4</td>
<td></td>
<td>PAM</td>
<td>52, Alive</td>
</tr>
<tr>
<td>16</td>
<td>E II C</td>
<td>1.4</td>
<td></td>
<td>PV</td>
<td>36, Dead</td>
</tr>
<tr>
<td>17</td>
<td>A III A</td>
<td>12.8</td>
<td></td>
<td>PV</td>
<td>9, Dead</td>
</tr>
<tr>
<td>18</td>
<td>E III A</td>
<td>-13.7, -17.5, 17.5</td>
<td></td>
<td>PV</td>
<td>10, Dead</td>
</tr>
<tr>
<td>19</td>
<td>A III A</td>
<td>15.2, -17.8, 37.4</td>
<td></td>
<td>PV</td>
<td>14, Dead</td>
</tr>
<tr>
<td>20</td>
<td>A III A</td>
<td>-32.2</td>
<td></td>
<td>PV</td>
<td>18, Alive</td>
</tr>
<tr>
<td>21</td>
<td>E III A</td>
<td>61.2, 42.1</td>
<td></td>
<td>MVP</td>
<td>25, Alive</td>
</tr>
<tr>
<td>22</td>
<td>A III A</td>
<td>-29.7, 17.9</td>
<td></td>
<td>MVP</td>
<td>26, Alive</td>
</tr>
<tr>
<td>23</td>
<td>E III A</td>
<td>59.8</td>
<td></td>
<td>MVP</td>
<td>31, Alive</td>
</tr>
<tr>
<td>24</td>
<td>A-S II B</td>
<td>-3.7, 6.7</td>
<td></td>
<td>PV</td>
<td>4, Dead</td>
</tr>
<tr>
<td>25</td>
<td>E II B</td>
<td>-22.6, -58.2</td>
<td></td>
<td>PV</td>
<td>7, Dead</td>
</tr>
<tr>
<td>26</td>
<td>L II B</td>
<td>31.7</td>
<td></td>
<td>PV</td>
<td>22, Alive</td>
</tr>
</tbody>
</table>

*1) A: Adenocarcinoma; E: Epidermoid carcinoma; A-S: Adenosquamous carcinoma; L: Large cell carcinoma
*2) N: Noncurative resection; C: curative resection
*3) 2PV, 2PAM, 2MVP: 2 courses of PV, PAM, or MVP, respectively
*4) TP: true positive; TN: true negative; FN: false negative
*5) p < 0.05 vs. control by Student's t test

rates are high for both surgical specimens and for cultured cell lines\(^5\). At least in the first generation after transplantation, the tumors histologically resemble the parent tumors\(^2\). In this study, the graft take rate was 100% and the histological characteristics of the parent tumors were maintained. According to Ossowski et al., at least within the first generation of transplantation onto the CAM, the malignant nature of the parent tumor is also maintained\(^2\). Seven days after transplantation, the tumors became large enough to be weighed and could be assessed for prediction of the efficacy of anticancer drugs. The test is simple, rapid, and inexpensive, but it requires some skill to perform. Prodrugs, such as cyclophosphamide, which require metabolic activation\(^5\), and combination chemotherapy can also be examined by this method\(^9\).
Using this assay system, we examined the effects of 3 combination chemotherapy regimens that are under clinical trial for lung cancer in Japan. Gralla et al. reported that the response to PV therapy was 23~46%, but that survival was not extended. The results of our chick embryo assay and the clinical follow-up study both indicated that PV therapy was not so effective. The efficacy rate of PAM therapy was 13.8% in the chick embryo assay, and its effect was also low in patients with Stage IV tumors and noncurative resection. On the other hand, the efficacy rate of MVP therapy in the chick embryo assay was 19.0% at the usual clinical dose and 30.8% at twice this dose. In our clinical study, 4 patients received MVP therapy and three of them showed a response. The overall agreement between our test and the clinical response was 79.2%, which is not inferior to other available chemosensitivity tests, including the in vitro human tumor clonogenic assay.

This study was preliminary, retrospective, and non-randomized, but the potential value of the chick embryo assay as a predictive test for tumor sensitivity to chemotherapy seems clear. As noted above, there was a good association between the results of sensitivity testing and the clinical outcome. However, before the routine use of this chemosensitivity test becomes possible, prospective studies are required, and a more definitive evaluation must depend upon the results of future randomized trials. Since only the MVP therapy was found to be active against lung cancer, there is little likelihood of finding drugs to which an individual tumor will be sensitive. Nevertheless, it should be emphasized that the predictive rate of our assay was quite high. Therefore, by using this test, we can at least avoid administering ineffective chemotherapy, which produces only side effects. In particular, the test should be useful to eliminate ineffective drugs for high-dose regimens in association with bone marrow transplantation.

In summary, the chick embryo assay can be applied for the in vivo chemosensitivity testing of lung cancer. While some technical problems remain, this assay may have various potential applications for predictive chemosensitivity testing.

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References
18) Gazdar AF, Steinberg SM, Russell EK, Linnoila RI, Oie HK, Ghosh BC, Cotelingam JD, Johnson BE, Minna JD, Inde DC: Correlation of in vitro drug sensitivity testing results with response to chemotherapy and survival in extensive-stage small cell lung cancer.


抗原（sialyl Tn antigen, STN）はモノクローナル抗体TKH2が認識する糖鎖抗原であり、母核糖鎖に属する。近年、STN抗原の癌関連抗原としての意義が認識され、各種癌において新しい腫瘍マーカーとして注目されている。

今回、筆者は術後再発および再発形態で予後悪化におけるSTN抗原の発現との関係について免疫組織化学的に検討した。

[対象と方法] 1986年、47年に来院した胃癌患者のうち、治療切除された125例を対象とした。

これらの症例の切除標本を10％ホルマリリン固定の後、パラフィン包埋し0.4μm切片を作製し、一次抗体とし
てTKH2（Osaka Assay Lab）を20倍希釈して用い、室温にて組織切片と1時間反応させ、streptavidin-biotin法にて免疫組織化学染色を行い、発色はdiaminobenzidineを用いた。判定は切片を光顕的に観察し、癌組織中の陽
性範囲が5％以上のものを陽性とした。

有意検定はX2検定を用いた。

[結果] STN抗原は胃癌組織、特に胞体質、細胞膜において強い発現を認めた。胃癌発生におけるSTNの発
現は74例（48.7％）にみられた。

臨床病理学の諸因子別にSTNの発現を検討した。リンパ節転移陽性症例ではリンパ節転移陰性の症例にくらべて有意に（P<0.01）STNの発現は高かった。また、壁深
度、組織学的進行度が進むにつれ、STN発現率は高値を示した。

STNの発現と予後の関係については、STN発現陽性
例は有意に（P<0.01）予後不良であった。

[結論] 胃癌組織中のSTN抗原の発現は組織学的進行度と関連し、STN抗原発現例では発現例陰性例にくらべて有意に（P<0.01）STNの発現率は低かった。また同一の組織学的進行度では、発現例の指標の一つとして、術後の補助療法の選択において有用であると思われた。

Changes in estrogen and progesterone receptor levels before and after preoperative treatments in primary advanced breast cancers  p 209～212

Yuichi Iino, Noritaka Sugamata et al.

原発癌進行症例において術前治療前に後のエストロゲンレセプターおよびプロゲステロンレセプターが
入射光を用いたningsoaked charcoal法で測定された。エストロゲンレセプター・レベルの平均値は、術前治療後有意に低下
（P<0.005）したが、プロゲステロンレセプター・レベルの平均値は有意に変動しなかった。すべての症例においてエストロゲンレセプター・およびプロゲステロンレセプターは陽性から陰性へと変動しなかった。治療前のレセプター・レベルの平均値は有効例のほうが無効例よりも高く、レセプター・レベルの平均値は、有効群では有意に低下（P<0.03）したが、無効群では有意には変動しなかった。

これらの結果は、ホルモンレセプターに関しては定性
により定量的のほうが臨床的より有効であることを示している。ヒト乳癌のエストロゲンレセプター・レベル

は通常、治療後に低下するかまたは変動しないかのどちら
らかであり、陽性から陰性に変動することは少ないと思われる。

Systemic induction chemotherapy in multidisciplinary treatment for locally advanced breast cancer  p 213～216

Yuichi Iino, Noritaka Sugamata et al.

21人の局所進行乳癌を対象にアスピラサイクリン系抗癌剤を用いた術前化学療法が行われた。発症は術
前ホルモン療法や術前照射を行った18人のhistorical control群の乳癌患者よりも高かった（48％対28％、P<0.10）。

化学療法後に意定的乳房切除術や拡大乳房切除術が
施行され、stage IIIまたは炎症性乳癌患者の90%が治療切
除であった。両群間の生存曲線有意差はなかったが、術前化学療法群の50%生存期間は術後に平均12ヶ月であった。

アスピラサイクリン系抗癌剤を用いた全化学療法は、集学的治療の一環として局所進行乳癌に有効である。

Chemoreactivity test of advanced lung cancers using the chick embryo assay  p 217～222

Motohiro Tanaka et al.

肺細胞に対する術後多剤併用化学療法の有用性を検討する目的で、受精卵の胚芽膜上にヒト腫瘍を植え付ける実験系（鶏卵法）を抗癌剤感受性試験として応用し、臨
床効果との比較を行った。

[対象と方法] 本実験において手術を施行された原発
性肺がん117症例に対し、その切除標本を用いて抗癌剤
感受性試験を行った。内訳は男19例、女26例で、年齢は
平均64.3歳、組織型別では腺腫51例、扁平上皮46例、
腺扁平上皮8例、大細胞癌5例、小細胞癌3例であった。

卵殻11日目の受精卵の卵渕部に細切した腫瘍を移植し、3日後抗癌剤を卵渕の血管内に投与した。腫瘍
移植の7日後に生著した腫瘍塊を摘出し抗癌剤効果を
判定した。抗癌剤は、臨床投与量を胎児の平均体重に換算して投与した。現在、肺腫瘍に対して非利用される
CDDP+VDS（PV療法）、CDPP+ADM+MMC（PAM療法）
MMC+VDS+CDDP（MPV療法）の3つの多剤併用
化学療法について鶏卵法と臨床効果との比較検討を行っ
た。感受性試験を行った117症例のうち、臨床効果との
相関性が検討可能な症例は26例であった。

臨床効果は、術後のfollow upを参考にし、PV療法または絶対非治療切除例では1年、それ以外のII期では2年、I
期では3年以上生存した場合その化学療法を“有効”と
判定した。

[結果] 鳥卵法を用いて感受性試験を行った117症
例に対する各化学療法の有効率は、PV療法が16.9％,
PAM療法が13.8％、MVP療法が19.0％であった。肺癌の
大肺を含む肺癌と扁平上皮癌についてプロトコール
別有効率をみると、肺癌に対してPV療法は14.8％、
MVP療法は17.6％であり、扁平上皮癌に対してPV療法は
23.8％、MVP療法は42.1％であり、特に扁平上皮癌に対
するMVP療法の有用性が示唆された。retoverspectiveに臨
床効果との相関性が評価可能な26症例のうち観察期間の
短い症例を除く24例の臨床相関性はtrue positiveが4例、
ture negativeが15例、false negativeが5例であった。以上
より鰓卵法の肺癌に対する臨床での併 Useful療法の予測
率は79.2％であった。

[考察] 肺癌は比較的早期から遠隔転移を生じやすいという癌器特異性があり、手術後の全
身化学療法の併用が不可欠である。したがって、肺癌の
個々の症例に対して有効な術後の多剤併用化学療法が選
択できる抗癌剤感受性試験法を発展させる。肺癌の治
療成績の向上に大きく貢献できると考えられる。本研究は、
臨床的に先の多剤併用化学療法を評価できる感受性
試験法としてin vivo鰓卵法の基礎的な検討を初め、臨床
効果との相関性を検討した。鰓卵法を用いた感受性試験
法は、短期間に効果判定が可能であり、試験成功率も高
く、肺癌に対する多剤併用療法が的確に評価可能である。
さらに、臨床効果の予測率が高くなり、再現性も良いこと
から、有用な抗癌剤感受性試験であると考えられた。

Recurrence of gastric cancer in the transverse colon 10 years after gastrectomy

Tatsuo Makino et al.

胃癌の直接浸潤または腹膜播種による横行結腸再発は
けっしてまれではないが、横行結腸への単発性再発は非
常によくまれである。今回筆者らは、胃癌根治術後10年を目
横行結腸に単発性の再発をきたした1例を経験したので
報告する。

症例は52歳の男性で、1976年に胃癌に対してAppleby
手術を施行した。肉眼的にはM領域症小弯を中心とした
浸潤性病変であり、組織学的には低分化腺癌でse, nlで
あった。術後経過は非常に順調であったが、1986年全腹部
を主訴に近医を受診し、注視検索にて横行結腸の狭窄
を指摘され当科を受診した。大腸内視鏡検査では、狭窄
部位結膜は浮腫を伴った不規則な多数の結節を呈してい
たが、潰瘍性病変は認められなかった。また、生検で
悪性組織は認められなかった。確定診断つかないも狭帯
部位切除の目的で手術を施行した。開腹所見では、横行結
腸の中央部に約10cmの腫瘤を認め、横行結腸切端を
施行した。検査の粘膜面は浮腫状を呈しており、一部に
結節を形成していた。組織学的には粘膜下を中心に低分
化腺癌を認め、癌細胞は粘膜下まで達していたが粘膜
面は正常であり、結腸外から浸潤してきたものと考えら
れた。また、癌組織所見が前回の胃癌組織と非常に類似
しており、以上より胃癌根治術後10年目に横行結腸再発をき
たした症例と診断した。
胃癌の再発は約80％が術後5年以内に起こるといわれ