Search was done to identify published and soft literature (not peer-reviewed but available through the web or other sources like books) using the following resources: PubMed, Scirus, ScienceDirect, references of published papers, and reference books.

Searched "yellow fever vaccine" and one of the following: BCG; dengue vaccine; cholera vaccine; hepatitis A vaccine; haemophilus influenza b or Hib vaccine; hepatitis B vaccine; HPV vaccine or human papillomavirus vaccine; influenza vaccine; Japanese encephalitis vaccine; measles vaccine; meningococcal vaccine; mumps vaccine; pneumococcal vaccine; rabies vaccine; rotavirus vaccine; rubella vaccine; smallpox vaccine; tetanus vaccine; tick-borne encephalitis vaccine; typhoid vaccine; varicella vaccine; zoster vaccine. Based on the titles, selected abstracts were reviewed. From the abstracts, a subset of articles was selected to review in detail. Articles with immunogenicity data and comparative groups are summarized below.

Available vaccines for co-administration with yellow fever vaccine listed by whether data are present on co-administration

Data present		***No data available***
Inactivated Vaccines	***Live (attenuated) vaccines***	
Cholera*	Bacillus Calmette-Guérin (BCG)	Anthrax
Diphtheria	Cholera*	Haemophilus Influenzae b; Hib
Hepatitis A	*Dengue chimera- recruiting*	Human papillomavirus
Hepatitis B	Measles	Influenza (lv)*
Influenza*	Mumps	Japanese encephalitis (iv)*
Meningococcal *recruiting*	Japanese encephalitis chimera*	*Malaria - recruiting*
Polio*	Polio*	Pneumococcal
Pertussis	Rubella	Rabies
Tetanus	Smallpox	Rotavirus
Typhoid*	Typhoid*	Tick-borne encephalitis
		Varicella virus, both Varicella and Zoster vaccines

* Both live and inactivate forms of vaccine; Abbreviations: iv = inactivated viral; lv = live viral; *Italic* indicate vaccines not yet licensed; ClinicalTrials.gov was used to determine if there were on-going studies and are indicated with "recruiting"

Abbreviations used in document: Ab = antibody; AE = adverse event; DTP = diphtheria, tetanus, and pertussis vaccine; ELISA = enzyme-linked immunosorbent assay; GMT = geometric mean titre; HAI = hemagglutination Inhibition Assay; Hep = hepatitis; LNI = log neutralization index; MMR = measles, mumps, and rubella; Ig = immunoglobulin; $PRNT_{\#}$ = plaque reduction neutralization test with the number as the proportion of the plaques inhibited where the titer was determined (e.g., 80% or 90% inhibition); RIA = radioimmunoassay; SCR = seroconversion rate; SPR = seropositive rate; YF = yellow fever

Table of Contents

Inactivated Vaccines

CHOLERA

1. Wolga J, et al. Evaluation of stabilized yellow fever vaccine Institut Pasteur on international travelers. J Biol Standard. 1986; 14: 289-295.
   Vaccines: Oral cholera vaccine (from A. Dodin); "classical yellow fever vaccine"; new stabilized YF vaccine; "classical diphtheria, tetanus" and either injectable or oral polio vaccine.
   Year: 1986 (published)
   Study population: Healthy adult travelers aged 16-71 years in France
   Number of Participants: 245 total (47-50 per group)
   Assays: YF $PRNT_{80}$ and HAI, with positive being defined as a titer of 5 for PRNT and 10 for HAI.
   Schedules: Group 1 – Cholera vaccine at day 0; Group 2 – YF "classic" vaccine at day 0; Group 3 – Cholera and YF "classic" vaccine at day 0; Group 4 – YF "classic" vaccine and DT-Polio vaccine; Group 5 – YF vaccine (new formulation; IP-Paris)
   Immunogenicity Results: All groups had similar rates of seroconversion to YF between 91.8% and 94%.
   Safety Results: No malaise, fever, or allergic reactions noted.
   Conclusions: Simultaneous vaccination is well tolerated and there is no impact of YF immunogenicity (immune responses to other vaccines were not measured).

2. Felsenfeld O, et al. Simultaneous vaccination against cholera and yellow fever. Lancet. 1973; 1: 457-8.
   Vaccines: Injectable cholera vaccine and YF vaccine (specific manufacturer unknown).
   Year: 1973 (published)
   Study population: "Individuals" in Colombia
   Number of Participants: ~300 total
   Assays: YF PRNT and cholera vibriocidal antibodies (per in-house protocol)
   Schedules: Group 1 – YF vaccine at 24 mo, 12-23 mo, 6-11 months, 5, 4, 3, 2, and 1 week before cholera; Group 2 – same schedule except cholera given both YF vaccine; Group 3 – Cholera alone; Group 4 – YF alone
   Immunogenicity Results: Significant decrease of both cholera and YF antibody if given within 3 weeks of the other vaccine.
   Safety Results: No note of safety
   Conclusions: Administration of YF and cholera vaccine, simultaneously or one to three weeks apart, reduced the vibriocidal and YF neutralizing antibody titres.

DIPHTHERIA

1. Wolga J, et al. Evaluation of stabilized yellow fever vaccine Institut Pasteur on international travelers. J Biol Standard. 1986; 14: 289-295.
   Vaccines: Oral cholera vaccine (from A. Dodin); "classical yellow fever vaccine"; new stabilized YF vaccine; "classical diphtheria, tetanus" and either injectable or oral polio vaccine.
   Year: 1986 (published)
   Study population: Healthy adult travelers aged 16-71 years in France
   Number of Participants: 245 total (47-50 per group)

Assays: YF $PRNT_{80}$ and HAI, with positive being defined as a titer of 5 for PRNT and 10 for HAI.
Schedules: Group 1 – Cholera vaccine at day 0; Group 2 – YF "classic" vaccine at day 0; Group 3 – Cholera and YF "classic" vaccine at day 0; Group 4 – YF "classic" vaccine and DT-Polio vaccine; Group 5 – YF vaccine (new formulation; IP-Paris)
Immunogenicity Results: All groups had similar SCR to YF between 91.8% and 94%.
Safety Results: No malaise, fever, or allergic reactions noted.
Conclusions: Simultaneous vaccination is well tolerated and there is no impact of YF immunogenicity (immune responses to other vaccines were not measured).

2. Yvonnet B, et al. Simultaneous administration of hepatitis B and yellow fever vaccines. J Med Virol. 1986; 19: 307-11.
Vaccines: DTP-Polio (pastuer); YF vaccine (IP-Dakar), Measles (Merieux), HepB (pasteur)
Year: 1986 (published)
Study population: Infants aged 9 to 36 months in Senegal
Number of Participants: 226 total (38-79 per group)
Assays: HepB commercial RIA; YF $PRNT_{90}$ (SCR not defined)
Schedules: Group 1 – no vaccines; Group 2 – HepB and DTP-polio at 3 doses 6 months apart with Measles and YF vaccine given at 3rd dose; Group 3 – same as Group 2 with 3 month dose interval; Group 4 – DTP-polio, YF, and measles vaccine
Immunogenicity Results: YF vaccine SCR was 92.4 to 93.5% regardless of HepB co-administration; GMTs were significantly lower with HepB administration (p=0.02). HepB GMTS were higher with YF co-administration than HepB alone.
Safety Results: "No evidence of untoward reactions was obtained during the study".
Conclusions: Co-administration of DTP-Polio, measles, and HepB did not significantly alter YF seroconversion (91.5%-93.5%; GMT 19.4-23.6) when compared to co-administration of DTP-Polio, measles and YF (SCR 93.6%; GMT 31.8). Titers to DPT-Polio were not evaluated.

3. Ruben et al. Simultaneous administration of smallpox, measles, yellow fever, and diphtheria-pertussis-tetanus antigens to Nigerian children. Bull WHO. 1973; 48: 175-181.
Vaccines: Smallpox (Dryvax, Wyeth); measles (Pitman-Moore), YF vaccine (National Drug, Nigeria); "commercial DPT"; blood before vaccination and at 3 months
Year: 1973 (published)
Study population: Children 6 months to 2 years in Nigeria
Number of Participants: 334 (119 between 6-11 months and 225 between 12-24 months)
Assays: HAI for measles; PRNT90 for YF; Rapid tube test for pertussis; haemagglutination for diphtheria and tetanus; smallpox visualization of scar
Schedules: Group 1 – Placebo at day 0; Group 2 – smallpox, measles, and YF vaccine at day 0; Group 3 – Smallpox, measles, yellow fever, and DPT vaccine at day 0 with DPT again at 2 months; Group 4 – DPT vaccine at day 0 and 2 months
Immunogenicity Results: The proportion with positive neut titers following YF vaccination was 5.3% in Group 1 (placebo) and 96.6 and 94.8% in Groups 2 and 3, respectively. There was no difference in the response to diphtheria, tetanus, or pertussis

when given in Group 4 versus Group 3; measles response was decreased when DPT was given versus just smallpox, measles, and yellow fever.
Safety Results: Not evaluated.
Conclusions: There was good SCR to YF vaccine regardless of whether it was coadministered with smallpox and measles vaccine or smallpox, measles, and DPT.

HEPATITIS A

1. Receveur MC, et al. Simultaneous vaccination against hepatitis A and yellow fever. Bull Soc Pathol Exot. 1993; 86: 406-9.
Vaccines: inactivated Hepatitis A (Havrix, GSK); and YF vaccine (Pasteur Merieux)
Year: 1993 (published)
Study population: Healthy adults in France
Number of Participants: 108 total (36 per group)
Assays: YF complement fixation; HepA ELISA
Schedules: Group 1 – HepA vaccine at Day 0, 15 and 6 months; Group 2 – YF vaccine at day 0; Group 3 – HepA vaccine and YF vaccine at day 0 and HepA at Day 15 and 6 months
Immunogenicity Results: YF SCR was 100% for Group 2 and 3; HepA SCR 100% for Group 3 and 1 (UI/l 481.8 and 557.1, respectively)
Safety Results: No SAEs; well tolerated
Conclusions: Simultaneous vaccination is well tolerated and immunogenicity is as good as it is for each vaccine separately.

2. Jong EC, et al. An open randomized study of inactivated hepatitis A vaccine administered concomitantly with typhoid fever and yellow fever vaccine. J Trav Med. 2002; 9: 66-70.
Vaccines: inactivated Hepatitis A (VAQTA, Merck); inactivated typhoid vaccine (Typhim Vi, sanofi pasteur); and YF vaccine (YF-VAX, sanofi pasteur)
Year: 1997
Study population: Healthy adults 18 to 55 years in USA
Number of Participants: 240 total (80 per group)
Assays: HAVAB assay for HepA with ≥10 mIU/mL positive (SPR); typhoid Vi RIA measuring seroconversion (SCR); YF PRNT with SCR being a titer >0.27IU/mL
Schedules: Group 1 - HepA, typhoid, and YF vaccines at Day 0 and HepA vaccine at Week 24; Group 2 – typhoid and YF vaccines at day 0 and HepA 1 month; Group 3 – HepA vaccine at day 0 and Week 24
Immunogenicity Results: YF SCR with HepA and typhoid vaccines was 98.6% (GMT 21.6; 95%CI 16.9-27.6) compared to YF and typhoid vaccines was 100% (GMT 20.2; 95%CI 15.8-25.6); HepA SPR with YF and typhoid vaccines was 95.9% (GMT 35.0, 95%CI 30.4-40.3) compared to HepA vaccine alone 100% (GMT 49.2, 95%CI 42.7-56.7); typhoid SCR with HepA and YF vaccines was 93.4% (GMT 2.9, 95%CI 2.3-3.7) compared to with YF vaccine is 89.7% (GMT 2.3, 95%CI 1.8-3.0)
Safety Results: No serious AEs; no difference in rates of injection or systemic reactions between groups.
Conclusions: No change in YF vaccine immunogenicity or reactogenicity when administered with inactivated HepA vaccine (though co-administered with inactivated

typhoid vaccine); HepA vaccine immunogenicity did decrease significantly when given with YF vaccine and typhoid vaccine but not believed to be of clinical significance.

3. Gil A, et al. Interference assessment of yellow fever vaccine with the immune response to single-dose inactivated hepatitis A vaccine (1440EL.U.). A controlled study in adults. Vaccine. 1996; 14: 1028-1030.
   Vaccines: inactivated Hepatitis A (HAVRIX, GSK) and YF vaccine (Stamaril, sanofi pasteur)
   Year: 1996 (published)
   Study population: Healthy adults 18 to 45 years in Spain
   Number of Participants: 110 total (55 per group with some attrition loss)
   Assays: HAVAB assay for HepA
   Schedules: Group 1 – HepA vaccine alone at day 0 and 6 months; Group 2 – HepA and YF vaccine at day 0 and HepA vaccine at 6 months with blood at Day 0, 1 month, 6 months, and 7 months
   Immunogenicity Results: No differences in HepA SCR and GMTs between groups at month 1, month 6 or 7
   Safety Results: No serious AEs; no difference in rates of injection or systemic reactions between groups.
   Conclusions: No change in HepA immunogenicity or reactogenicity when administered with yellow fever vaccine; yellow fever vaccine immunogenicity was not measured and yellow fever vaccine was not administered alone to determine if reactogenicity differed.

4. Dumas R, et al. Safety and immunogenicity of a new inactivated hepatitis A vaccine in concurrent administration with a typhoid fever vaccine or a typhoid fever + yellow fever vaccine. Adv Ther. 1997; 14: 160-7.
   Vaccines: inactivated Hepatitis A (Avaxim, Pasteur Merieux Connaught); inactivated typhoid vaccine (Typhim Vi, Pasteur Merieux Connaught/sanofi pasteur); and YF vaccine (Stamaril, Pasteur Merieux Connaught/sanofi pasteur)
   Year: 1996
   Study population: Healthy adults (18-60 years) in Switzerland
   Number of Participants: 121 total (62 and 59 per group)
   Assays: $PRNT_{80}$; HepA by RIA (HAVAB); typhoid by modified RIA
   Schedules: Group 1 – HepA with typhoid at day 0 and 6 months; Group 2 – HepA with typhoid and YF vaccines at day 0; with blood at Day 0, 14 (Group 2 only) and 28
   Immunogenicity Results: No differences in HepA and typhoid SCR between groups at 1 month; YF vaccine SCR at one month in Group 2 was 100%. Typhoid SCR was 90% and 92% for Group 1 and 2, respectively.
   Safety Results: No serious AEs; no difference in rates of injection or systemic reactions between groups.
   Conclusions: Developed 100% SCR to YF vaccine and HepA following vaccination without changes in reactogenicity profile. No comparison arm with YF alone to know if GMTs were lower when coadministered.

5. Bovier PA, et al. Tolerance and immunogenicity of the simultaneous administration of virosome hepatitis A and yellow fever vaccines. J Travel Med. 1999; 6: 228-33.

Vaccines: inactivated Hepatitis A (Epaxal, Berna/Crucell) and YF vaccine (Stamaril, sanofi pasteur)
Year: 1999 (published)
Study population: Healthy adults aged 18 to 40 years
Number of Participants: 105 total (52 and 53 per group)
Assays: HepA automated sandwich ELISA (Enaymun test) with SCR >20mIU/Ml; YF mouse brain neutralization with SCR >1:5%.
Schedules: Group 1 – HepA and YF vaccines at day 0; Group 2 – Hep A vaccine alone at day 0; both group received HepA vaccine at 12 months; blood at Day 0, 14, and 28, Month 3, 12, 13, Year 2
Immunogenicity Results: No statistically significant differences in HepA SCR and GMT at any time point; YF vaccine SCR at one month in Group 1 was 96%
Safety Results: No serious AEs; no difference in rates of injection or systemic reactions between groups.
Conclusions: Developed 96% and 100% SCR to YF vaccine and HepA vaccine, respectively without changes in reactogenicity profile to HepA.

HEPATITIS B

1. Yvonnet B, et al. Simultaneous administration of hepatitis B and yellow fever vaccines. J Med Virol. 1986; 19: 307-11.
   Vaccines: DTP-Polio (pastuer); YF vaccine (IP-Dakar), Measles (Merieux), HepB (pasteur)
   Year: 1986 (published)
   Study population: Infants aged 9 to 36 months in Senegal
   Number of Participants: 226 total (38-79 per group)
   Assays: HepB commercial RIA; YF $PRNT_{90}$
   Schedules: Group 1 – no vaccines; Group 2 – HepB and DTP-polio at 3 doses 6 months apart with Measles and YF vaccine given at 3rd dose; Group 3 – same as Group 2 with 3 month dose interval; Group 4 – DTP-polio, YF, and measles vaccine
   Immunogenicity Results: YF vaccine SCR was 92.4 to 93.5% regardless of HepB co-administration; GMTs were significantly lower with HepB administration (p=0.02). HepB GMTS were higher with YF co-administration than HepB alone.
   Safety Results: "No evidence of untoward reactions was obtained during the study".
   Conclusions: "YF antibodies were detected in a similar proportion of infants immunized with either YF alone or an association of YF and hepatitis B vaccines. However, a lower proportion of high YF antibody titers were observed when the vaccines were injected at the same time."

2. Coursaget P, et al. Simultaneous injection of plasma-derived or recombinant hepatitis B vaccines with yellow fever and killed polio vaccines. Vaccine. 1995; 13: 109-111.
   Vaccines: Plasma-derived HB vaccine (Hevac B, Pasteur-Merieux); recombinant HB vaccine (Gen-Hevac B, Pasteur-Merieux); and YF vaccine (Pasteur-merieux) [DTP-Polio also studied but only with HepB]
   Year: 1986 (published)
   Study population: Infants aged 9 to 36 months in Senegal
   Number of Participants: 176 total (55-62 per group)

Assays: YF $PRNT_{90}$
Schedules: HepB given at 2, 4, and 9 or 10 months of age; YF vaccine and measles given at 9 months of age; blood samples taken at 9 and 10 months.
Immunogenicity Results: YF vaccine SCR was 95-96% regardless of HepB co-administration; GMTs were similar with 16.6 for YF with measles alone compared to 17.6 and 16.9 with plasma-derived or recombinant HepB vaccine administration, respectively.
Safety Results: "No untoward reactions were observed during the study".
Conclusions: "The serological antibody response to YF vaccine administered with plasma-derived or recombinant HB vaccine was found to be similar to that observed after administration of YF vaccine alone. These results show that HB vaccine given simultaneously with YF vaccine at 9 months of age does not interfere with the development of an immune response to yellow fever as suspected in [Yvonnet et al]."

INFLUENZA

1. Goullin B, et al. Efficacy of the association of flu-vaccine and yellow-fever vaccine. Med Armees. 1993; 21: 115-117.
   Vaccines: Inactivated flu vaccine (Mutagrip R) and YF vaccine (Pasteur-merieux)
   Year: 1988
   Study population: Military male soldiers (adults) in France
   Number of Participants: 92 total (65 and 27 per group)
   Assays: YF $PRNT_{80}$ and Influenza used HAI
   Schedules: Group 1 received YF and Influenza at day 0; Group 2 received YF vaccine at day 0; blood taken at day 30.
   Immunogenicity Results: YF SCR and log titers were not significantly different between the groups (Group 1 SCR=100% and log titer 1.76 versus Group 2 SCR = 96% and log titer 1.88). Flu titers were 78-80% to the three strains in the vaccine which were noted to the same as those seen for the vaccine released the previous year.
   Safety Results: No data obtained.
   Conclusions: Effective protection against yellow fever regardless of the coadministration of inactivated influenza vaccine. Although the immune response to influenza vaccine was not evaluated alone, it was reported to be "as usually obtained".

MENINGOCOCCAL

1. There was an abstract presented at the 36th ICAAC meeting that suggested that co-administration of inactivated typhoid vaccine, YF vaccine and meningococcal (A,C,W-135,Y without conjugate) did not impact the immunogenicity or reactogenicity of the vaccines. The original data were not published. (Ref: Dukes C, et al. Safety and immunogenicity of simultaneous administration of Typhim Vi (TV), YF-VAX (YF and Menomune (MV) [Abstract]. Presented at the 36th International Conference on Antimicrobial Agents and Chemotherapy; September 15-18, 1996; New Orleans, Louisiana).

2. ClinicalTrial.gov has a trial (NCT01466387) listed where YF vaccine (YF-VAX, sanofi pasteur) and typhoid vaccine with to be given together or co-administered with MenA,C,W-135,Y-CRM (Novartis); enrolling through May 2012.

POLIO

1. Wolga J, et al. Evaluation of stabilized yellow fever vaccine Institut Pasteur on international travelers. J Biol Standard. 1986; 14: 289-295.
   Vaccines: Oral cholera vaccine (from A. Dodin); "classical yellow fever vaccine"; new stabilized YF vaccine; "classical diphtheria, tetanus" and either injectable or oral polio vaccine.
   Year: 1986 (published)
   Study population: Healthy adult travelers aged 16-71 years in France
   Number of Participants: 245 total (47-50 per group)
   Assays: YF $PRNT_{80}$ and HAI, with positive being defined as a titer of 5 for PRNT and 10 for HAI.
   Schedules: Group 1 – Cholera vaccine at day 0; Group 2 – YF "classic" vaccine at day 0; Group 3 – Cholera and YF "classic" vaccine at day 0; Group 4 – YF "classic" vaccine and DT-Polio vaccine; Group 5 – YF vaccine (new formulation; IP-Paris)
   Immunogenicity Results: All groups had similar rates of seroconversion to YF between 91.8% and 94%.
   Safety Results: No malaise, fever, or allergic reactions noted.
   Conclusions: Simultaneous vaccination is well tolerated and there is no impact of YF immunogenicity (immune responses to other vaccines were not measured).See Wolga et al under inactivated cholera.

2. Yvonnet B, et al. Simultaneous administration of hepatitis B and yellow fever vaccines. J Med Virol. 1986; 19: 307-11.
   Vaccines: DTP-Polio (pastuer); YF vaccine (IP-Dakar), Measles (Merieux), HepB (pasteur)
   Year: 1986 (published)
   Study population: Infants aged 9 to 36 months in Senegal
   Number of Participants: 226 total (38-79 per group)
   Assays: HepB commercial RIA; YF $PRNT_{90}$
   Schedules: Group 1 – no vaccines; Group 2 – HepB and DTP-polio at 3 doses 6 months apart with Measles and YF vaccine given at 3rd dose; Group 3 – same as Group 2 with 3 month dose interval; Group 4 – DTP-polio, YF, and measles vaccine
   Immunogenicity Results: YF vaccine SCR was 92.4 to 93.5% regardless of HepB co-administration; GMTs were significantly lower with HepB administration (p=0.02). HepB GMTS were higher with YF co-administration than HepB alone.
   Safety Results: "No evidence of untoward reactions was obtained during the study".
   Conclusions: Co-administration of DTP-Polio, measles, and HepB did not significantly alter YF seroconversion (91.5%-93.5%; GMT 19.4-23.6) when compared to co-administration of DTP-Polio, measles and YF (SCR 93.6%; GMT 31.8). Titers to DPT-Polio were not evaluated.

PERTUSSIS

1. Ruben et al. Simultaneous administration of smallpox, measles, yellow fever, and diphtheria-pertussis-tetanus antigens to Nigerian children. Bull WHO. 1973; 48: 175-181.

Vaccines: Smallpox (Dryvax, Wyeth); measles (Pitman-Moore), YF vaccine (National Drug, Nigeria); "commercial DPT"; blood before vaccination and at 3 months
Year: 1973 (published)
Study population: Children 6 months to 2 years in Nigeria
Number of Participants: 334 (119 between 6-11 months and 225 between 12-24 months)
Assays: HAI for measles; PRNT90 for YF; Rapid tube test for pertussis; haemagglutination for diphtheria and tetanus; smallpox visualization of scar
Schedules: Group 1 – Placebo at day 0; Group 2 – smallpox, measles, and YF vaccine at day 0; Group 3 – Smallpox, measles, yellow fever, and DPT vaccine at day 0 with DPT again at 2 months; Group 4 – DPT vaccine at day 0 and 2 months
Immunogenicity Results: The proportion with positive neut titers following YF vaccination was 5.3% in Group 1 (placebo) and 96.6 and 94.8% in Groups 2 and 3, respectively. There was no difference in the response to diphtheria, tetanus, or pertussis when given in Group 4 versus Group 3; measles response was decreased when DPT was given versus just smallpox, measles, and yellow fever.
Safety Results: Not evaluated.
Conclusions: There was good SCR to YF vaccine regardless of whether it was coadministered with smallpox and measles vaccine or smallpox, measles, and DPT.

TETANUS

1. Gateff C, et al. Pentavalent vaccine association: a preliminary study. Ann Microbiol (Inst Pasteur). 1973; 124B: 387-409.
   Vaccines: Smallpox (Dryvax, Wyeth); BCG (IP-Dakar); YF (IP-Dakar); Measles (Lyovac, Merck); Tetanus (IP-Paris)
   Year: 1973 (published)
   Study population: Children aged 1 to 5 years in Cameroon
   Number of Participants: 600 total (100 per group)
   Assays: YF HAI at 60 days post vaccination; Smallpox – response to vaccine (local reaction); Measles HAI at 60 days post vaccination; Tetanus – neutralization test
   Schedules: Group 1 – Smallpox, YF, Measles, BCG, and tetanus vaccine at day 0; Group 2 – Smallpox and YF vaccine at day 0; Group 3 – Measles and Smallpox vaccine at day 0; Group 4 – Smallpox and BCG vaccine at day 0; Group 5 – Smallpox, Measles, and Tetanus vaccine at day 0; Group 6 – Placebo and Smallpox vaccine at day 0
   Immunogenicity Results: YF protective level of antibodies achieved in 84.4% (Titre base 2: 56) of Group 1 and 86.7 (Titre base 2: 68) of Group 2. There was no significant difference in the response to the other vaccines between Group 1 and Group 2. BCG response, however, was suboptimal with just over half responding in any group; Tetanus had 93% protection in Group 5 versus 84% in Group 1.
   Safety Results: No comment.
   Conclusions: "The association of the 5 antigens gives protection to at least 80% of those subjects vaccinated against smallpox, yellow fever, measles and tetanus, when the level of protection following BCG administration is normal. A firm position which out of respect for the possible saturation phenomenon would accept the following quadruple associates": small pox, YF, measles, and tetanus vaccine; or smallpox, YF, measles, and BCG.

2. Wolga J, et al. Evaluation of stabilized yellow fever vaccine Institut Pasteur on international travelers. J Biol Standard. 1986; 14: 289-295.
   Vaccines: Oral cholera vaccine (from A. Dodin); "classical yellow fever vaccine"; new stabilized YF vaccine; "classical diphtheria, tetanus" and either injectable or oral polio vaccine.
   Year: 1986 (published)
   Study population: Healthy adult travelers aged 16-71 years in France
   Number of Participants: 245 total (47-50 per group)
   Assays: YF $PRNT_{80}$ and HAI, with positive being defined as a titer of 5 for PRNT and 10 for HAI.
   Schedules: Group 1 – Cholera vaccine at day 0; Group 2 – YF "classic" vaccine at day 0; Group 3 – Cholera and YF "classic" vaccine at day 0; Group 4 – YF "classic" vaccine and DT-Polio vaccine; Group 5 – YF vaccine (new formulation; IP-Paris)
   Immunogenicity Results: All groups had similar rates of seroconversion to YF between 91.8% and 94%.
   Safety Results: No malaise, fever, or allergic reactions noted.
   Conclusions: Simultaneous vaccination is well tolerated and there is no impact of YF immunogenicity (immune responses to other vaccines were not measured).

3. Yvonnet B, et al. Simultaneous administration of hepatitis B and yellow fever vaccines. J Med Virol. 1986; 19: 307-11.
   Vaccines: DTP-Polio (pastuer); YF vaccine (IP-Dakar), Measles (Merieux), HepB (pasteur)
   Year: 1986 (published)
   Study population: Infants aged 9 to 36 months in Senegal
   Number of Participants: 226 total (38-79 per group)
   Assays: HepB commercial RIA; YF $PRNT_{90}$
   Schedules: Group 1 – no vaccines; Group 2 – HepB and DTP-polio at 3 doses 6 months apart with Measles and YF vaccine given at 3rd dose; Group 3 – same as Group 2 with 3 month dose interval; Group 4 – DTP-polio, YF, and measles vaccine
   Immunogenicity Results: YF vaccine SCR was 92.4 to 93.5% regardless of HepB co-administration; GMTs were significantly lower with HepB administration (p=0.02). HepB GMTS were higher with YF co-administration than HepB alone.
   Safety Results: "No evidence of untoward reactions was obtained during the study".
   Conclusions: Co-administration of DTP-Polio, measles, and HepB did not significantly alter YF seroconversion (91.5%-93.5%; GMT 19.4-23.6) when compared to co-administration of DTP-Polio, measles and YF (SCR 93.6%; GMT 31.8). Titers to DPT-Polio were not evaluated.

4. Ruben et al. Simultaneous administration of smallpox, measles, yellow fever, and diphtheria-pertussis-tetanus antigens to Nigerian children. Bull WHO. 1973; 48: 175-181.
   Vaccines: Smallpox (Dryvax, Wyeth); measles (Pitman-Moore), YF vaccine (National Drug, Nigeria); "commercial DPT"; blood before vaccination and at 3 months
   Year: 1973 (published)
   Study population: Children 6 months to 2 years in Nigeria
   Number of Participants: 334 (119 between 6-11 months and 225 between 12-24 months)

Assays: HAI for measles; PRNT90 for YF; Rapid tube test for pertussis; haemagglutination for diphtheria and tetanus; smallpox visualization of scar
Schedules: Group 1 – Placebo at day 0; Group 2 – smallpox, measles, and YF vaccine at day 0; Group 3 – Smallpox, measles, yellow fever, and DPT vaccine at day 0 with DPT again at 2 months; Group 4 – DPT vaccine at day 0 and 2 months
Immunogenicity Results: The proportion with positive neut titers following YF vaccination was 5.3% in Group 1 (placebo) and 96.6 and 94.8% in Groups 2 and 3, respectively. There was no difference in the response to diphtheria, tetanus, or pertussis when given in Group 4 versus Group 3; measles response was decreased when DPT was given versus just smallpox, measles, and yellow fever.
Safety Results: Not evaluated.
Conclusions: There was good SCR to YF vaccine regardless of whether it was coadministered with smallpox and measles vaccine or smallpox, measles, and DPT.

TYPHOID

1. Jong EC, et al. An open randomized study of inactivated hepatitis A vaccine administered concomitantly with typhoid fever and yellow fever vaccine. J Trav Med. 2002; 9: 66-70.
Vaccines: inactivated Hepatitis A (VAQTA, Merck); inactivated typhoid vaccine (Typhim Vi, sanofi pasteur); and YF vaccine (YF-VAX, sanofi pasteur)
Year: 1997
Study population: Healthy adults 18 to 55 years in USA
Number of Participants: 240 total (80 per group)
Assays: HAVAB assay for HepA with ≥10 mIU/mL positive (SPR); typhoid Vi RIA measuring seroconversion (SCR); YF PRNT with SCR being a titer >0.27IU/mL
Schedules: Group 1 - HepA, typhoid, and YF vaccines at Day 0 and HepA vaccine at Week 24; Group 2 – typhoid and YF vaccines at day 0 and HepA 1 month; Group 3 – HepA vaccine at day 0 and Week 24
Immunogenicity Results: YF SCR with HepA and typhoid vaccines was 98.6% (GMT 21.6; 95%CI 16.9-27.6) compared to YF and typhoid vaccines was 100% (GMT 20.2; 95%CI 15.8-25.6); HepA SPR with YF and typhoid vaccines was 95.9% (GMT 35.0, 95%CI 30.4-40.3) compared to HepA vaccine alone 100% (GMT 49.2, 95%CI 42.7-56.7); typhoid SCR with HepA and YF vaccines was 93.4% (GMT 2.9, 95%CI 2.3-3.7) compared to with YF vaccine is 89.7% (GMT 2.3, 95%CI 1.8-3.0)
Safety Results: No serious AEs; no difference in rates of injection or systemic reactions between groups.
Conclusions: No change in YF vaccine immunogenicity or reactogenicity when administered with inactivated HepA vaccine (though co-administered with inactivated typhoid vaccine); HepA vaccine immunogenicity did decrease significantly when given with YF vaccine and typhoid vaccine but not believed to be of clinical significance.

2. Dumas R, et al. Safety and immunogenicity of a new inactivated hepatitis A vaccine in concurrent administration with a typhoid fever vaccine or a typhoid fever + yellow fever vaccine. Adv Ther. 1997; 14: 160-7.
Vaccines: inactivated Hepatitis A (Avaxim, Pasteur Merieux Connaught); inactivated typhoid vaccine (Typhim Vi, Pasteur Merieux Connaught/sanofi pasteur); and YF vaccine (Stamaril, Pasteur Merieux Connaught/sanofi pasteur)

Year: 1996
Study population: Healthy adults (18-60 years) in Switzerland
Number of Participants: 121 total (62 and 59 per group)
Assays: $PRNT_{80}$; HepA by RIA (HAVAB); typhoid by modified RIA
Schedules: Group 1 – HepA with typhoid at day 0 and 6 months; Group 2 – HepA with typhoid and YF vaccines at day 0; with blood at Day 0, 14 (Group 2 only) and 28
Immunogenicity Results: No differences in HepA and typhoid SCR between groups at 1 month; YF vaccine SCR at one month in Group 2 was 100%. Typhoid SCR was 90% and 92% for Group 1 and 2, respectively.
Safety Results: No serious AEs; no difference in rates of injection or systemic reactions between groups.
Conclusions: Developed 100% SCR to YF vaccine and HepA following vaccination without changes in reactogenicity profile. No comparison arm with YF alone to know if GMTs were lower when coadministered.

3. There was an abstract presented at the 36th ICAAC meeting that suggested that co-administration of inactivated typhoid vaccine, YF vaccine and meningococcal (A,C,W-135,Y without conjugate) did not impact the immunogenicity or reactogenicity of the vaccines. The original data were not published. (Ref: Dukes C, et al. Safety and immunogenicity of simultaneous administration of Typhim Vi (TV), YF-VAX (YF and Menomune (MV) [Abstract]. Presented at the 36th International Conference on Antimicrobial Agents and Chemotherapy; September 15-18, 1996; New Orleans, Louisiana).

Live Vaccines

BACILLUS CALMETTE-GUÉRIN; BCG

1. Gateff C, et al. Pentavalent vaccine association: a preliminary study. Ann Microbiol (Inst Pasteur). 1973; 124B: 387-409.
   Vaccines: Smallpox (Dryvax, Wyeth); BCG (IP-Dakar); YF (IP-Dakar); Measles (Lyovac, Merck); Tetanus (IP-Paris)
   Year: 1973 (published)
   Study population: Children aged 1 to 5 years in Cameroon
   Number of Participants: 600 total (100 per group)
   Assays: YF HAI at 60 days post vaccination; Smallpox – response to vaccine (local reaction); Measles HAI at 60 days post vaccination; Tetanus – neutralization test
   Schedules: Group 1 – Smallpox, YF, Measles, BCG, and tetanus vaccine at day 0; Group 2 – Smallpox and YF vaccine at day 0; Group 3 – Measles and Smallpox vaccine at day 0; Group 4 – Smallpox and BCG vaccine at day 0; Group 5 – Smallpox, Measles, and Tetanus vaccine at day 0; Group 6 – Placebo and Smallpox vaccine at day 0
   Immunogenicity Results: YF protective level of antibodies achieved in 84.4% (Titre base 2: 56) of Group 1 and 86.7 (Titre base 2: 68) of Group 2. There was no significant difference in the response to the other vaccines between Group 1 and Group 2. BCG response, however, was suboptimal with just over half responding in any group; Tetanus had 93% protection in Group 5 versus 84% in Group 1.
   Safety Results: No comment.
   Conclusions: "The association of the 5 antigens gives protection to at least 80% of those subjects vaccinated against smallpox, yellow fever, measles and tetanus, when the level of protection following BCG administration is normal. A firm position which out of respect for the possible saturation phenomenon would accept the following quadruple associates": small pox, YF, measles, and tetanus vaccine; or smallpox, YF, measles, and BCG.

CHOLERA

1. Kollartsch et al. Safety and immunogenicity of live cholera and typhoid vaccines administered alone or in combination with antimalarial drugs, oral polio vaccine, or yellow fever. J Infect Dis. 1997; 175: 871-875 (Cholera and typhoid results). ***AND*** Tsai TF et al. Compatible concurrent administration of yellow fever 17D vaccine with oral, live, attenuated cholera CVD103-HgR and typhoid Ty21a vaccines. J Infect Dis. 1999; 179: 522-523 (yellow fever testing results).
   Vaccines: Oral cholera (CVD103-HgR, Berna); oral typhoid (Ty21a, Berna); and YF vaccine (Arilvax, Burroughs Wellcome)
   Year: 1997 and 1999 (published)
   Study population: Healthy adults ≥ 18 years in Austria.
   Number of Participants: 150 total (30 to 45 per group)
   Assays: YF $PRNT_{90}$; cholera microtiter plate assay; S typh IgG and IgA ELISA
   Schedules: Several group including ones with anti-malarials; main group of interest were Group 1 – oral cholera vaccine at day 0; Group 2 – oral cholera and YF vaccine; Group 3 – oral cholera and oral typhoid vaccines at day 0; Group 4 – oral cholera, oral typhoid, and YF vaccines

Immunogenicity Results: All subjects developed YF antibodies with an overall GMT of 178; subjects who received cholera, typhoid, and YF vaccine had higher (not significant) GMTs versus those who received cholera and YF vaccine GMTs (213 vs149, respectively). YF coadministration improved cholera SCR and GMTs when compared to the vaccine alone; the effect was not maintained when oral typhoid was also given. S typh antibodies were unaffected by the addition of YF vaccine.
Safety Results: "No concomitant treatment resulted in a statistically significant higher rate for any type of adverse event."
Conclusions: No impact on the immunogenicity or safety profile of YF vaccine when concomitantly administered with oral cholera or oral cholera and oral typhoid (there was also no impact on immunogenicity and safety for the other agents).

DENGUE CHIMERIA (*on YF vaccine backbone*)

1. Qiao M, et al. Priming effect on dengue and yellow fever vaccination on the immunogenicity, infectivity, and safety of a tetravalent dengue vaccine in humans. Am J Trop Med Hyg. 2011; 85: 724-31.
Vaccines: tetravalent chimeric dengue vaccine (TDV, sanofi pasteur); YF vaccine (Stamaril, sanofi pasteur); and monovalent dengue 1 or 2 chimeric vaccine (Acambis)
Year: 2011 (published)
Study population: Healthy adults 18-40 years old in Australia
Number of Participants: 35 (8-15/group)
Assays: Dengue and YF $PRNT_{50}$
Schedules: Group 1 – DEN1 or DEN2 chimeric vaccine 1 year previously and TDV at day 0; Group 2 – YF vaccine 1 year previously and TDV at day 0; Group 3 – Flavivirus naïve and TDV at day 0; Blood day 0, 28, 60, and 180.
Immunogenicity Results: Four weeks after TDV vaccination, a higher proportion of participants in the dengue monovalent or YF-primed groups than in the naïve group were seropositive to 4 dengue serotypes (with higher GMTs); vaccination with TDV did not seem to boost YF immune response. Delayed response to DEN1 seen in YF-primed persons but it increased over time.
Safety Results: No SAEs, not powered to detect significant differences, only systemic severe reactions reported in those with YF or monovalent dengue prior to TDV
Conclusions: YF immune response not affected by TDV, however previous YF delayed DEN1 antibody formation

2. Poo J, et al. Live-attenuated tetravalent dengue vaccine in dengue-naïve children, adolescents, and adults in Mexico City. Pediatr Infect Dis. 2011; 30: e9-e17.
Vaccines: tetravalent chimeric dengue vaccine (TDV, sanofi pasteur); YF vaccine (Stamaril, sanofi pasteur)
Year: 2006
Study population: Healthy 2-45 year olds in Mexico
Number of Participants: 126 (18-36/group)
Assays: dengue $PRNT_{50}$
Schedules: Group 1 – TDV at 0, 3.5, and 12 mo; Group 2 – YF at 0 months and TDV at 3.5 and 12 mo

Immunogenicity Results: Similar seropositive rates to all 4 dengue strains in those who received TDV initially (60%, 95%CI 48-72) versus YF vaccine initially (71%, 95%CI 53-85); GMTs were not significantly different if YF or TDV was given as initial vaccine.
Safety Results: No significant difference if YF given first or TDV though a slight increase in systemic reactions was observed in those receiving TDV after initial YF or TDV dose.
Conclusions: YF vaccine did not adversely impact response to TDV; in fact if gave similar if not better GMTs than TDV as initial vaccination.

3. Guirakhoo F, et al. Live attenuated chimeric yellow fever dengue type 2 (ChimeriVax-DEN2) vaccine: phase I clinical trial for safety and immunogenicity: effect of yellow fever pre-immunity in induction of cross neutralizing antibody responses to all 4 dengue serotypes. Hum Vaccin. 2006; 2: 60-7.
Vaccines: chimeric dengue 2 vaccine on YF vaccine backbone (sanofi pasteur); YF vaccine (YF-VAX, sanofi pasteur);
Year: 2006 (published)
Study population: Healthy adults 18-49 years old in USA
Number of Participants: 56 (42 naïve, 14 prior YF vaccine)
Assays: YF Log neutralization index (LNI); Dengue $PRNT_{50}$
Schedules: Group 1 – Low dose ChimeriVax-DEN2 at day 0; Group 2 – High dose ChimeriVax-DEN2 at day 0; Group 3 – YF vaccine at day 0; and Group 4 – YF vaccine 24-27 months previously and ChimeriVax-DEN2 at day 0
Immunogenicity Results: YF immune persons given ChimeriVax-DEN2 had higher GMTs and SCR to other dengue strains, also overall had a better immune response that was sustained at 6 and 12 mo (except for serogroup 4)
Safety Results: No SAEs, increase in AEs in YF immune persons versus naïve (uncertain significance)
Conclusions: YF vaccine 2 years pre single dose ChimeriVax-DEN2 resulted in similar if not better SCR and GMTs to DEN2 as well as eliciting DEN1, 3, and 4 responses which was not seen in YF vaccine naïve persons. YF primed persons had a slightly higher rate in AEs but not clear if significant.

4. ClinicalTrials.gov has a trial (NCT01488890) that is currently recruiting health adults 18-45 years in USA to receive YF vaccine with first dose TDV followed by dose additional doses of TDV at 2 and 6 months; also have YF alone and three dose TDV alone arms – data anticipated in 2014.

JAPANESE ENCEPHALITIS CHIMERA (*on YF vaccine backbone*)

1. Nasveld PE, et al. Concomitant or sequential administration of live attenuated Japanese encephalitis chimeric virus vaccine and yellow fever 17D vaccine: randomized double-blind phase II evaluation of safety and immunogenicity. Hum Vacc. 2010; 6:906-914.
Vaccines: JE chimeric vaccine (sanofi pasteur) and YF vaccine (Stamaril, sanofi pasteur)
Year: 2004-2005
Study population: Healthy adults aged 18-55 years
Number of Participants: 108 (90 in YF treatment arms)
Assays: $PRNT_{50}$ for both JE and YF vaccines

Schedules: Group 1 – JE vaccine at day 0 and YF vaccine at day 30; Group 2 – YF vaccine at day 0 and JE vaccine at day 0; and Group 3 – JE and YF vaccines at day 0 or day 30 and placebo at the other time point.
Immunogenicity Results: All participants seroconverted to YF vaccine with no significant difference between anti-YFV antibody GMTs when YF vaccine was administered 30 days before or after JE vaccine (ratio of means 1.1, 95%CI 0.5, 2.6) or when co-administered with JE vaccine (ratio of means 0.6, 95% CI 0.1, 1.2). Although the rates of SCR to JE vaccine were not significantly different between groups (91-100%) the GMTs for anti-JEV antibodies was significantly higher when JE was given 30 days before YF when compared to YF given prior to JE vaccine. When JE and YF were co-administered the GMTs were significantly lower when compared to JE then YF vaccine arm.
Safety Results: No serious AEs and co-administration did increase systemic or local symptoms.
Conclusions: SCR did not differ if chimeric JE was administered either concomitantly or in series with YF vaccine; however JE GMTs were lower with concomitant and coadministration.

2. Monath TP, et al. Chimeric live, attenuated vaccine against Japanese encephalitis (ChimeriVax-JE): phase 2 clinical trials for safety and immunogenicity, effect of vaccine dose and schedule, and memory response to challenge with inactivated Japanese encephalitis antigen. J Infect Dis. 2003; 188: 1213-30.
Vaccines: JE chimeric vaccine (sanofi pasteur) and YF vaccine (YF-VAX, sanofi pasteur)
Year: 2003 (published)
Study population: Healthy adults 18-59 years in USA
Number of Participants: 22 (total study 99 but only 22 received YF vaccine)
Assays: PRNT and expressed as $\log_{10}$ neutralization index with ≥ 0.7 being protection
Schedules: Group 1 - JE vaccine at day 0 and YF vaccine at day 30; Group 2 – YF vaccine at day 0 and JE vaccine at day 30.
Immunogenicity Results: 64% of persons in Group 1 had seroconversion to YF versus 91% in Group 2; the difference was not significant. Also the LNI was lower for persons who received YF vaccine after JE vaccine (1.59) than persons who received YF vaccine before JE vaccine (2.29); the difference was not significant.
Safety Results: No SAEs; with no differences in systemic or local reactions
Conclusions: There are no safety concerns when YF vaccine is given within 30 days of the chimeric JE vaccine; there was a lower, non-significant immune response to YF vaccine if it was given 30 days after JE chimeric vaccine.

MEASLES

1. Nascimento Silva JR, et al. Mutual interference on the immune response to yellow fever vaccine and a combined vaccine against measles, mumps, and rubella. Vaccine. 2011; 29: 6327-6334.
Vaccines: MMR (both MSD and BioManguinhos); YF vaccine (17DD, BioManguinhos; 17D-213, WHO)
Year: 2006

Study population: Healthy children 12-23 months in Brazil
Number of Participants: 1828 (1723 per protocol YF groups)
Assays: YF PRNT to log10 (>2.7log10 mIU/mL considered positive; four-fold increase in titer considered seroconversion); Measles PRNT; Mumps IgG ELISA; Rubella IgG ELISA
Schedules: Group 1 – MMR and YF vaccines at day 0; Group 2 – MMR at day 0 and YF at day 30; Blood at day 0 and 30 days post YF vaccine (varied time to measles titer measurement); AEs recorded 10 days post vaccination
Immunogenicity Results: When combined with MMR YF SCR (69.7%, 95%CI 66.4-72.8), GMT (1064.6, 95%CI 976.0-1161.2), and titer distribution were all significantly decreased when compared to YF vaccine given 30 days post MMR (SCR 87.7, 95%CI 85.3-89.8; GMT 3385.2, 95%CI 3105.2-3690.4). There was no difference in the responses between 17DD and 17D-213.
Measles SCR and GMTs were not significantly different between groups
Mumps and Rubella SCR and GMTs were significantly lower in Group 1 versus Group 2
Safety Results: No serious AEs; higher proportion of AEs reported in Group 1 than Group 2 but it was not significant (16.6% versus 11.8%, respectively); no difference between the Groups in the time to develop AEs or the duration of AEs
Conclusions: Coadministration of YF and MMR vaccine decreases the SCR and GMTs against YF, mumps, and rubella (measles not affected). Safety was not significantly different.

2. Stefano I, et al. Recent immunization against measles does not interfere with the sero-response to yellow fever vaccine. Vaccine. 1999; 17: 1042-46.
Vaccines: Measles (Merieux and Sclavo); YF vaccine (17DD, BioManguinhos)
Year: 1999 (published)
Study population: Healthy children 9 month old (vaccine naïve) in Brazil
Number of Participants: 294 per protocol (53-65/group)
Assays: YF PRNT to log10 (>2.7log10 mIU/mL considered positive; four-fold increase in titer considered seroconversion); Measles ELISA and PRNT
Schedules: Group 1 – Measles at day 0 and YF vaccine at day 1-6; Group 2 – Measles at day 0 and YF vaccine at day 7-13; Group 3 – Measles at day 0 and YF vaccine at day 14-21; Group 4 – Measles at day 0 and YF vaccine at 22-27 days; Group 5 – Measles at day 0 and YF vaccine at ≥28 days; Blood at day 0 and 6 weeks post YF vaccine (varied time to measles titer measurement)
Immunogenicity Results: There was no difference in YF SCR (67.9-84.6%) or GMTs (4.24-4.57) between groups; not specifically shown but measles SCR and GMTs were reported to be not significantly different between groups
Safety Results: Safety data not reported
Conclusions: YF vaccine given at varying times post measles vaccine does not significantly impact the SCR and GMTs to YF or measles.

3. Adu FD, et al. Field trial of combined yellow fever and measles vaccines among children in Nigeria. East African Med J. 1996; 73: 579-82.
Vaccines: Measles (MOH); YF vaccine (Federal YF Production Laboratory, Lagos)
Year: 1996 (published)

Study population: Healthy child 6-12 months in Nigeria
Number of Participants: 1177 (340-485/group)
Assays: YF ELISA; measles HAI
Schedules: Group 1 – Measles vaccine at day 0; Group 2 – YF vaccine at day 0; Group 3 – Measles and YF vaccines at day 0; Blood at 7 weeks post vaccination; AEs recorded 8 days post vaccination
Immunogenicity Results: No significant difference between Group 2 and 3 by age group 6-8 mo versus 9-12 mo for YF SCR (87.1-96.9%) and GMTs (130-163); measles SCR were lower in 6-8 mo but this was unaffected by co-administration
Safety Results: No difference between Groups.
Conclusions: YF and measles vaccines coadministration did not affect immunogenicity or reactogenicity of either vaccine.

4. Soula G et al. Study of a new combined yellow fever measles vaccine in children 6 to 24 months old in Mali. Bull Soc Path Ex. 1991; 84: 885-97.
Vaccines: Measles (Rouvax, Merieux); YF vaccine (Stamaril, sanofi) – vaccines mixed together prior to administration
Year: 1988-1989
Study population: Healthy children 4-24 months in Mali
Number of Participants: 453 (249 with YF titres)
Assays: YF seroneutralization; Measles HAI
Schedules: Group 1 – Measles and YF vaccines at day 0; Group 2 – Measles at day 0 and YF vaccine at day 45; Group 3 – YF at day 0 and Measles vaccine at day 45; Blood at day 0, 45, 240, and 270; AEs recorded 14 days post vaccination
Immunogenicity Results: YF SCR did not differ by Group and age strata (92.7-96.2%); GMTs higher in 12-24mo (19.4-29.5) compared to 4-8mo (16.5-19.8) and for Group 3 (19.8-29.5) versus Group 1 (16.5-19.4) but the difference was not significant. For measles, coadministration did not affect SCR of GMTs, however 6-8mo had a significantly lower SCR compared to 12-24mo for measles alone.
Safety Results: No difference in rates of local or systemic side effects except that measles had lower AE rates than YF alone or YF and measles vaccines combined.
Conclusions: "The results demonstrate the satisfactory immunogenicity and safety of the combined yellow fever measles vaccine."

5. Mouchon D, et al. Study of the combined vaccination against measles and yellow fever in African infants aged 6-10 months. Bull Soc Path Ex. 1990; 83: 537-551.
Vaccines: YF vaccine (17D, Pasteur); Measles (Rouvax, Merieux)
Year: 1990 (published)
Study population: Healthy infants 6-10 months old in Cameroun
Number of Participants: 319 (75-89/group)
Assays: YF $PRNT_{80}$; Measles HAI
Schedules: Group 1 – YF vaccine at day 0 and measles at day 30; Group 2 – Measles at day 0 and YF vaccine at day 30; Group 3 – YF and measles combined together in same syringe at day 0; Blood D0 and 30
Immunogenicity Results: YF SCR and GMTs were not significantly different between Group 1 (92.6% and 22.63) versus Group 3 (95.8% and 34.05). YF response did not

differ by age group. Measles SCR and GMTs not significantly different between Group 2 and Group 3 but GMTs increased with increasing age (significantly)
Safety Results: No undesirable effects secondary to vaccination
Conclusions: GMTs against YF are increased with coadministration with measles vaccine; SCR and safety are not different with coadministration

6. Lhuillier M, et al. Study of combined vaccination against yellow fever and measles in infants from six to nine months. J Biol Stand. 1989; 17: 9-15.
Vaccines: YF vaccine (Stamaril, sanofi); measles (Rouvax, Merieux)
Year: 1989 (published)
Study population: Healthy children 5-11mo in Ivory Coast
Number of Participants: 410 (219 per protocol)
Assays: YF HAI and PRNT; Measles HAI
Schedules: Group 1 – YF vaccine at day 0, measles at day 45; Group 2 – Measles at day 0 and YF vaccine at day 45; Group 3 – YF and measles vaccines at day 0; Blood at day 45
Immunogenicity Results: YF SCR (88-92%) and GMTs (13.8-15) were not significantly different by age group (<7mo versus >8mo) or single versus concomitant administration. Measles response was impacted by age by not by whether YF vaccine was coadministered.
Safety Results: "The vaccines administered separately or together were well tolerated."
Conclusions: Coadministration does not impact YF immunogenicity or reactogenicity.

7. Gateff C, et al. Pentavalent vaccine association: a preliminary study. Ann Microbiol (Inst Pasteur). 1973; 124B: 387-409.
Vaccines: Smallpox (Dryvax, Wyeth); BCG (IP-Dakar); YF (IP-Dakar); Measles (Lyovac, Merck); Tetanus (IP-Paris)
Year: 1973 (published)
Study population: Children aged 1 to 5 years in Cameroon
Number of Participants: 600 total (100 per group)
Assays: YF HAI at 60 days post vaccination; Smallpox – response to vaccine (local reaction); Measles HAI at 60 days post vaccination; Tetanus – neutralization test
Schedules: Group 1 – Smallpox, YF, Measles, BCG, and tetanus vaccine at day 0; Group 2 – Smallpox and YF vaccine at day 0; Group 3 – Measles and Smallpox vaccine at day 0; Group 4 – Smallpox and BCG vaccine at day 0; Group 5 – Smallpox, Measles, and Tetanus vaccine at day 0; Group 6 – Placebo and Smallpox vaccine at day 0
Immunogenicity Results: YF protective level of antibodies achieved in 84.4% (Titre base 2: 56) of Group 1 and 86.7 (Titre base 2: 68) of Group 2. There was no significant difference in the response to the other vaccines between Group 1 and Group 2. BCG response, however, was suboptimal with just over half responding in any group; Tetanus had 93% protection in Group 5 versus 84% in Group 1.
Safety Results: No comment.
Conclusions: "The association of the 5 antigens gives protection to at least 80% of those subjects vaccinated against smallpox, yellow fever, measles and tetanus, when the level of protection following BCG administration is normal. A firm position which out of respect for the possible saturation phenomenon would accept the following quadruple

associates": small pox, YF, measles, and tetanus vaccine; or smallpox, YF, measles, and BCG.

8. Yvonnet B, et al. Simultaneous administration of hepatitis B and yellow fever vaccines. J Med Virol. 1986; 19: 307-11.
Vaccines: DTP-Polio (pastuer); YF vaccine (IP-Dakar), Measles (Merieux), HepB (pasteur)
Year: 1986 (published)
Study population: Infants aged 9 to 36 months in Senegal
Number of Participants: 226 total (38-79 per group)
Assays: HepB commercial RIA; YF $PRNT_{90}$
Schedules: Group 1 – no vaccines; Group 2 – HepB and DTP-polio at 3 doses 6 months apart with Measles and YF vaccine given at 3rd dose; Group 3 – same as Group 2 with 3 month dose interval; Group 4 – DTP-polio, YF, and measles vaccine
Immunogenicity Results: YF vaccine SCR was 92.4 to 93.5% regardless of HepB co-administration; GMTs were significantly lower with HepB administration (p=0.02). HepB GMTS were higher with YF co-administration than HepB alone.
Safety Results: "No evidence of untoward reactions was obtained during the study".
Conclusions: Co-administration of DTP-Polio, measles, and HepB did not significantly alter YF seroconversion (91.5%-93.5%; GMT 19.4-23.6) when compared to co-administration of DTP-Polio, measles and YF (SCR 93.6%; GMT 31.8). Titers to DPT-Polio were not evaluated.

9. Ruben et al. Simultaneous administration of smallpox, measles, yellow fever, and diphtheria-pertussis-tetanus antigens to Nigerian children. Bull WHO. 1973; 48: 175-181.
Vaccines: Smallpox (Dryvax, Wyeth); measles (Pitman-Moore), YF vaccine (National Drug, Nigeria); "commercial DPT"; blood before vaccination and at 3 months
Year: 1973 (published)
Study population: Children 6 months to 2 years in Nigeria
Number of Participants: 334 (119 between 6-11 months and 225 between 12-24 months)
Assays: HAI for measles; PRNT90 for YF; Rapid tube test for pertussis; haemagglutination for diphtheria and tetanus; smallpox visualization of scar
Schedules: Group 1 – Placebo at day 0; Group 2 – smallpox, measles, and YF vaccine at day 0; Group 3 – Smallpox, measles, yellow fever, and DPT vaccine at day 0 with DPT again at 2 months; Group 4 – DPT vaccine at day 0 and 2 months
Immunogenicity Results: The proportion with positive neut titers following YF vaccination was 5.3% in Group 1 (placebo) and 96.6 and 94.8% in Groups 2 and 3, respectively. There was no difference in the response to diphtheria, tetanus, or pertussis when given in Group 4 versus Group 3; measles response was decreased when DPT was given versus just smallpox, measles, and yellow fever.
Safety Results: Not evaluated.
Conclusions: There was good SCR to YF vaccine regardless of whether it was coadministered with smallpox and measles vaccine or smallpox, measles, and DPT.

MUMPS

1. Nascimento Silva JR, et al. Mutual interference on the immune response to yellow fever vaccine and a combined vaccine against measles, mumps, and rubella. Vaccine. 2011; 29: 6327-6334.
   Vaccines: MMR (both MSD and BioManguinhos); YF vaccine (17DD, BioManguinhos; 17D-213, WHO)
   Year: 2006
   Study population: Healthy children 12-23 months in Brazil
   Number of Participants: 1828 (1723 per protocol YF groups)
   Assays: YF PRNT to log10 (>2.7log10 mIU/mL considered positive; four-fold increase in titer considered seroconversion); Measles PRNT; Mumps IgG ELISA; Rubella IgG ELISA
   Schedules: Group 1 – MMR and YF vaccines at day 0; Group 2 – MMR at day 0 and YF at day 30; Blood at day 0 and 30 days post YF vaccine (varied time to measles titer measurement); AEs recorded 10 days post vaccination
   Immunogenicity Results: When combined with MMR YF SCR (69.7%, 95%CI 66.4-72.8), GMT (1064.6, 95%CI 976.0-1161.2), and titer distribution were all significantly decreased when compared to YF vaccine given 30 days post MMR (SCR 87.7, 95%CI 85.3-89.8; GMT 3385.2, 95%CI 3105.2-3690.4). There was no difference in the responses between 17DD and 17D-213.
   Measles SCR and GMTs were not significantly different between groups
   Mumps and Rubella SCR and GMTs were significantly lower in Group 1 versus Group 2
   Safety Results: No serious AEs; higher proportion of AEs reported in Group 1 than Group 2 but it was not significant (16.6% versus 11.8%, respectively); no difference between the Groups in the time to develop AEs or the duration of AEs
   Conclusions: Coadministration of YF and MMR vaccine decreases the SCR and GMTs against YF, mumps, and rubella (measles not affected). Safety was not significantly different.

POLIO

1. Wolga J, et al. Evaluation of stabilized yellow fever vaccine Institut Pasteur on international travelers. J Biol Standard. 1986; 14: 289-295.
   Vaccines: Oral cholera vaccine (from A. Dodin); "classical yellow fever vaccine"; new stabilized YF vaccine; "classical diphtheria, tetanus" and either injectable or oral polio vaccine.
   Year: 1986 (published)
   Study population: Healthy adult travelers aged 16-71 years in France
   Number of Participants: 245 total (47-50 per group)
   Assays: YF $PRNT_{80}$ and HAI, with positive being defined as a titer of 5 for PRNT and 10 for HAI.
   Schedules: Group 1 – Cholera vaccine at day 0; Group 2 – YF "classic" vaccine at day 0; Group 3 – Cholera and YF "classic" vaccine at day 0; Group 4 – YF "classic" vaccine and DT-Polio vaccine; Group 5 – YF vaccine (new formulation; IP-Paris)
   Immunogenicity Results: All groups had similar rates of seroconversion to YF between 91.8% and 94%.
   Safety Results: No malaise, fever, or allergic reactions noted.

Conclusions: Simultaneous vaccination is well tolerated and there is no impact of YF immunogenicity (immune responses to other vaccines were not measured).

2. Kaplan JE, et al. The effect of immune globulin on the response to trivalent oral poliovirus and yellow fever vaccinations. Bull WHO. 1984; 62: 585-590.
Vaccines: oral Polio; YF vaccine; (and other vaccines administered at a different time include: DT; typhoid; smallpox; cholera and rabies vaccines); immune globulin
Year: 1978
Study population: Healthy adults (Peace Corps volunteers) aged 20-70 years
Number of Participants: 201
Assays: YF PRNT and Polio microneutralization test with response being defined as a four-fold greater change in Ab titers.
Schedules: Oral polio and YF at day 0; IgG was given 0-7 days before, 3-5 days after, or 28-32 days after vaccination
Immunogenicity Results: Main comparison was relative to immunoglobulin administration; YF antibody response rates were 82%; Polio SCR was 100% with YF administration. Cholera coadministration did not impact YF response.
Safety Results: None given.
Conclusions: Study not designed to clearly note interactions with vaccines but YF did not appear to be affected by co-administration of oral polio.

RUBELLA

1. Nascimento Silva JR, et al. Mutual interference on the immune response to yellow fever vaccine and a combined vaccine against measles, mumps, and rubella. Vaccine. 2011; 29: 6327-6334.
Vaccines: MMR (both MSD and BioManguinhos); YF vaccine (17DD, BioManguinhos; 17D-213, WHO)
Year: 2006
Study population: Healthy children 12-23 months in Brazil
Number of Participants: 1828 (1723 per protocol YF groups)
Assays: YF PRNT to log10 (>2.7log10 mIU/mL considered positive; four-fold increase in titer considered seroconversion); Measles PRNT; Mumps IgG ELISA; Rubella IgG ELISA
Schedules: Group 1 – MMR and YF vaccines at day 0; Group 2 – MMR at day 0 and YF at day 30; Blood at day 0 and 30 days post YF vaccine (varied time to measles titer measurement); AEs recorded 10 days post vaccination
Immunogenicity Results: When combined with MMR YF SCR (69.7%, 95%CI 66.4-72.8), GMT (1064.6, 95%CI 976.0-1161.2), and titer distribution were all significantly decreased when compared to YF vaccine given 30 days post MMR (SCR 87.7, 95%CI 85.3-89.8; GMT 3385.2, 95%CI 3105.2-3690.4). There was no difference in the responses between 17DD and 17D-213.
Measles SCR and GMTs were not significantly different between groups
Mumps and Rubella SCR and GMTs were significantly lower in Group 1 versus Group 2
Safety Results: No serious AEs; higher proportion of AEs reported in Group 1 than Group 2 but it was not significant (16.6% versus 11.8%, respectively); no difference between the Groups in the time to develop AEs or the duration of AEs

Conclusions: Coadministration of YF and MMR vaccine decreases the SCR and GMTs against YF, mumps, and rubella (measles not affected). Safety was not significantly different.

SMALLPOX

1. Gateff C, et al. Pentavalent vaccine association: a preliminary study. Ann Microbiol (Inst Pasteur). 1973; 124B: 387-409.
   Vaccines: Smallpox (Dryvax, Wyeth); BCG (IP-Dakar); YF (IP-Dakar); Measles (Lyovac, Merck); Tetanus (IP-Paris)
   Year: 1973 (published)
   Study population: Children aged 1 to 5 years in Cameroon
   Number of Participants: 600 total (100 per group)
   Assays: YF HAI at 60 days post vaccination; Smallpox – response to vaccine (local reaction); Measles HAI at 60 days post vaccination; Tetanus – neutralization test
   Schedules: Group 1 – Smallpox, YF, Measles, BCG, and tetanus vaccine at day 0; Group 2 – Smallpox and YF vaccine at day 0; Group 3 – Measles and Smallpox vaccine at day 0; Group 4 – Smallpox and BCG vaccine at day 0; Group 5 – Smallpox, Measles, and Tetanus vaccine at day 0; Group 6 – Placebo and Smallpox vaccine at day 0
   Immunogenicity Results: YF protective level of antibodies achieved in 84.4% (Titre base 2: 56) of Group 1 and 86.7 (Titre base 2: 68) of Group 2. There was no significant difference in the response to the other vaccines between Group 1 and Group 2. BCG response, however, was suboptimal with just over half responding in any group; Tetanus had 93% protection in Group 5 versus 84% in Group 1.
   Safety Results: No comment.
   Conclusions: "The association of the 5 antigens gives protection to at least 80% of those subjects vaccinated against smallpox, yellow fever, measles and tetanus, when the level of protection following BCG administration is normal. A firm position which out of respect for the possible saturation phenomenon would accept the following quadruple associates": small pox, YF, measles, and tetanus vaccine; or smallpox, YF, measles, and BCG.

2. Ruben et al. Simultaneous administration of smallpox, measles, yellow fever, and diphtheria-pertussis-tetanus antigens to Nigerian children. Bull WHO. 1973; 48: 175-181.
   Vaccines: Smallpox (Dryvax, Wyeth); measles (Pitman-Moore), YF vaccine (National Drug, Nigeria); "commercial DPT"; blood before vaccination and at 3 months
   Year: 1973 (published)
   Study population: Children 6 months to 2 years in Nigeria
   Number of Participants: 334 (119 between 6-11 months and 225 between 12-24 months)
   Assays: HAI for measles; PRNT90 for YF; Rapid tube test for pertussis; haemagglutination for diphtheria and tetanus; smallpox visualization of scar
   Schedules: Group 1 – Placebo at day 0; Group 2 – smallpox, measles, and YF vaccine at day 0; Group 3 – Smallpox, measles, yellow fever, and DPT vaccine at day 0 with DPT again at 2 months; Group 4 – DPT vaccine at day 0 and 2 months
   Immunogenicity Results: The proportion with positive neut titers following YF vaccination was 5.3% in Group 1 (placebo) and 96.6 and 94.8% in Groups 2 and 3, respectively. There was no difference in the response to diphtheria, tetanus, or pertussis

when given in Group 4 versus Group 3; measles response was decreased when DPT was given versus just smallpox, measles, and yellow fever.
Safety Results: Not evaluated.
Conclusions: There was good SCR to YF vaccine regardless of whether it was coadministered with smallpox and measles vaccine or smallpox, measles, and DPT.

3. Tauraso et al. Effect of interval between inoculation of live smallpox and yellow fever vaccines on antigenicity in man. J Infect Dis. 1972; 126: 362-371.
Vaccines: Smallpox (NY) and YF vaccine (precursor YF-VAX, sanofi)
Year: 1972 (published)
Study population: Healthy male adults in USA
Number of Participants: 483 (27 to 49 per group)
Assays: Log neutralization index (LNI) for both YF and smallpox; also HAI for both vaccines
Schedules: 12 Groups in which YF and smallpox vaccine were given either together or were separated by 3, 7, 14, or 28 days
Immunogenicity Results: All but one vaccinee (482/483) developed a protective level of YF antibodies (LNI $\geq$ 0.7) following vaccination regardless of the interval with smallpox. Universally the response to smallpox was low (7-26%) but most of the recipients had previously been vaccinated and there was no difference between groups.
Safety Results: "generally well tolerated"
Conclusions: "The results of our study show that the reactogenicity and antigenicity of live smallpox and yellow-fever vaccines and unaffected by the interval between inoculation."

4. Meyer HM, et al. Response of Volta children to jet inoculation of combined live measles, smallpox, and yellow fever vaccines. Bull WHO; 1964; 30: 783-94.
Vaccines: Measles (Enders, Merck); Smallpox (Lederle, NY); YF vaccine (YF-VAX precursor, Philadelphia)
Year: 1962
Study population: Children aged 5 to 54 months in Burkina Faso (all vaccine naïve and 89-93% lacked prevaccination antibodies)
Number of Participants: 545 (101-124 per group)
Assays: HAI for measles and smallpox; mouse neutralization test for YF (conversion defined as prevaccination less than 25 LD_{50} and postvaccination $\geq$25 LD_{50}
Schedules: Group 1 – Measles at day 0; Group 2 – Smallpox at day 0; Group 3 – YF at day 0; Group 4 – measles and smallpox at day 0; Group 5 – measles, smallpox, and YF vaccines at day 0
Immunogenicity Results: There was a lower but non-significant seroconversion seen when YF was given with measles and smallpox versus YF alone (85% versus 97%). Measles GMTs did not vary by group; there was a significant trend to lower antibody titer to smallpox with the more antigens that were co-administered.
Safety Results: "No indication that any of these combinations potentiated the characteristic clinical reactions elicited by the individual attenuated viruses."
Conclusions: There was no evidence that combined vaccinations caused "significant immunological inference" and there were no safety concerns.

[Note: Dick et al reported on concomitant administration of YF and smallpox vaccines delivered through scarification at the same location – there was an impact in the immune response to suggest that not be done. Further information is not provided since scarification is not the method of choice for delivery of YF vaccine.]

TYPHOID

1. Kollartsch et al. Safety and immunogenicity of live cholera and typhoid vaccines administered alone or in combination with antimalarial drugs, oral polio vaccine, or yellow fever. J Infect Dis. 1997; 175: 871-875 (Cholera and typhoid results). ***AND*** Tsai TF et al. Compatible concurrent administration of yellow fever 17D vaccine with oral, live, attenuated cholera CVD103-HgR and typhoid Ty21a vaccines. J Infect Dis. 1999; 179: 522-523 (yellow fever testing results).
   Vaccines: Oral cholera (CVD103-HgR, Berna); oral typhoid (Ty21a, Berna); and YF vaccine (Arilvax, Burroughs Wellcome)
   Year: 1997 and 1999 (published)
   Study population: Healthy adults ≥ 18 years in Austria.
   Number of Participants: 150 total (30 to 45 per group)
   Assays: YF $PRNT_{90}$; cholera microtiter plate assay; S typh IgG and IgA ELISA
   Schedules: Several group including ones with anti-malarials; main group of interest were Group 1 – oral cholera vaccine at day 0; Group 2 – oral cholera and YF vaccine; Group 3 – oral cholera and oral typhoid vaccines at day 0; Group 4 – oral cholera, oral typhoid, and YF vaccines
   Immunogenicity Results: All subjects developed YF antibodies with an overall GMT of 178; subjects who received cholera, typhoid, and YF vaccine had higher (not significant) GMTs versus those who received cholera and YF vaccine GMTs (213 vs149, respectively). YF coadministration improved cholera SCR and GMTs when compared to the vaccine alone; the effect was not maintained when oral typhoid was also given. S typh antibodies were unaffected by the addition of YF vaccine.
   Safety Results: "No concomitant treatment resulted in a statistically significant higher rate for any type of adverse event."
   Conclusions: No impact on the immunogenicity or safety profile of YF vaccine when concomitantly administered with oral cholera or oral cholera and oral typhoid (there was also no impact on immunogenicity and safety for the other agents).

2. There was an abstract presented at the 36th ICAAC meeting that suggested that co-administration of inactivated typhoid vaccine, YF vaccine and meningococcal (A,C,W-135,Y without conjugate) did not impact the immunogenicity or reactogenicity of the vaccines. The original data were not published. (Ref: Dukes C, et al. Safety and immunogenicity of simultaneous administration of Typhim Vi (TV), YF-VAX (YF and Menomune (MV) [Abstract]. Presented at the 36th International Conference on Antimicrobial Agents and Chemotherapy; September 15-18, 1996; New Orleans, Louisiana).